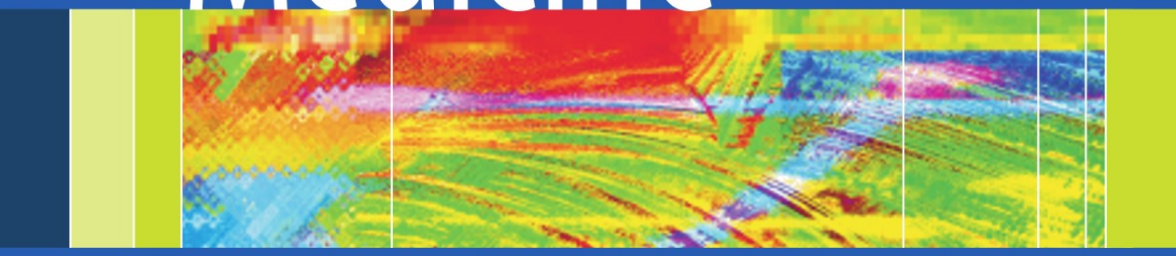
James E. Lessenger *Editor*

Agricultural Medicine



A Practical Guide

Springer

Agricultural Medicine

James E. Lessenger, MD, FAAFP, FACOEM
Morinda Medical Group, Inc., Porterville, California
Editor

Agricultural Medicine

A Practical Guide

With 15 Illustrations

Foreword by Stan Schuman, MD, DrPH, LLD

Springer

James E. Lessenger, MD, FAAFP, FACOEM
Morinda Medical Group, Inc.
Porterville, CA 93257
USA

Library of Congress Control Number: 2005928355

ISBN 10: 0-387-25425-0
ISBN 13: 978-0387-25425-8

Printed on acid-free paper.

Printed in the United States of America. (SPI/MVY)

9 8 7 6 5 4 3 2 1

springeronline.com

Foreword

The reader of this volume will experience a voyage of discovery with one of the finest guides available. James E. Lessenger has combined experience in private practice, preventive medicine, and public service in California's San Joaquin Valley, one of the most productive agricultural regions in the world. His experience and selection of chapter authors is, in every sense, a contribution to illuminating the art and science of agromedicine. As one examines the table of contents, one is impressed by the range of topics and the importance of each concern. Covering both injury prevention and environmental hazards, this innovative work is a practical guide for the family physician working in a rural area. The contents demonstrate the vitality of agromedicine and the vision and insight of the authors.

The chapters on farm chemicals provide thorough information about the many types of chemicals commonly used in the farm environment, how they are applied, and the principles of diagnosis and management for family physicians treating patients for toxic chemical exposure. These chapters underscore the fact that the use of farm chemicals is one of the things responsible for the increase in worldwide agricultural production and that risks can be managed through preventive measures.

The *Agricultural Medicine* represents a benchmark in the evolution of a concept begun in South Carolina over two decades ago called agromedicine. Several faculty members at two state-supported universities in South Carolina needed a shortened name for our closer partnership between the land grant campus of Clemson University and the Medical University of South Carolina at Charleston. In 1983 the agromedicine program was only an idea: how to provide an innovative public service program to benefit farmers and farm families with the most useful information on health, safety, nutrition, and preventive medicine. The new term *agromedicine* connotes an update of the traditional terms *agricultural health and safety* and *agricultural medicine*.

The need for the agromedicine partnerships is just as real now as it was in its inception. The target population of farmers, farm families, and consumers of food and fiber are underserved by direct and effective forms of preventive medicine. These forms include health education, patient motivation, and food safety. Dr. Lessenger's book addresses these issues as well as preventable disorders such as noise-induced hearing loss, ultraviolet light–induced skin cancers, heat and humidity syndromes, allergic anaphylaxis, zoonoses, injuries, and pulmonary disorders.

Complex agromedicine questions keep arising: How should we focus on the most practical health measures for the average hard-working rural farm

family and consumer? How should we react to illnesses resulting from hazards such as infectious rodents and ticks, noxious hog-farm odors, botanical toxins and dermatitis, pesticide residues measured in food at parts per billion or trillion, self-medication with herbal preparations, and excessive stress predisposing farmers to depression and suicide? How should we define the problem, select countermeasures, and communicate to farmers and farm families at risk?

The average farm family today differs from that of the 1980s. Rural patients and extension clients in the past were less oriented to the media and untouched by cyberspace. Today's farm family can be deluged with health information and misinformation. One constant issue is that health insurance is still an unmet need for many farm families. Chapters 1 and 2 of this book address the context of agricultural medicine and traditions that affect treatment. Health issues of migrant farm workers are also covered.

Our experience in South Carolina helped other southeastern states initiate similar interuniversity partnerships for their farmers and farm families. Naturally, priorities and methods of outreach vary with the types of agriculture. Grain farmers endure different hazards than orchard sprayers; the ergonomics of dairy farmers differ from those of vineyard workers; heat stress and cold injury vary with climate. Client-based research will lead to a broadened range of preventable health problems, whether they involve food bioterrorism, the Norwalk virus in oyster beds, immunodeficiency in poultry workers, asthma in hog-confinement operations, or anaphylaxis from fire ant stings.

In South Carolina, in the 1980s, client-based research led us into medical entomology and epidemiology: How many cases of Lyme-like illness are never reported? How can people protect themselves from unnecessary tick-borne disease? How can patients get specific antibiotic/antiinflammatory treatment early? How can primary care physicians offer earlier diagnosis and treatment? It is clear that agromedicine is not a subspecialty of occupational medicine seeking academic or grant recognition as it is a responsive programmatic approach to emerging rural health problems in exposed segments of the population.

Stan Schuman, MD, DrPH, LLD

Preface

This is the book I wish I had when I started practicing medicine in an agricultural community. During 22 years of researching, practicing, and teaching agricultural medicine, I have encountered bat bites, thorn punctures from citrus, grain harvester machine entrapments, and pesticide exposures. I have seen packing-house women who routinely got into fist fights, and a lawyer run over by a bull while visiting a dairy. I've treated farm laborers from Mexico who worked 12 hours a day, and millionaires dressed in mud-caked jeans and boots, looking not much different from the day laborers.

People in agriculture are a hearty and bull-headed group. You can tell a cowboy to wear a cast; the next day he will be riding a bull with the cast missing. He will tell you he "lost" it. Or the farmer will insist on working even though his finger was just cut off by a machine: "It's just bleeding a little, Doc. Can't you put a butterfly on it?"

This book cuts across several different medical disciplines to include those subjects of importance to a physician practicing in an agricultural area. As such, it is a reference and overview of those subjects that form the core of primary care in farming communities. Important topics include the broad field of farm chemicals, the nexus of food safety and employee health, common injuries seen in agriculture, and special topics including mental health, diseases and injuries of veterinarians, and zoonoses.

This book is intended for students, researchers, academicians, and, most important, physicians on the front lines of illness and disease among agricultural workers. It is designed to be as useful as a text to students new to the field and as a reference for those of us who have been in the field for decades.

The authors of this book are as diverse as the field of agriculture is broad. Professionals from around the world and representing multiple scientific disciplines have contributed. They come from academia, clinical practice, scientific institutions, and industry to present a broad-based introduction to the care of individuals in a diverse field.

I am indebted to Dr. Stan Schuman, editor emeritus of the *Journal of Agromedicine*, and Dr. Robert Taylor, editor of *Family Medicine: Principles and Practice*, for their guidance and help over the last decade.

I am grateful to Robert Albano for the opportunity to write this book. Developmental editor Merry Post was instrumental in bringing it to fruition. My son Ernest, now an MBA student at Rice University, helped me with all the computer setups. My wife, Leslie, who has a Ph.D. in psychology and

keeps me sane, helped with research, reviewed manuscripts, and gave encouragement. My deepest thanks to all those involved in this project.

James E. Lessenger, MD, FAAFP, FACOEM
Porterville, California

Contents

Contributors

Karl Auerbach, MD
Assistant Professor, Department of Occupational and Environmental Medicine, University of Rochester, Rochester, NY 14642, USA

A. Nelson Avery, MD
Associate Professor and Director, Department of Occupational and Environmental Health Services, University of Texas Medical Branch, Galveston, TX 77555, USA

James B. Becker, MD
Associate Professor, Department of Family and Community Health, Joan C. Edwards School of Medicine, Marshall University; Chief of Industrial, Department of Occupational and Environmental Health at Marshall University; Director, Office of Medical Management, West Virginia Office of Workers' Compensation, Marshall University, Huntington, WV 25701, USA

James M. Daniels, MD, MPH, FACOEM, FAAFP, FACPM
Director, Primary Care Sports Medicine Fellowship, Associate Professor, Department of Family and Community Medicine, Southern Illinois University School of Medicine, Quincy, IL 62301, USA

Victor Duraj, BS
Associate Development Engineer, Department of Biological and Agricultural Engineering, University of California, Davis, Davis, CA 95616, USA

Antonio Durazo, MD
Chair, Department of Family Practice, Sierra View District Hospital, Porterville, CA 93257, USA

Guilia Earle-Richardson, MPH
Research Supervisor, New York Center for Agricultural Medicine and Health, Cooperstown, NY 13326, USA

Louise Ferguson, PhD
Horticulture Specialist, Department of Plant Sciences, Kearney Agricultural Center, University of California, Davis, Parlier, CA 93648, USA

William E. Field, EdD
Professor, Department of Agricultural and Biological Engineering, Purdue University, West Lafayette, IN 47907, USA

Capri-Mara Fillmore, MD, MPH, MSc
Associate Medical Director, Department of Health of Milwaukee; Assistant Professor, Epidemiology, Health Policy Institute, Preventive Medicine and Family and Community Medicine; Associate Director, Preventive Medicine Residency, Medical College of Wisconsin, Milwaukee, WI 53226, USA

John E. Furman, PhD, MSN, CIC, COHN-S
Occupational Nurse Consultant, Department of Labor and Industries of Washington, WISHA Services Division, Policy and Technical Services, Olympia, WA 98504, USA

Robert L. Goldberg, MD, FACOEM
Associate Professor, Department of Medicine, Division of Occupational and Environmental Medicine, University of California, San Francisco; University of California Ergonomics Program, Richmond, CA 94804, USA

Joseph D. Hovey, PhD
Chair, Department of Psychology; Director, Program for the Study of Immigration and Mental Health; Co-director, Center for the Study of Anxiety Disorders and Depression, University of Toledo, Toledo, OH 43606, USA

Sarah Janssen, MD, PhD
Occupational Medicine Fellow, Division of Occupational and Environmental Medicine, University of California, San Francisco, San Francisco, CA 94143, USA

Royce H. Johnson, MD, FACP
Vice Chair, Professor of Medicine, University of California, Los Angeles; Chair Department of Medicine and Chief Infectious Diseases, Kern Medical Canter, Bakersfield, CA 93305, USA

Paul Jones, BA
Manager, Breaking New Ground Resource Center, Purdue University, West Lafayette, IN 47907, USA

Nikita B. Katz, MD, PhD
Senior Lecturer, Department of Neurology, INR/Biomed, Inc., Concord, CA 94520, USA

Olga Katz, MD, PhD
Clinical Instructor, Department of Neurology, Jefferson Medical College; Neurology and Neurophysiology Associates, Philadelphia, PA 19107, USA

Steven R. Kirkhorn, MD, MPH, FACOEM
Medical Director, National Farm Medicine Center and Occupational Health, Marshfield Clinic, Editor, Journal of Agromedicine, Marshfield, WI 54449, USA

Ricky Lee Langley, MD, MPH, FACP, FACOEM, FACPM
Department of Health and Human Services of North Carolina, Division of Public Health, Raleigh, NC 27699, USA

James E. Lankford, PhD
Professor, Emeritus and Former Dean of the College of Health and Human Sciences, Northern Illinois University, DeKalb, IL 60115, USA

Bruce J. Lanser, BS
Senior Clinical Research Assistant, Medical College of Wisconsin, Milwaukee, WI 53226, USA

James E. Lessenger, MD, FAAFP, FACOEM
Morinda Medical Group, Inc., Porterville, CA 93257, USA

Gideon Letz, MD
Medical Director, State Compensation Insurance Fund, San Francisco, CA 94103, USA

Stephen A. McCurdy, MD, MPH
Professor, Department of Public Health Sciences, Division of Environmental and Occupational Health, University of California, Davis, Davis, CA 95616, USA

Steven Mandel, MD
Clinical Professor, Department of Neurology, Jefferson Medical College; Neurology and Neurophysiology Associates, Philadelphia, PA 19107, USA

Deanna K. Meinke, MA
Assistant Professor, Department of Audiology and Speech-Language Sciences, University of Northern Colorado, Greeley, CO 80639, USA

Augustine D. Muñoz, MD
Associate Clinical Professor of Medicine, David Geffen School of Medicine at University of California, Los Angeles; Vice-Chair, Department of Medicine, Director, Pulmonary Medicine, Kern Medical Canter, Bakersfield, CA 93305, USA

Hitoshi Nakaishi, MD, DMSc
Chief Executive Officer of Y.N. Medical Company; Former Lecturer of University of Tsukuba, Hon-amanuma 3-18-15, Suginami-ku, Tokyo, 167-0031, Japan

Michael Nasterlack, MD
Department of Occupational Medical and Health Protection, BASF Aktiengesellschaft, GOA/C, 67056 Ludwigshafen, Germany

Robert Bhavesh J. Pandya, MD, MPH
Los Angeles Medical Center, Los Angeles, California; Occupational Health Services, Kaiser Permanente, West Los Angeles, CA 90034, USA

Danny B. Pence, PhD
Professor, Department of Entomology, Texas Tech Medical Center, Lubbock, TX 79430, USA

Scott Prince, MD, MSPH
Department of Preventive Medicine and Environmental Health, Southeast Center for Agricultural Safety, Lexington, KY 40504, USA

Mark A. Purschwitz, PhD
Research Engineer, Agricultural Safety, National Farm Medicine Center, Marshfield, WI 54449, USA

Alan Scott Ragland, DO, MS
Assistant Clinical Professor of Medicine, David Geffen School of Medicine at University of California, Los Angeles; Associate Program Director, Internal Medicine; Director, Ambulatory Care, Internal Medicine; Director, Medical Student Program, Kern Medical Canter, Bakersfield, CA 93305, USA

Laura D. Seligman, PhD
Assistant Professor, Department of Psychology, Co-director, Center for the Study of Anxiety Disorders and Depression, University of Toledo, Toledo, OH 43606, USA

William M. Simpson, Jr., MD
Medical Director, South Carolina Agromedicine Program; Professor of Family Medicine, Department of Family Medicine, Medical University of South Carolina, Charleston, SC 29425, USA

Lorann Stallones, MPH, PhD
Professor of Epidemiology and Director of the Colorado Injury Control Research Center, Department of Psychology, Colorado State University, Fort Collins, CO 80526, USA

Roger L. Tormoehlen, PhD
Professor, Youth Development and Agricultural Engineering, Department of Agriculture and Biological Engineering, Purdue University, West Lafayette, IN 47907, USA

Mitchell S. Wachtel, MD
Associate Professor, Department of Pathology, School of Medicine, Texas Tech Medical Center, Lubbock, TX 79430, USA

Carl John Williams, DVM
Department of Health and Human Services of North Carolina, Division of Public Health, Raleigh, NC 27699, USA

Huiyun Xiang, MD, MPH, PhD
Assistant Professor, Center for Injury Research and Policy Columbus Children's Research Institute and Columbus Children's Hospital, College of Medicine and Public Health, Ohio State University, Columbus, OH 43205, USA

Andreas Zober, MD, PhD
Director, Department of Occupational Medical and Health Protection, BASF Aktiengesellschaft, GOA, 67056 Ludwigshafen, Germany UL

1

The Agricultural Environment

William M. Simpson, Jr.

Key words: developing world, genetically modified foods, genetically modified organisms, migrant workers, seasonal workers, sensitive population

Of the more than 6 billion people in the world, more than half live in rural areas and more than 40% are involved in the production of food and fiber. But, as would be expected, there are substantial differences between the developed and developing worlds in how much human effort it takes to supply the food and fiber needs of their populations. In the developed world, only 7% of the population is involved in agriculture, while in the developing world just over half spend their working lives in farming activities. The importance of an adequate supply of food cannot be overemphasized. Adequate fuel for mental and physical activity is necessary for life and health. In addition, the value of food and fiber to the world economy is not trivial. The worldwide gross domestic product (GDP), the total value of goods and services produced, is approximately $7600 per capita or $46 trillion; agriculture accounts for 6.2% of the GDP or nearly $3 trillion. The world system of production, processing, distribution, and marketing is incredibly complex. We will review the highlights of that system here (1).

Agriculture in the United States

From 1950 to 1980, United States farm output doubled. At the same time, the number of farms fell from over 5 million to approximately 2 million, averaging 400+ acres in size and covering a total of nearly a billion acres. The farm population shrank from 23 million to 6 million (from 15% to 2.7% of the population). The number of persons supplied with farm products grew from 15 to 65 for each farm worker. The estimated market value of land and buildings on an average farm is over $500,000 or over $1200 per acre. Equipment is valued at nearly $70,000 per farm. Averages are somewhat misleading since 1.8 million of the 2 million farms in the United States are less than 500 acres. The market value of agricultural products sold in 2002 was

more than $2 billion, or almost $100,000 per farm. Again, averages are misleading since the top 15% of farms, in terms of size, produced almost 80% of the gross farm income.

The 2002 Census of Agriculture by the United States Department of Agriculture found a slight decline in the total number of farms, but a much more significant loss (18%) in the number of corporate farms (74,000 from 90,000), reversing a trend of increasing corporate ownership of farms that began in the 1970s (nearly doubling between 1978 and 1997). Sixty percent of principal operators of U.S. farms have farming as their primary occupation, so 40% of farm operators have jobs off the farm that they consider their primary employment. The average age of principal farm or ranch operators was 55.3 years compared to 54 years in 1997, which continues a 25-year trend of aging among American farmers. The typical family farm today is a commercialized and specialized business, concentrating on one or two commercial crops. It utilizes machinery to the greatest extent possible on large fields and usually depends on borrowed capital to purchase equipment, seed and feed, fertilizer, pesticides, and veterinary treatments and services to maximize yields. In an environment such as this, much more than just farming skills are needed to be successful (2).

Agriculture in the World

To go beyond the distorted view presented by statistical averages about world agriculture requires dividing the world into at least three groups; the "haves" or "First World," for whom food security is not an issue, the "have nots" or "Third World," who live on less than $1 a day, and the large group of "in-betweens" or "Second World."

The First World consists of approximately 1 billion people who are largely removed from their agricultural roots, take a plentiful and inexpensive food supply for granted, and are increasingly conscious of environmental issues. For them, international aid and development are low priorities. In the Third World, another billion people, mainly rural and chronically malnourished, are living in countries where the free market economic model does not work. This group qualifies most for humanitarian assistance but they need much more than that. They need to learn better farming practices to increase yields while decreasing soil erosion and desertification. In the Second World, 4 billion people live in countries where the state and market economy generally do not function well, but there is a widespread desire to do better. Doing better requires assistance in developing markets, protection of distribution, implementation of good agricultural practices, and application of biotechnology (3).

More than half of the "have nots" are found in Asia and the Pacific (60%) and 24% are found in sub-Saharan Africa. However, the proportion of the population that is undernourished is very different in the two

regions. In sub-Saharan Africa one third of the population is undernourished, while one sixth is undernourished in Asia and the Pacific, and one tenth in Latin America, the Caribbean, the Near East, and North Africa. The incidence of undernourishment has declined from 28% of the population of the world in 1980 to 17% in 2000. Most of the improvement has been in Asia and the Pacific, which halved their incidence of undernourishment. Undernourishment in other areas of the world has only slightly improved or remained stagnant during the same time period. As of late 2003, food emergencies exist in nearly 40 countries, more than half in Africa, eight in Asia, five in Latin America, and two in Europe. In many of these countries, food shortages are compounded by the impact of HIV-AIDS on food production, transport, distribution, and utilization (4).

The Farm Culture

Ownership Patterns

Patterns of ownership and control of farm resources vary around the world depending on the philosophy and activity of government, stage of economic development, type of agriculture engaged in, and practices of inheritance and tradition. Farming in the United States, Canada, and most Western countries was founded on the family-farm concept. The head of the family is the head of the farm. The farm is large enough to provide most or all of the family income but small enough to be operated largely by members of the family. In the United States the concept of the family farm was supported in government policy (homesteading, squatter's rights, etc.) that encouraged settlers to take up farming on plots of land that were "family-farm sized."

In Latin America, family farms exist, but a larger proportion of land is concentrated in large holdings, and as a result there are a large number of very small farms and relatively poor farmers. Land reform (more equitable distribution of land resources) is one of the recognized needs for farm progress and for development in this region. The tropical (or sub-Saharan) portion of Africa is, for the most part, agriculturally backward. Farms are most often very small and primitive and a large part (80% or more) of the total population is engaged in farming. Much of this region is a pattern of shifting, "bush-fallow" agriculture, where land is farmed for a few years, then allowed to return to bush for a few years. Intermixed among these millions of small farms are plantations and large farms, many operated by Europeans, producing specialized commodities (cocoa, coffee, peanuts, palm oil, tobacco, etc.) mostly for export. The temperate part of Africa is a mixture of large and small farms that emphasize grains and grass/livestock.

In Asia, farm organization varies from the nomadic agriculture of the Arabian desert, to the traditional peasant economies of India and Southeast Asia, to the post-Communist economy of the People's Republic of China.

In Western Europe, farms are generally smaller than in the United States, Canada, and Australia, but productivity per acre is high, and land resources are intensively farmed. In Eastern Europe, the fall of the Soviet Union has left agriculture in disarray, but the possibility of westernization exists and has begun to a limited extent.

Farm Workers

In addition to the farm owner, who usually serves as the primary farm worker, other family members often serve as part-time farm workers. Women have been involved in the production of food and fiber for millennia but have only recently begun to take on farm management roles. Children have been pressed into agricultural work at times of high labor need on the family farm and find themselves helping to make ends meet on subsistence farms around the world and as migrant laborers working with their parent(s).

Seasonal agricultural workers are usually employed in agriculture 1 to 5 months a year. Their numbers have decreased in the recent past due to mechanization of many farm practices. Now in the United States, only 1 in 20 agricultural workers is seasonal. Eighty percent of the seasonal workers move considerable distances to find work on a daily basis but never sleep away from their homes for employment purposes. Twenty percent are truly migrant workers. These migrant workers usually travel in one of three streams—in the east from Florida to New York and New Jersey, in the mid-continent from Mexico across the middle of the country as far east as Ohio and as far west as Oregon and Washington, and in the west from Mexico to California and Arizona. Migratory and stable seasonal agricultural laborers are among the lowest paid and least protected American workers. A number of legislative and legal interventions have been undertaken to improve conditions for migrant workers. Child labor has been outlawed, minimum housing standards have been set, systems for forwarding health and school records have been established, and farm labor contractors are required by law to register. Despite these improvements on paper, enforcement is sometimes inadequate. Unionization of farm workers has, in most instances, improved working and living conditions for their members (5).

Sensitive Human Populations

Groups have been referred to as "sensitive populations" because their response to particular exposures is presumed to be greater than that of the general population. Very young and very old individuals have traditionally been considered sensitive to various stresses (heat, cold, infectious agents). On the family farm, the youngest and the oldest members of the family are sometimes pressed into service in times of heavy work demands or just because they want to help out. This may put these populations at greater risk

for injury or illness. The elder person with poor eyesight because of a cataract is more likely to have an accident while operating machinery. The youth who is inexperienced may take unnecessary risks or fail to utilize personal protective equipment. These sensitive populations require education and supervision to ensure safe participation in farming. Groups such as "Farm Safety 4 Just Kids" (www.fs4jk.org), 4-H Clubs, and Future Farmers of America help to provide this education.

In addition to sensitive populations that actually work on farms, additional sensitive populations are exposed to potential agricultural risks because of encroachment of housing and business development into areas that were previously farmland and immediately adjacent to land currently under cultivation or used as pasture. Drift of fertilizers, pesticides, herbicides, and odors only rarely have true adverse health effects, but involuntary exposures of any kind are emotionally and physically stressful and may lead to symptoms and legal conflicts. Persons with immunosuppression for organ transplant or due to infection have additional theoretical risk from living in close proximity to an agricultural operation.

More general concerns have been raised about the effect of genetically modified foods and organisms on the quality and safety of the food supply and risks for the development of "super-weeds" and highly resistant organisms. The issues are controversial and much additional data is needed for final answers, but a recent (2004) Food and Agriculture Organization (FAO) conference on genetically modified crops has shed some light on these concerns. More than 80% of genetically modified crops are herbicide resistant, meaning herbicides can be applied to the crop to control weeds without affecting the crop itself. This decreases the rate of soil erosion, preserves moisture in the soil, and decreases hand labor use, all positive impacts. While some weed resistance has developed, it appears that the rate of resistance development is not significantly different from that which occurs naturally. More study of the issue was recommended. Crops that include *Bacillus thuringiensis* (Bt) are resistant to many pests (the Bt incorporated in the plant material is toxic to the insect that ingests it). While pest species may develop resistance over time, decreasing rates of pesticide use on crops with Bt may decrease resistance pressure, making other pesticides that are used more effective. Again, the issues are complex and the FAO study group recommended further study. Drought and salinity tolerance are additional characteristics that may be engineered into plant species. While commercial crops with these characteristics are probably years away, basic research suggests that crops of this type may allow wider areas of the planet to be successfully cultivated (6).

Concerns about changes in soil ecosystems as a result of genetically modified (GM) crop cultivation were also discussed. Thus far, research on GM crops has shown very minor alterations in these characteristics compared to those produced by other sources of variation (temperature, moisture level, or organic matter level) in soil-borne ecosystems.

Production: Farming as an Industry

In highly developed countries, farming ranks with manufacturing, construction, transportation, and the service industries as a major component of the economy. Improvements in farming have been basic to the progression of industrial growth. Efficiency in farming saves labor and permits a modern industrial nation to produce an adequate food supply using only a small part of the total labor force. The greatest industrial growth has occurred in those countries where agriculture is most progressive and efficient (most of North America, Europe, Japan, Australia, New Zealand, and smaller parts of Latin America, Asia, and Africa). Exports of farm products are a significant source of strength in the economies of most advanced countries. The United States is, by far, the largest exporter of farm products, totaling 20% to 25% of all exports.

In less developed countries, labor use is less efficient, and farms are generally smaller and less well-organized. Mechanization of agriculture should increase the amount of food that can be produced by each agricultural worker, reducing the need for on-farm jobs. In many poor nations where labor is plentiful and rural incomes are extremely low, reducing farm employment is not a desired outcome. As a result, appropriate technologies, scaled to the small farm and improving labor efficiency without eliminating agricultural jobs are being sought, rather than simply applying modern, large-scale agricultural technology to subsistence agricultural systems. Agricultural industries, both those supplying services to farmers and those marketing crops, are not as well-organized or sophisticated as in highly developed countries, making it more difficult in less developed countries to make use of these advances in agricultural techniques and to benefit from outside trade.

Processing and Transportation

The processing of food and fiber crops in the developed world is highly organized, leading to widespread availability of a dizzying array of food and nonfood products at relatively low cost. Refrigerated cargo ships and refrigerated trailers transport more than 200 types of fresh fruits and vegetables, making them available year-round at most supermarkets in the developed world. Large food processors can, box, bag, bottle, and freeze more than 10,000 different products in the United States alone. In contrast, in the developing world, food is much more likely to be of limited variety, and is produced very close to where it is consumed at a cost that is proportionally greater than in the developed world. Nonfood items are similarly limited in variety and relatively high in cost.

Health Care for the Farm Population

About 10% of physicians practice in rural areas of the United States, despite the fact 25% of the population lives in those same areas (7). Rural residents

are less likely to have employer-provided health care coverage or prescription drug coverage. The rural poor are less likely to be covered by Medicaid than their urban counterparts. The rural population is more likely to be over 65 (18% vs. 15%) and poor (14% below the poverty level vs. 11%). Nearly 25% of rural children live in poverty.

Risky health behaviors are more common among rural youth. The rate of drunk driving arrests is significantly greater in nonurban counties. Forty percent of rural 12th graders report using alcohol while driving compared to 25% of their urban counterparts. Rural 8th graders are twice as likely to smoke cigarettes (more than 26% vs. 13% in large metropolitan areas).

Most studies of specific disease states, with the notable exception of cancers other than skin, show higher rates in rural versus urban areas. Cerebrovascular disease and hypertension are both at least 25% higher in rural versus urban populations. Suicide rates for both men and women are higher in rural areas—mental health services are less accessible (87% of mental health professional shortage areas were in nonmetropolitan counties). The rural, "healthy" lifestyle (greater physical activity, diets heavy in fruits and vegetables), which has previously been credited with lower rates of cancer and some chronic diseases, appears to be overwhelmed by behaviors and diseases associated with stress and lack of self-care. Relative lack of mental and physical health professionals in rural areas only exacerbates the problem.

Rural Health in the Third World

If statistics regarding health in rural areas of developed countries such as the United States are discouraging, rural health statistics for developing countries are even more so. Infant mortality is 60% higher in rural versus urban South Africa. Rural children are 77% more likely to be underweight or under height for age. Eighty percent of the poor in Latin America, 60% in Asia, and 50% in Africa live on marginal agricultural lands of low productivity and great susceptibility to degradation, encouraging migration from rural to urban areas. This exacerbates the already terrible problems of the world's cities where more than a billion people live without garbage disposal or water drainage facilities and breathe heavily polluted air. If this unhealthy urban drift is to be reversed, both the economic and physical health of rural populations must be addressed. Poverty leading to ill health and low productivity is a vicious downward spiral (8).

Patterns of illness and injury in rural areas are not only related to poverty. Work injuries, in general, are more serious and more severe in rural areas, following from the stoic attitude and "too tough to care" mindset of farmers and agricultural workers. The specifics differ from country to country, but there are always diseases and illnesses that are peculiar to living and working in rural areas such as zoonoses and other animal or insect-borne diseases. In many rural areas, at least some of the time, there is no means of transportation or

evacuation for critically ill or injured patients. In addition, simple communication between rural areas and sites of higher level care is inconsistent to nonexistent.

In response to these problems, the World Health Organization has initiated the Towards Unity for Health (TUFH) project, which will attempt to integrate individual health and community health-related activities through involvement of traditional medicine and public health. WONCA, the World Organization of Family Doctors, has been a co-leader in the development of this project.

Conclusion

The health of agriculture varies from robust to moribund. The developed world struggles with diseases of excess nutrition, while developing nations deal with millions of deaths annually from starvation. The world has the capacity to provide enough food for all of its inhabitants, but individual productivity, local politics and structures, national priorities and interconnections, and international trade patterns make distribution inequitable, difficult, and sometimes dangerous and ineffective.

References

1. The State of Food and Agriculture 2003–2004. Rome: Food and Agriculture Organization, 2004.
2. United States Department of Agriculture. 2002 Census of Agriculture. Washington: USDA, National Agricultural Statistics Service, 2004.
3. United States Department of Agriculture. Shaping the future of agriculture. Agriculture 21 (Agriculture Department: FAO) 2003;1–4.
4. The State of Food and Agriculture 2003–2004. Rome: Food and Agriculture Organization, 2004.
5. Griffith D, Kissam E. Working Poor: Farmworkers in the United States. Philadelphia: Temple University Press, 1995.
6. Report of the Expert Consultation on Environmental Effects of Genetically Modified Crops. Rome: Agriculture Department, Food and Agriculture Organization, 2004. ftp://ftp.fao.org/docrep/fao/fild/006/ad690e/ad690e00.pdf.
7. Gramm LD, Hutchison LL, Dabney BJ, Dorsey AM, eds. Rural Healthy People 2010: A Companion Document to Healthy People 2010. Volume 1. College Station, TX: Texas A&M University System Health Sciences Center, School of Rural Public Health, 2003. http://www.srph.tamushsc.edu/rhp2010/litreview/Volume1.pdf.
8. Strasser R. Rural health around the world: challenges and solutions. Family Practice 2003;20(4):457–63.

2

Food Safety and Agricultural Medicine

Robert Bhavesh J. Pandya

Key words: safety, threats, hunger, malnutrition

Food safety and security are important public health issues for agriculture and other food production sectors. As the global population continues to grow past 6 billion, food safety, food insecurity, and hunger remain major problems in the world. Hunger and malnutrition are the primary risk to global health, killing more people than AIDS, malaria, and tuberculosis combined by claiming 10 million lives each year, 25,000 lives each day, and one life every 5 seconds (1–3).

Sustaining the growing world population with adequate and safe food and water supplies is the major global nutritional and public health priority for the 21st century. To meet this challenge, the 53rd World Health Assembly, the governing body of the World Health Organization (WHO), adopted a resolution in May 2000 calling upon WHO and its member nations to recognize food safety as an essential public health function. In addition, WHO has made food safety one of its top 11 priorities and calls for more systematic and aggressive steps to significantly reduce the risk of microbial foodborne illnesses. This will require major redirections of food microbiology efforts and cooperation on a global scale (2,3).

To decrease the risk of microbial foodborne illnesses, the main methods of increasing food safety use pesticides and chemicals, food irradiation, and combined nonthermal technologies. Newer agricultural methods of genetically modified foods and organic farming have been advanced as ways of increasing global food supply while reducing the use of chemicals and pesticides. Organic farming has been popular over the past decade but may pose some risks for food safety.

Although these technological advances help increase food safety and supply, they may have potential occupational effects on agricultural workers and on the environment. This chapter briefly reviews the history of food safety, discusses the sources of risk for food safety, reviews the main methods currently used for ensuring food safety, and highlights potential occupational consequences of these methods for agricultural workers. Evolving potential threats to food safety from bioterrorism and agroterrorism are also discussed.

Brief History of Food Safety and Agriculture

Agriculture has evolved since humans first domesticated plants such as corn more than 6000 years ago. Although current agricultural practices vary worldwide, in the United States and developed countries agriculture has become increasingly industrialized since the 1940s and 1950s, resulting in more efficiency and production on the farm. Mechanical inventions such as the self-propelled combine reduced the need for manual labor and encouraged the production of grain commodities, which led to the practice of monocropping or monoculture, as farmers began to focus on growing the most profitable crops such as corn, soy, and wheat. Though profitable, monocropping reduced the previous soil-enriching practices of crop rotation and livestock grazing, making agriculture more dependent on synthetic or petroleum-based fertilizers in place of natural manure for amending the soil. Furthermore, although arsenic and lead-based pesticides had been used widely since the late 1800s, new pesticide formulations came on the market during the agricultural boom of the mid–20th century. These included methylbromide, a fumigant once widely applied to soil and crops to kill insects and weeds that was approved for use in 1947, atrazine, a herbicide approved in 1959, and chlorpyrifos, an organophosphate pesticide approved for use in 1965. Since the 1960s, pesticide use in the United States has more than tripled. Despite the ban on several toxic pesticides, like the organochlorines in the United States over the past several years, currently more than 1 billion pounds of agricultural pesticides are still purchased each year in the United States. Globally, pesticide use also has increased, and the type used, amount, and regulations vary regionally (4–6).

Since 1962, the Codex Alimentarius Commission (CAC) of the Food and Agricultural Organization of WHO has been responsible for developing standards, guidelines, and other recommendations on the quality and safety of food to protect the health of consumers and to ensure fair practices in food trade. In the United States, various regulations exist to enhance food safety. Early actions of the U.S. Department of Agriculture (USDA) culminated in the passage of the 1906 Food and Drug Act that helped increase food safety for the public. In 1910, the Insecticide Act established product-labeling provisions. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) of 1947 required registration of pesticide products with the USDA prior to domestic or foreign sales. The Federal Food, Drug, and Cosmetics Act that evolved from the 1906 statute was expanded in 1954 by the Miller Amendment that established pesticide tolerances in or on agricultural commodities based primarily on good agricultural practices. The Delaney Clause of 1958 prohibited use of any carcinogenic food additive in processed foods. Subsequently, regulatory authority was enhanced by creation of the U.S. Environmental Protection Agency (EPA) in 1970 and an additional 1972 FIFRA amendment that required manufacturers to demonstrate that use of a product "would not cause adverse effects on human health or the environment" (7–9).

Recurrent outbreaks of food and water diseases have highlighted the importance of sustaining safe food and water supplies. In response to threats to food safety, the United States government and other entities have made several changes in the United States food safety regulatory structure. These include implementation by USDA of the Pathogen Reduction: Hazard Analysis Critical Control Point (HAACP) in 1995, Final Rule for Meat and Poultry (from USDA's Food Safety and Inspection Service (FSIS), creation of FoodNet (a sentinel surveillance system for active collection of foodborne disease surveillance data), creation of PulseNet (a national molecular subtyping network for foodborne bacterial disease surveillance), and revisions to the Food Code and the National Primary Drinking Water Regulations (10–12).

Threats to Food Safety

Despite regulations and increasing awareness, food supplies continue to be at risk from contamination by microbial pathogens and chemicals used to control pests. Food handlers are another potential source of foodborne illness if they do not practice good hygiene when handling food items.

Microbial Contamination of Food

Foodborne illnesses remain a major risk globally. Each year, unsafe food makes at least 2 billion people ill worldwide, which is about one third of the global population. Furthermore, food- and waterborne diarrheal diseases are leading causes of illness and death in less developed countries, killing approximately 1.8 million people annually, most of whom are children. Obtaining accurate estimates of the incidence of specific microbial foodborne illnesses is often difficult in many areas of the world. A population-based study in the Netherlands estimated a total annual incidence of gastroenteritis to be 28%, without attributing the degree of foodborne or microbiological etiology. In the United States, it has been estimated that 76 million cases of foodborne diseases may occur each year, resulting in 325,000 hospitalizations and 5000 deaths. Important sources of foodborne pathogens include contaminated produce and improperly cooked, handled, or stored meat and poultry products. Major pathogens in foodborne diseases worldwide include salmonella, campylobacter, *Escherichia coli* 0157, cholera, and listeriosis. Furthermore, microbial and chemical sources can pose significant health risks for certain vulnerable populations such as the elderly, children, pregnant women, those in institutionalized settings, and the immunocompromised (13–21).

Milk and meat obtained from infected animals is another threat to food safety. Important zoonotic foodborne illnesses worldwide are tuberculosis due to *Mycobacterium bovis, Campylobacter* spp., verotoxigenic *E. coli,* and *Brucella abortis* from ingestion of contaminated, raw unpasteurized milk.

Farmers, farm families, and visitors to farms should be advised about the risks associated with the consumption of unpasteurized milk from any animal species. *M. bovis* infection in humans has also been reported to occur after consumption of contaminated meat (22).

To reduce the global burden of foodborne illnesses, the WHO and the Food and Agricultural Organization of the United Nations released the Five Keys Strategy on October 13, 2004, in Bangkok, Thailand at the second Global Forum of Food Safety Regulators. The five simple measures consist of:

1. Keeping hands and cooking surfaces clean.
2. Separating raw and cooked food.
3. Cooking food thoroughly.
4. Keeping food stored at safe temperatures.
5. Using safe water and raw ingredient(s) (13).

Other methods recommended by WHO in the past include eating cooked food immediately, reheating cooked food thoroughly, keeping all kitchen surfaces meticulously clean, and protecting food from insects, rodents, and other animals (23).

Agricultural Workers as Vectors for Foodborne Illness

Occupational health and hygiene during the course of handling food items should be a top priority for food safety. However, agricultural workers and food handlers are potential vectors of foodborne illnesses when handling food items in the course of customary work practices. Many agricultural practices, such as harvesting, are labor-intensive operations involving direct human contact with fresh produce. In fact, humans and animals are major sources of pathogens in our food supply. Major pathogens such as *E. coli* 0157.H7, *Salmonella* spp., *Shigella* spp., *Staphylococcus aureus, Giardia lamblia,* and *Cryptosporidium parvum* can often be traced back to human or animal sources. Hepatitis A outbreaks have also occurred via food contaminated by infected food handlers in several areas worldwide (24–28).

Prevention is the mainstay to decrease morbidity from spread of transmissible diseases by food handlers. In the United States, food preparation and service regulations are issued by state health departments and may vary from state to state. For instance, routine hepatitis A vaccination of all food handlers is not recommended because their profession does not put them at higher risk for infection. However, local regulations mandating proof of vaccination for food handlers or offering tax credits for food service operators who provide hepatitis A vaccine to employees has been implemented in some areas. One economic analysis concluded that routine vaccination of all food handlers would not be economical from a societal or restaurant owner's perspective. However, the Centers for Disease Control and

Prevention (CDC) in the United States have supported use of the hepatitis A vaccine among dietary workers who may be at risk for contracting or spreading the disease (29–31).

The CDC has also supported screening for tuberculosis (TB) in high-risk groups such as foreign-born or recent immigrants from outside the United States. Screening of food handlers for TB has been found to be cost-effective in high-risk populations. However, this recommendation is to identify high-risk individuals who may be candidates for preventive treatment for latent TB and not to protect the public from contaminated food as *Mycobacterium tuberculosis* is not transmitted through food (32–35).

The WHO does not recommend routine medical and microbial screening of agricultural workers and food handlers. However, workers suffering from an illness that includes symptoms such as jaundice, diarrhea, vomiting, fever, sore throat, skin rash, or skin lesions such as boils or cuts should report this to their supervisor prior to starting work and should be temporarily excluded from activities requiring food handling (23,36).

Good worker hygiene practices during production, harvest, and food-handling activities can help prevent or minimize microbial contamination of food. Simple preventive practices such as teaching employees how to effectively wash their hands (i.e., wet the hands, use soap, rub hands together for at least 20 seconds to develop a lather, clean under fingernails, rinse, and dry with a paper towel) and when to wash hands (i.e., before starting to pack or process, after each break, after handling unsanitary items such as decayed produce, and after using the toilet facilities) are recommended. Other useful strategies include prohibiting workers from smoking or eating in the fields, where saliva could accidentally be sprayed on produce, and encouraging use of impermeable, nonlatex gloves when handling fresh produce. Multilingual signs and direct communication between supervisor and employee are also important (24).

Food Contamination from Pesticides and Chemicals

Pesticides, herbicides, fungicides, and other chemicals have been used globally for decades to increase food supply and eliminate pests. Data on worldwide pesticide sales and use are remarkably difficult to find, and survey results from countries are often not reliable. The EPA estimates that each year domestic users in the United States spend $8.5 billion for 1.1 billion pounds of pesticides active ingredients. Many of the banned or withdrawn pesticides from developed countries are still produced and sold in developing countries or by some multinationals acting through subsidiaries or joint ventures. These include DDT and other persistent organochlorine (OC) insecticides, which represent about 15% of the sales in regions outside the United States, Western Europe, and Japan. Estimates indicate that 70,000 to 80,000 tons of these compounds were applied in 1995 in developing and formerly socialist countries (Table 2.1) (37–39).

TABLE 2.1. Regulatory status of some organochlorine pesticides in different countries.

	U.S.	China	India	Mexico	U. K.	Canada
DDT	B	R	R	R	B	Not registered
Aldrin	B	Not banned	Not banned	B	B	Not registered
Dieldrin	B	Not banned	R	B	B	Not registered
Endrin	B	Not banned	Not registered	B	B	Not registered
Heptachlor	(R)	Not banned	Not banned	Not registered	B	Not registered
Hexachlorobenzene	B				B	Not registered
Mirex	B	R		R		Banned
Toxaphene	B	Not banned	B	B	B	Not registered

Adapted from Garcia AM. Pesticide exposure and women's health. Am J Ind Med 2003;44:585.
Note: Blank spaces above indicate no available data.
R, registered; B, banned; (R), restricted.

Banned pesticides have recently been reintroduced into certain environments such as DDT sprayed in several areas of Africa as a preventive measure against malaria. Older and more toxic organophosphate (OP) and carbamate insecticides and herbicides also have very significant sales in the Third World (e.g., alachlor, aldicarb, benomyl, captan, carbofuran, chlordane, cyanazine, dimethoate, endosulfan, EPN, mancozeb, lindane, monocrotophos, paraquat, parathion, toxaphene, zineb, carbaryl, atrazine, glyphosate, 2-4-D, dichlorovos, phorate, and many others). In developing countries, these pesticides are still preferred by the small farmers because they are less costly, easily available, and display a wide spectrum of bioactivity. Globally, OPs account for nearly 40% of total insecticide sales by volume, followed by carbamates (20.4%), pyrethroids (18.4%), and others (6.1%) (5,6,40).

Persistent pesticides travel through the air, soil, and water into living tissues where they can bioaccumulate up the food chain into human diets. In fact, it has been estimated that approximately 85% to 90% of pesticides applied agriculturally never reaches the target pest organisms but disperses through the air, soil, and water. As an example, the half-life of toxaphene in soil is up to 29 years (5,41,42).

Humans bioaccumulate organochlorine and metal-containing pesticides in their body fat, where they tend to stay unless the fat is metabolized for energy, such as during an illness. For example, in Latin American countries, the pattern of residues found in human body tissues consisted of high levels of DDT and its metabolites, followed by benzene hexachloride (BHC), dieldrin, heptachlor epoxide, and hexachlorobenzene (HCB). Interestingly, these organochlorines were also found in people's body tissues in 22 Third World and formerly socialist countries. Furthermore, food standards in developing countries are typically not as well regulated as those in industrialized

countries, and pesticide residues are frequently found on agricultural products. For instance, in Brazil, pesticide residues in 13.6% of fruits and 3.7% of vegetables exceeded tolerance limits (5,43,44).

Although less is known of the toxicological consequences of chemical contamination of food items, the WHO has identified acrylamide and semicarbazide as emerging contaminants that may have potential health consequences for humans, although more investigation is needed. Acrylamide is a chemical that has several uses including manufacture of polyacrylamide materials, treatment of drinking water and wastewater to remove particles and other impurities, and the construction of dam foundations and tunnels. Interestingly, acrylamide also appears to be produced in some foods at high temperatures (45).

Acrylamide is known to cause cancer in animals; certain doses are toxic to the nervous system of both humans and animals. In humans, studies of workers exposed to acrylamide through air and skin contact found no evidence of cancer. However, the International Agency for Research on Cancer (IARC) has classified acrylamide as "probably carcinogenic to humans" on the basis of the evidence from research studies on animals (45).

There is currently little information about, and poor understanding of, how acrylamide forms in foods. It appears to be produced naturally in some foods that have been cooked or processed at high temperature, and the levels appear to increase with the duration of heating. Acrylamide has also been found in home-cooked foods as well as precooked, packaged, and processed food and seems to arise when different food components react together. Although the exact temperature at which acrylamide forms in food is not currently known, acrylamide has not been found in food prepared at temperatures below 120°C. Thus far, the highest levels have been in starchy foods such as potato and cereal products (45,46).

The WHO has also highlighted public health concerns of semicarbazide (SEM) in food at the request of several member states and based on information provided by the European Food Safety Authority. Semicarbazide is found in food products packaged in glass jars with metal lids that have formed plastic seals. Semicarbazide has been detected at low levels in a number of such food products, including baby foods. The origin of SEM is not clear but has been linked to the permitted use of azodicarbonamide in the plastic seals. The presence of SEM has raised concerns since it has weak carcinogenic activity when fed to laboratory animals at high doses. Based on levels reported in food, the health risk, if any, to consumers, including infants, seems quite small. However, since the relatively high consumption of products in glass jars by infants can result in higher exposure as compared to other consumers, the presence of SEM in baby foods is considered particularly undesirable. The WHO has recommended that alternative materials be evaluated for their suitability, including their microbial and chemical safety, and introduced as rapidly as possible for baby foods and subsequently other foods (47).

Other examples of chemical contaminants in food include polychlorinated biphenyls (PCBs), dioxins, and mercury contamination in seafood. Some aquatic organisms can convert inorganic mercury into organic methylmercury, with resulting bioaccumulation in large carnivorous fish such as swordfish. Soils and water used for agriculture may also contain regional environmental hazards such as the widespread arsenic contamination of ground water in Bangladesh (48–50).

Organic Farming and Food Safety

Conventional and organic farming are two major forms of agricultural practices today. Although organic farming can be traced back to England in the 1920s, it has been embraced over the last several years due to concerns over use of pesticides and genetically modified organisms in large-scale conventional agriculture. Organic farming avoids use of synthetic chemicals and genetically modified organisms (GMOs) and follows the principles of naturally sustainable agriculture (51).

Despite many favorable characteristics of organic farming, one of several criticisms about organic farming is the increased potential for microbial food contamination. A French study in 1999 to 2000 warned that biological toxins in certain organic products (i.e., apples and wheat) should be closely monitored. Another major concern is the use of manure as a fertilizer in organic farming. Manure can carry human pathogens and mycotoxins from molds. It is well known that *E. coli* 0157:H7 originates primarily from ruminants such as cattle, sheep, and deer, which shed it through their feces. In addition, growers must also be alert to the potential contamination of produce growing and handling environments by human or animal fecal material, which is known to harbor *Salmonella, Cryptosporidium,* and other pathogens. However, properly treated manure (and other biosolids) can be an effective and safe fertilizer. Other sources of contamination related to organic farming may arise from nearby composting or manure storage areas, livestock, or poultry operations, nearby municipal wastewater or biosolids storage, treatment or disposal area, and high concentrations of wildlife in the growing and harvesting environment, such as nesting birds in a packing shed, or heavy concentrations of migratory birds, bats or deer in fields (51,52).

Occupational Risk from Methods to Increase Food Safety

Use of Pesticides and Chemicals

Although it is well established in the medical literature that acute and subacute exposure to pesticides and other chemicals poses major health issues, less is currently known about low-level chronic occupational or environmental exposures to residues of pesticides and chemicals. However, evidence

exists for potential chronic health effects of exposure to several pesticide classes at chronic low levels such as the association of chronic neurological effects with exposure to several pesticide classes. Examples include the association of increased vibration sense, motor-sensory neuropathy, and cognitive and affective deficits after exposure to organophosphates; the association of olfactory, cognitive, and behavioral deficits after exposure to methylbromide; and the association of symptoms of Parkinson's disease after paraquat exposure. Another example is association of oligospermia and azoospermia after exposure to dibromochloropropane (DBCP), which is now banned in the United States. There is also evidence of associations of chronic low-level exposure to pesticide residues and cancer (5,6,53–56).

A major area of interest in relation to pesticides and cancer has concentrated on pesticides acting as endocrine disrupters, mostly organochlorinated insecticides, and on hormone-related cancers. Research has largely focused on the association of breast cancer and exposure to DDT and its metabolites, although a causal inference has not been established. A recent study carried out in India, a country in which exposure to organochlorinated pesticides is expected to be higher and more recent than in populations from developed countries, found significantly higher levels of organochlorinated pesticides (DDT and its metabolites and others) in the blood of women with breast cancer as compared to reference women. In a Danish study, a modifying effect of p53 mutations on the breast cancer risk associated with exposures to organochlorines was observed, suggesting a potential for gene-environment interactions as an important factor in pesticide-related carcinogenicity (56–58).

Other pesticides have also been linked to cancer. For example, an Italian study observed a significantly increased risk for ovarian cancer in women exposed to triazines, a class of herbicides including the frequently used atrazine, simazine, and others (56,59).

Workplace factors and work practices influence the magnitude and amount of exposure. In addition, workers are often exposed to mixtures of pesticides and chemicals in the occupational setting. Other relevant factors contributing to the significance of the occupational exposure to pesticides and chemicals in the agricultural setting are the nature of the pesticide, shorter versus longer duration pesticide, type of work activity (e.g., pesticide operators versus reentry workers), and length of exposure. For example, a study in California determined that certain organophosphate application variables were significantly related to systemic illness. These included application to fleshy fruit, vegetables, and melons; air application drift; and specific OPs such as mevinphos, demeton, oxydemeton-methyl, methamidophos, and azinphos-methyl. California's unique pesticide mandatory reporting requirements make it the only state in which data are available on both pesticide use and suspected pesticide-related illnesses (59,60).

Studies evaluating the health effects of pesticides have mainly addressed the oral route of exposure after consumption. However, exposure to pesticide

and chemical residues primarily involves the dermal route and, to a lesser extent, the inhalation route and typically occurs intermittently. However, despite the relatively high dermal exposure in occupational settings, existing regulations such as the FIFRA in the United States have primarily evolved from concerns about the oral route of exposure. Therefore, to accurately estimate occupational exposures to residues in agricultural work, more dermal toxicodynamic studies focusing on intermittent exposures are needed. Furthermore, the bioavailability of bound skin residues of pesticides and chemicals and the effects of the parent compound or relevant metabolite(s) in the context of various agricultural practices and work activities are other areas that need to be researched (9,59,61–63).

Gender-specific research is also needed. There are a number of major gender-related variables in agriculture that may lead to occupational exposure in females to pesticides. For example, compared to men, women working in agriculture may be found in lower-paid and lower-status jobs, with less access to promotion, information, and safety measures. In a survey of over 500 farmers in Thailand, in which all male and female farmers applied pesticides, 53% of the women were not able to read, compared to 29% of men, decreasing their ability to heed the safety warnings written on the labels of pesticides. Another occupational group that has often been overlooked is children. Child labor persists globally. The International Labor Organization estimates that approximately 250 million children between the ages of 5 and 14 work part-time or full-time around the world. Although they engage in various jobs, by far the largest number work in agriculture where they may be exposed to various hazards, including toxic chemicals (see Chapter 12) (56,64–67).

Food Irradiation

Irradiation of food has the potential to decrease the incidence of foodborne disease and makes possible the replacement of toxic and environmentally harmful chemical fumigants such as methylbromide, ethylene oxide, and propylene oxide. Irradiation can also increase the shelf life of certain food items and decrease losses from spoilage and pests. Decreasing losses is important in the context of global storage of food supplies. Although it remains controversial, food irradiation is widely supported by various international and national medical, scientific, and public health organizations, as well as groups involved with food processing and food services. Many countries have started to irradiate food, including France, the Netherlands, Portugal, Israel, Thailand, Russia, China, and South Africa. However, in the United States, only 10% of herbs and spices and less than 0.002% of fruits, vegetables, meats, and poultry are currently irradiated (18,68–70).

The technology of food irradiation involves use of high-energy radiation in any of three approved forms: gamma rays, electron beams, or x-rays. Gamma rays can be generated by either of two approved radionuclide

sources, cobalt-60 or cesium-137, which give off high-energy photons, called gamma rays, that can penetrate foods to a depth of several feet. The radioactive substances emit gamma rays all the time, and massive concrete walls are needed to contain them. Foods to be irradiated are brought into a chamber on conveyor systems and are exposed to the rays for a defined time period. Although some fear that foods become radioactive, since gamma irradiation does not emit neutrons, foods are not made radioactive by the procedure (71,72).

Electron beam (e-beam) technology uses a stream of high-energy electrons propelled from an electron gun. No radioactivity is involved, but shielding is needed to protect workers from the electron beam (72).

The newest technology is x-ray irradiation, an outgrowth of e-beam technology, and is still being developed. The x-ray machine is a more powerful version of the machines used in many hospitals to take radiographs. To produce the x-rays, a beam of electrons is directed at a thin plate of gold, producing a stream of x-rays coming out on the other side. Like gamma rays, x-rays can pass through thick foods and require shielding for worker safety. Four commercial x-ray units have been built in the world since 1996 (73).

The absorption of gamma rays, x-ray photons, or electrons produces ionization. Water is the principal target for the radiation since it is the largest component of most foods and microorganisms. Normally, approximately 70% of the radiation-induced ionization occurs in cellular water, and the target organisms are inactivated because of secondary reactions, not because of a direct effect on bacterial DNA. However, others have proposed that DNA damage is the mechanism by which irradiation acts (68,74–76).

Radiation doses used in the irradiation process are measured in units of grays (Gy) or kilograys (kGy), with 1 Gy equal to 100 rads. Doses can be divided into three groups: low dose (less than 1 kGy); pasteurizing dose (1 to 10 kGy) used for pasteurization of meats, poultry, and other foods; and high dose (more than 10 kGy) for sterilization or for reduction of the number of microbes in spices. Some bacterial spores may be more resistant to irradiation than vegetative cells and require doses substantially higher than those used in pasteurization. In general, inactivation of viruses also requires higher doses of radiation than doses used to sterilize pests in plants or for pasteurization (18,77–79).

In the United States, the Nuclear Regulatory Commission (NRC) regulates facilities that utilize radioactive sources. To be licensed, the facility must have been designed with multiple fail-safe measures, and must establish extensive and well-documented safety procedures and worker training. The occupational risk in working in areas where food irradiation takes place is minimal if safe work practice guidelines are followed. Outside the United States, a small number of fatal incidents have been documented in which a worker bypassed multiple safety steps to enter the chamber while the radioactive source was exposed, resulting in a severe or even lethal radiation injury (73).

Alternative Nonthermal Methods

Nonthermal technologies that appear promising include high hydrostatic pressure (HHP), pulsed electric fields (PEF), and high-intensity ultrasound combined with pressure, or combinations of these methods, or with irradiation. As with food irradiation, occupational health and safety guidelines and worker education and training would prevent injuries or accidents (74).

Influence of Biotechnology on Food Safety

The influence of biotechnology on agriculture has already led to profound and revolutionary developments through genomics and transgenics and continues to transform agriculture. Whereas genomics seeks to understand and modify the chromosomal traits of a species, transgenics focuses on changing traits of an organism by transferring individual genes from one species to another. Estimates indicate that the world market for genetically modified (GM) plants will be $8 billion in 2005 and $25 billion by 2010. The number of countries growing transgenic crops commercially has increased from 1 in 1992 to 13 in 1999. Furthermore, between 1996 and 2000, the global area of agriculture devoted to growing transgenic crops increased by more than 25-fold, from 1.7 million hectares in 1996 to 44.2 million hectares in 2000. The United States, Canada, and Argentina grew approximately 98% of the total amount. Within transgenic plants, herbicide tolerance is the most common trait, accounting for 74% of all transgenic crops in 2000 (80).

Genetically modified crops can directly benefit the farmer by altering the inputs needed to produce a crop, such as herbicides or fertilizer. Other plants are designed to benefit the consumer when the end product expresses a desirable outcome, such as improved quality, nutritional content, or storability (81,82).

Examples of genetic engineering to benefit the farmer/grower include the following:

1. Glyphosate or round-up tolerant soybeans: A gene from another plant is introduced into the soybean plant, allowing farmers to spray the glyphosate herbicide and kill weeds without harming the genetically engineered (GE)-soybean plant.
2. Bt crops: *Bacillus thuringiensis* (Bt) is an aerobic, motile, gram-positive endospore-forming bacillus initially isolated in Japan and described by Berlinger in 1915 (80).

Bt has insecticidal activity from endotoxins included in crystals formed during sporulation, but vegetative insecticidal proteins (VIPs) from before sporulation are also being developed. The crystals of different strains of most Bts contain varying combinations of insecticidal crystal proteins (ICPs), and

different ICPs are toxic to different groups of insects. To confer resistance to insects in specific plants, a gene from the Bt bacteria is introduced into corn, cotton, or other plant types. The plants then produce the same protein crystal that the bacteria produce that is toxic to many types of insects that would normally harm the plant, such as the European corn borer (80).

Two examples of genetic engineering to benefit the consumer include the following:

1. High-oleic soybeans: These contain less saturated fat than conventional soybeans, leading to consumer health benefits, lower processing costs, and longer shelf life for oil.
2. High-lauric canola: An inserted gene allows the plant to produce an oil composed of 40% lauric acid, a key ingredient in many soaps, detergents, lubricants, and cosmetics.

Similar applications are occurring in animal agriculture. These include the creation of a synthetic version of a naturally occurring hormone to boost milk production in dairy cows and development of low-phytate corn and other types of animal feeds that lead to the decrease of phosphorus in animal waste, leading to less pollution and lower cost of animal feeds (81).

Potential Occupational Risk

Regulatory frameworks exist to address vital issues related to food safety and environmental protection in regard to GMO applications. However, little research or regulatory oversight currently exists addressing the potential impact of genetically modified/engineered crops on the health and safety of agricultural workers. Some studies have evaluated the health effects of Bt in agricultural workers. In a public health survey, a large number of individuals were exposed to a massive Bt pesticide spraying program. Some of the symptoms reported included rash and angioedema. One of the spray workers developed dermatitis, pruritus, swelling, and erythema with conjunctival injection. Bt was cultured from the conjunctiva in this case. In 1992 the use of Bt as part of an Asian gypsy moth control program was associated with symptoms of allergic rhinitis, exacerbations of asthma, and skin reactions among individuals exposed to the spraying operations. However, no follow-up was performed to determine if these events were a result of hypersensitivity to Bt or possible toxic reactions, or were secondary to common aeroallergens coincidental to the season when the spraying was performed. Similar results were produced during another spraying of Bt in 1994 (82–88).

Given that approximately 75% of asthma cases are triggered by allergens, the potential allergenicity of Bt is important to investigate further. A study by Bernstein et al. (83) measured immune responses in seasonal migrant farm workers exposed to Bt pesticides in the muck crops region of Northern Ohio in the United States in October 1995. This study included questionnaires, nasal and mouth lavages, ventilatory function assessment, and skin tests to

indigenous aeroallergens and to a variety of Bt spores and vegetative preparations. The exposure group consisted of farmers who picked vegetables (celery, parsley, cabbage, kale, spinach, and strawberries) that required Bt pesticide spraying soon after the first crops were planted and continuing until the harvesting of the last crop in early October. Positive skin-prick tests to several Bt spore extracts were seen chiefly in exposed workers. Specifically, there was a significant ($p < .05$) increase in the number of positive skin tests to spore extracts at 1 and 4 months after exposure to Bt spray. The number of positive skin test responses was significantly higher in high-versus low-to-moderately exposed workers. The majority of nasal lavage cultures from exposed workers were positive for the commercial Bt organism, as demonstrated by specific molecular genetic probes. Specific immunoglobulin E (IgE) antibodies were also more present in workers exposed to high Bt spray levels, and specific IgG and IgE levels were present in all groups of exposed workers. However, there was no evidence found of occupationally related respiratory symptoms. Another study by Pearce et al. (87) studied the effects of aerial spraying with the *Kurstaki* species of Bt on children with asthma within the Bt spray area in Victoria, British Columbia, in 1999. The study found no difference in asthma symptom scores between exposed and gender and age-matched controls either before or after the spray. No significant changes were found for the peak expiratory flow rates for subjects after the spray period.

From a consumer standpoint, concerns have been raised about the allergenic potential of GM foods. For example, the CDC investigated 51 reports of possible adverse reactions to corn that occurred after Starlink, a corn variety modified to produce a Bt endotoxin, Cry9C, was allowed for animal feed and was found in the human food supply. However, allergic reactions were apparently not confirmed. More research is needed to better comprehend the health effects of Bt and other biological sources such as novel proteins found in genetically modified foods from an occupational, environmental, and consumer perspective (88,89).

Terrorism and Food Safety

Given the reality of the geopolitical terrorism threats facing the world today, agriculture can also be a potential target for terrorism. For instance, agroterrorism, the use of microbes and poisons to shake the confidence in the food supply, could cripple the $201 billion agricultural economy in the United States. Diseases such as swine fever and citrus greening can potentially spread across the land silently. The impact of a single case of foot-and-mouth disease could require the destruction of millions of cows and result in a worldwide ban on United States cattle export for years. Furthermore, unlike the most feared bioterrorism threats, such as anthrax or smallpox, some virulent agricultural diseases are harmless to humans and can be trans-

ported from great distances from infected crops and animals worldwide. To defend against this threat in the United States, the USDA is building or modernizing laboratories to quickly screen disease samples from around the country. Some have advocated greater use of vaccines, but this is problematic due to high cost and logistical complexity. With increasing global trade, another concern is that many nations cannot readily distinguish between infected and vaccinated animals and may reject either at their border. Some private companies have developed a suitcase-size device that can detect DNA from the air to determine the presence of a deadly microbe within about half an hour. Such devices may help localize and map outbreaks (90).

Global Issues Related to Food Safety

Cooperation between nations will help achieve food safety on a global scale. The concept of good agricultural practices (GAP) has evolved in recent years to meet the needs of a rapidly changing and globalizing food economy and to address concerns of a wide range of stakeholders about food production and security, food safety and quality, and the environmental sustainability of agriculture. The Committee on Agriculture (COAG) of the Food and Agricultural Organization (FAO) of the United Nations in 2003 adopted a holistic food chain (sometimes called "farm to table" or "farm to fork") approach that encompasses the whole food chain to maximize food safety and quality worldwide. The FAO defines the food chain approach as recognition that the responsibility for the supply of food that is safe, healthy, and nutritious is shared along the entire food chain by all involved with the production, processing, and trade of food on a global scale (91–93).

References

1. Schlundt J. New directions in foodborne disease prevention. Int J Food Microbiol 2002;78:3–17.
2. Pimentel D, Wilson A. World population, agriculture, and malnutrition. WorldWatch 2004;SeptOct:22–5.
3. World Health Organization (WHO) Food and Agriculture Organization (FAO)quoted in http://www.wfp.org/aboutwfp/facts/hunger_facts.html.
4. Joachim D, Davis R. From farm to fork: good reasons to choose pure food. In: Fresh Choices. New York: St. Martin's Press, 2004.
5. Mansour S. Pesticide exposure: Egyptian scene. Toxicol 2004;198:91–115.
6. Gupta PK. Pesticide exposure: Indian scene. Toxicol 2004;198:83–90.
7. Randall AW, Whitehead AJ. Codex alimentarius: food quality and safety standards for international trade. Rev Sci Tech 1997;16:313–21.
8. Oser BL. Toxicology then and now. Regul Toxicol Pharmacol 1997;7:427–43.
9. Ross JH, Driver JH, Cochran RC, et al. Could pesticide toxicology studies be more relevant to occupational risk management? Ann Occup Hyg 2001;45:S5–S17.

10. Morris JG. The color of hamburger: slow steps toward the development of a science-based food safety system in the United States. Trans Am Clin Climatol Assoc 2003;114:191–201.
11. Swaminathan B, Barrett TJ, Hunter SB et al. PulseNet: the molecular subtyping network for foodborne bacterial disease surveillance, United States. Emerg Infect Dis 2001;7:382–9.
12. Gerald BL, Perkin JE. Position statement of the American dietetic association: food and water safety. J Am Diet Assoc 2003;103:1203–18.
13. World Health Organization. Five simple measures could significantly reduce the global incidence of foodborne illness. http://www.who.int/mediacentre/news/releases/2004/pr72/en/.
14. World Health Organization. Food safety. http://www.who.int.foodsafety/en/.
15. Murray CJL, Lopez AD, eds. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020. Boston: Harvard University Press; 1996.
16. Wit MAS, de Koopmans, MPG, Kortbeek LM, et al. Sensor, a population-based cohort study on gastroenteritis in the Netherlands: incidence and aetiology. Am J Epidemiol 2001;154:666–74.
17. Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. Emerg Infect Dis 1999;5:607–25.
18. Osterholm MT, Norgan A. The role of irradiation in food safety. N Engl J Med 2004;350:1898–1901.
19. Foodborne Outbreak Response and Surveillance Unit. 2000 Foodborne diseases outbreaks due to bacterial etiologies. http://www.cdc.gov/foodborneoutbreaks/us_outb/fbo2000/bacterial00.html.
20. Food Safety and Inspection Service. 2003 Recall cases. http://www.fsis.usda.gov/OA/recalls/rec_actv.htm#2003.
21. WHO. Food safety and foodborne illness. *http://www.who.int/mediacentre/factsheets/fs237/en/*.
22. FSAI Scientific Committee. Zoonotic tuberculosis—final Report, July 2003:1–18. http://www.fsai.ie/publications/other/zoonotic_tuberculosis.pdf.
23. Foodborne intoxications (Food poisoning). In: Chin J, ed. Control of Communicable Diseases Manual, 17th ed. 2000:202–12. Washington, DC: American Public Health Association; 2000.
24. Good Agricultural Practices. In the field of worker health and hygiene. New England extension of food safety consortium. http://hort.uconn.edu/IPM/foodsafety/manbiosolids.htm.
25. Viral hepatitis A. In: Chin J, ed. Control of Communicable Diseases Manual, 17th ed. 2000:238–43. Washington, DC: American Public Health Association; 2000.
26. Center for Disease Control and Prevention. Foodborne transmission of hepatitis A: Massachusetts, 2001. MMWR 2003;52:565–7.
27. Chaudhuri AK, Cassie G, Silver M. Outbreak of food-borne type-A hepatitis in Greater Glasgow. Lancet 1975;2:223–5.
28. Jones AE, Smith JL, Hindman SH, et al. Foodborne hepatitis A infection: a report of two urban restaurant-associated outbreaks. Am J Epidemiol 1977;105:156–62.
29. Food preparation and service—part 1. Self inspection checklist. http://www.cdc.gov/niosh/docs/2004–101/chklists/r1n32f~1.htm. (NOTE: to see all five parts of this checklist, insert numbers 33 to 36 instead of "32" in the Web site address.)
30. Fiore AE. Hepatitis A transmitted by food. Clin Infect Dis 2004;38:705–715.

31. Alagappan K, Barnett B, Napolitano A, et al. Seroprevalence of hepatitis A among hospital dietary workers: implications for screening and immunization. Am J Med Qual 2001;16:145–8.
32. Center for Disease Control. Screening for tuberculosis and tuberculosis infection in high-risk populations. Recommendations of the advisory committee for elimination of tuberculosis. MMWR 1990;39:1–7.
33. Judson FN, Sbarbaro JA, Tapy JM, et al. Tuberculosis screening. Evaluation of a food handlers' program. Chest 1983;83:879–82.
34. Food Safety and Inspection Service. U.S. Department of Agriculture. Tuberculosis. What you need to know. August 1997:1–3. http://www.fsis.usda.gov/ophs/TBBROCH.HTM.
35. Center for Disease Control. Traveler's health. Tuberculosis, pp. 1–3. http://www.cdc.gov/travel/diseases/tb/htm.
36. World Health Organization. Hygiene in food preparation. http://www.who.int/foodsafety/publications/capacity/en/6.pdf.
37. Curti T. Statistical department, Food and Agricultural Organization (FAO), Rome, Italy, June 1994.
38. Dalaker J, Naifeh M. Poverty in the United States: 1997. U.S. Bureau of the Census, Current Population Reports, Series P60–201. Washington, DC: U.S. Government Printing Office, 1997.
39. Wood-Mackenzie Consultants, Ltd., Agrochemical division, 1994. Update of the Country report, Ref. Vol. Agrochem. Serv.,Edinburgh, Scotland (cited in Mansour S. Pesticide exposure-Egyptian scene. Toxicology 2004;198:91–115).
40. Wendo C. Uganda considers DDT to protect homes from malaria. Lancet 2004;363:1376.
41. Moses M, Johnson ES, Anger WK et al. Environmental equity and pesticide exposure. Toxicol Ind Health 1993;9:913–59.
42. Pesticide Action Network. Toxaphene in North Sea Fish. Global Pesticide Campaigner. Pesticide Action Network 1993;3(4):17 (cited in Mansour S. Pesticide exposure-Egyptian scene. Toxicology 2004;198:91–115).
43. Henao S, Finkelman J, Albert L, et al. Pesticides and health in America. Environ. Ser. No. 12, Plant American Health Organization, Division of Health and Environment, Washington, DC (cited in Mansour S. Pesticide exposure-Egyptian scene. Toxicology 2004;198:91–115).
44. Kaloyanova FP, El-Batawi MA. Organochlorine Compounds. Human Toxicology of Pesticides. Boca Raton, FL: CRC Press, 59–100 (cited in Mansour S. Pesticide exposure-Egyptian scene. Toxicology 2004;198:91–115); 1991.
45. World Health Organization. Frequently asked questions—acrylamide in food, pp. 1–4. http://www.who.int/foodsafety/publications/chem/acrylamide_faqs/ en/print.html; 1991.
46. FAO/WHO consultation on the health implications of acrylamide in food, Geneva, 25–27, June 2002. http:www.who.int/foodsafety/publications/chem/acrylamide_june2002/en/.
47. World Health Organization. Semicarbizide. http://www.who.int/foodsafety/chem/sem/en/print.html.
48. World Health Organization. PCBs and dioxin in salmon. http://www.who/int/foodsafety/chem/pcbsalmon/en/.
49. Williams S. Mercury. In: Olson KR, ed. Poisoning and drug overdose. Stamford, CT: Appleton & Lange, 1999.

50. Das HK, Mitra AK, Sengupta PK, et al. Arsenic concentrations in rice, vegetables, and fish in Bangladesh: a preliminary study. Environ Int 2004;30:383–7.
51. Organic farming. http://fact-index.com/o/or/organic_farming.html.
52. Guidance for industry. Guide to minimize microbial food safety hazards for fresh fruits and vegetables. http://www.foodsafety.gov/~dms/prodguid.html.
53. Ecobichon DJ. Toxic effects of pesticides. In: Klaassen CD, ed. Casarett and Doull's Toxicology, 5th ed. New York: McGraw-Hill 1996.
54. Das R, O'Malley M, Styles L. Pesticide illness. Part 4. Chronic health effects. Laws and regulations. http://www.aoec.org/LLDIR.htm#powerpoint.
55. Blanc PD. Evaluation of the patient with occupational chemical exposure. In: Olson KR, ed. Poisoning and Drug Overdose. Stamford, CT: Appleton & Lange; 1999.
56. Garcia AM. Pesticide exposure and women's health. Am J Ind Med, 2003;44:584–94.
57. Mathur V, Bhatnagar P, Sharma RG, et al. Breast cancer incidence and exposure to pesticides among women originating from Jaipur. Environ Int 2002;28:331–6.
58. Hoyer AP, Gerdes AM, Jorgensen T, et al. Organochlorines, p53 mutations in relation to breast cancer risk and survival. A Danish cohort-nested case-control study. Breast Cancer Res Treat 2002;71:59–65.
59. Donna A, Crosignani P, Robutti F, et al. Trazine herbicides and ovarian epithelial neoplasms. Scand J Work Environ Health 1989;15:47–53.
60. Weinbaum Z, Schenker MB, Gold EB, et al. Risk factors for systemic illnesses following agricultural exposures to restricted organophosphates in California, 1984–1988. Am J Ind Med, 1997;31:572–9.
61. Carmichael NG. Critique of the paper: Could pesticide toxicology studies be more relevant to occupational risk assessment? (by Ross et al., 2001). Ann Occup Hyg 2001;45(suppl 1):S5–S17.
62. Hakkert BC. Refinement of risk assessment of dermally and intermittently exposed pesticide workers: a critique. Ann Occup Hyg 2001;45:S23–8.
63. Von Hemmen JJ, Groeneveld CN, Van Drooge H, et al. Risk assessment of worker and residential exposure to pesticides: conclusions and recommendations. Ann Occup Hyg 2001;45:S171–4.
64. London L, De Grosbois S, Wesseling C, et al. Pesticide usage and health consequences for women in developing countries: out of sight, out of mind? Int J Occup Environ Health 2002;8:46–59.
65. Kunstadter P, Prapamontol T, Sirirojn B, et al. Pesticide exposures among Hmong farmers in Thailand. Int J Occup Environ Health 2001;7:313–25.
66. Bachman SL. A stitch in time? In the decade since the last United Nations special session of children, the world has become painfully aware of the child labor problem. As the delegates convene again, they face the hardest question of all: now what? Los Angeles Times Magazine 2001, September 16:10–19.
67. International Labor Organization. Child Labor 101. http://www.ilo.org/teachin/ilou101.cfm?&bsuppresslayout=1.
68. Crawford LM. Challenges and opportunities for food irradiation in the 21st century. In: Loaharanu P, Thomas P, eds. Irradiation for Food Safety and Quality. Lancaster, PA: Technomic Publishing, 2001.
69. Food loss prevention in perishable crops. Agricultural Services Bulletin No. 43. Rome: Food and Agricultural Organization of the United Nations, 1981. http://www.fao.org/docrep/s8620e/s8620e00.htm.

70. Food irradiation: available research indicates that benefits outweigh risks. (GAO)/RCED-00–217. Washington, DC: General Accounting Office, August 2000.
71. Schmidt C. Safe food: an all-consuming issue. Environ Health Perspect 1999;107:A144–69.
72. Thayer DW. Irradiation of food: Helping to ensure food safety. N Engl J Med 2004;350:1811–12.
73. Frequently asked questions about food irradiation. Center for Disease Control. Division of bacterial and mycotic diseases. http://www.cdc.gov/ncidod/dbmd/diseaseinfo/foodirradiation.htm.
74. Ross A, Griffiths MW, Mittal GS, et al. Combining nonthermal technologies to control foodborne microorganisms. Int J Food Microbiol 2003;89:125–38.
75. DeRuiter FE, Dwyer J. Consumer acceptance of irradiated foods: dawn of a new era? Food Service Technol 2002;2:47–58.
76. Dickson JS. Radiation inactivation of microorganisms. In: Molins R, ed. Food Irradiation: Principles and Applications. New York: Wiley, 2001.
77. Loaharanu P. Irradiated Foods, 5th ed. New York: American Council on Science and Health, 2003.
78. Molins R, ed. Food Irradiation: Principles and Applications. New York: Wiley, 2001.
79. Diehl JF. Safety of Irradiated Foods, 2nd ed. New York: Marcel Dekker, 1995.
80. Shelton AM. Zhao JZ, Roush RT. Economic, ecological, food safety, and social consequences of the deployment of Bt transgenic plants. Annu Rev Entomol 2002;47:845–81.
81. Shutske JM, Jenkins SM. The impact of biotechnology on agricultural worker safety and health. J Agric Saf Health 2002;8(3):277–87.
82. Riley PA, Hoffman L. Value-enhanced crops: Biotechnology's next stage. Agric Outlook 1999;259:18–23.
83. Bernstein IL, Bernstein JA, Miller M, et al. Immune responses in farm workers after exposure to bacillus thuringiensis pesticides. Environ Health Perspect 1999;107(7):575–82.
84. Green M, Heumann M, Foster LR, et al. Public health implications of the microbial pesticide Bacillus thuringiensis: an epidemiological study, Oregon 1985–85. Am J Public Health 1990;80:848–52.
85. Asian Gypsy Moth Control Program, Report of Health Surveillance Activities. Olympia, WA: Washington State Department of Health, 1993.
86. Bender C, Peck S. Health symptoms reported during BTK spraying spring 1994 in the capital region district. Environ Health Rev 1996(Summer):42–4.
87. Pearce M, Habbick B, Williams J, et al. The effects of aerial spraying with *Bacillus thuringiensis kurstaki* on children with asthma. Can J Public Health 2002;93(1):21–5.
88. Bernstein JA, Bernstein IL, Bucchini L, et al. Clinical and laboratory investigation of allergy to genetically modified foods. Environ Health Perspect 2003;111(8):1114–21.
89. Bannon G, Tong-Jen F, Kimber I et al. Protein digestibility and relevance to allergenicity. Environ Health Perspect 2003;111(8):1122–4.
90. Piller C. Farmlands seen as fertile fields of terrorism. Los Angeles Times, Sunday Preview, August 22, 2004:A1,A14–A15.
91. FAO's Strategy for a Food Chain Approach to Food Safety and Quality: A Framework Document for the Development of Future Strategic Direction.

Committee on Agriculture, 17th session, Rome, Italy, March 31–April 4, 2003. Food and Agricultural Organization of the United Nations, pp. 1–15. http://www.fao.org/DOCREP/MEETING/006/Y8350e.HTM.
92. Development of a framework for good agricultural practices. Committee on Agriculture, 17th Session, Rome, Italy, March 31–April 4, 2003. Food and Agricultural Organization of the United Nations, pp. 1–14. http://www.fao.org/DOCREP/MEETING/006/Y8350e.HTM.
93. Protecting the food chain. http://www.fao.org/ag/magazine/0304spl.htm.

3

Overview of Hazards for Those Working in Agriculture

Scott Prince

Key words: job task, hazards, injury, illness, allergy, stress

Despite a dramatic shift in agricultural production methods in the developed nations over the past several decades, agricultural work remains one of the most hazardous occupations. In the United States during the 10 years from 1992 to 2002, the annual rate of fatal occupational injuries in agriculture (including forestry and fishing) declined 5%, from 23.9 to 22.7 per 100,000 workers. During the same time period, the rate among those employed in the private sector declined by 21% and, by the end of that period, was 4.2 per 100,000 workers, over five times lower than in agriculture. Injury and illness rates, which are more difficult to estimate, also are significantly elevated for farmers compared to workers in the private sector, though the difference is less pronounced (1–3).

The number of U.S. agricultural workers has been relatively stable over the past decade at approximately 3.3 million, though farming populations, particularly migrant workers, are difficult to count accurately. Whatever the exact number, these workers comprise only a small percentage of the population, which is similar to the situation in other industrialized nations. This is in sharp contrast to the preindustrial age, and the current situation in much of the world, where overall 70% of all workers farm. Fewer farmers means that fewer people are directly aware of the risks of agriculture. With the shift of the population to cities, most people tend to have a romanticized view of rural life and farming as peaceful and healthy. Even the health care providers who care for farmers may not be uniformly aware of the increased risks associated with their patients' occupation (3–6).

The ability to dramatically increase farming productivity, accomplished primarily through mechanization and use of chemicals, is also a significant contributor to the risks faced by those who remain in agriculture. More productivity does not necessarily translate into lower risk for the farmer, particularly for fatal and disabling injuries. While hand tilling and walking behind an animal-powered plow have certain associated hazards, those activities do not have the same risk for sudden, catastrophic injury present in operating mechanized farm equipment, especially earlier models that had little or no

safety engineering. Similarly, pest control and the use of fertilizer in the preindustrial, prechemical age may have been inefficient, but it gave rise to a narrower range of serious hazards than the substances and methods in use today.

Just as agriculture is possibly the most diverse occupational classification in terms of the wide variation in products, methods, and job tasks, agricultural hazards are present in a multitude of ways—obvious or subtle, acute or chronic. Table 3.1 lists job tasks and associated hazards to provide a brief overview of the most common risks faced by farmers. It is not meant to be as detailed as the discussions in the following chapters but outlines categories of risk by general farm activities and exposures.

TABLE 3.1. Common agricultural hazards by job task.

Job task	Hazards	Outcomes
Primarily crop-related		
Field preparation, cultivation, harvesting	Inorganic dust (silica) (7)	Silicosis
	Allergens	Dermatitis, respiratory effects
Handling pesticides, herbicides	Chemical exposure	*Acute*: toxicity
		Chronic: neuropathy (organophosphates)
		Possible: cancer, adverse reproductive events (4,8)
Handling fertilizer	Ammonia	Burns, respiratory damage
Working in grain elevators	Organic dust (7) (allergens, endotoxins, irritants)	Allergies, other respiratory diseases
	Oxygen displacement	Asphyxia
	Entrapment	Trauma, asphyxia
Working in silos	Nitrogen oxides	Silo-fillers' lung
Handling cotton	Cotton dust/endotoxin	Byssinosis
Harvesting tobacco	Nicotine	Green tobacco illness (9)
Primarily animal-related		
Contact with animals in general (10–13)	Bites, scratches, stings	Trauma, infection, envenomation
	Allergens	Dermatitis, respiratory effects
	Infectious agents	Zoonoses
	Feed additives	Dermatitis, other toxicity
	Pesticides	Acute/chronic toxicity (see above)
Working with large animals	Being stepped on/ pinned	Trauma, crush injuries
Working in animal confinement buildings (including manure pits) (12)	Organic dust	Allergies, other respiratory disease
	Hydrogen sulfide	Asphyxia, pulmonary edema
	Ammonia	Respiratory irritation, disease
	Methane	Asphyxia, explosion
	Disinfectants	Dermatitis, respiratory disease
	Carbon dioxide	Asphyxia
	Inhalation of manure	Asphyxia, pneumonia

TABLE 3.1. Common agricultural hazards by job task. (continued)

Job task	Hazards	Outcomes
Handling hay/straw/feed	Moldy dusts	Farmers' hypersensitivity pneumonitis (7)
Veterinary treatment (11,12)	Anesthetic gases/ medications	Acute systemic toxicity, dermatitis
	Ionizing radiation	Burns, tissue damage, cancer
	Laser	Burns
Primarily machinery-related		
Loud processes (common in machinery tasks)	Noise	Hearing loss, increased risk of injury (loss of situational awareness)
Operating electrical equipment	Electrical shock	Burns, electrocution
	Fire	Burns, smoke inhalation
Operating gasoline/diesel equipment	Heat	Burns
	Fire	Burns, smoke inhalation
	Carbon monoxide	Carbon monoxide poisoning
	Diesel fumes	Respiratory irritation
Driving tractor/other vehicle	Rollover	Trauma
	Falling from seat	Trauma
	Collisions (MVA)	Trauma
	Chronic vibration (posture)	Hip arthritis
Operating field implements	Entrapment	Trauma
Operating hydraulic systems/pressure washers (14)	Wet surfaces: falls	Trauma
	High pressure fluid	Injection injury, infection
Welding	Welding fumes	*Acute*: welding fume fever
	Ultraviolet (UV) light	*Chronic*: metal toxicity/lung disease
	Heat/fire	*Acute*: UV keratitis/flash burns
		Chronic: cataracts
		Burns, smoke inhalation
Other general tasks/exposures		
Strenuous physical work	Ergonomic stress	Cumulative trauma syndrome
Outdoor work	UV radiation	*Acute*: sunburn
	Heat	*Chronic*: skin damage/cancer, cataracts
	Cold	Dehydration, cramps, hyperthermia
	Lightning	Frostbite, hypothermia
	Noncrop plants	Burns, electrocution
		Allergy, dermatitis
Work at heights	Falls	Trauma

Using tractors and other vehicles, operating power equipment, and working with large animals are the primary farm activities associated with traumatic injury. The majority of agricultural fatalities involve tractor-related injuries, and the annual rate of fatal injuries per tractor has remained around

8 per 100,000 for the most recent decade for which there are data. Tractor rollovers account for 50% to 60% of these fatalities. This is particularly troubling since the majority of these deaths could be prevented with the use of rollover protective structures (ROPS) and seat belts. Runovers accounted for approximately another quarter of the tractor-related fatalities, with children, either nearby or as extra passengers, at particular risk (3,4,6,7,15–18).

Farm machinery and equipment also require maintenance and repair, much of which is performed by the farmer. Because this is an occasional activity, the skill, understanding of hazards, and use of engineering controls or personal protective equipment may be lower for the farmer than for someone who performs these same jobs full-time. However, the farmer is also less likely to become complacent about performing hazardous tasks or to suffer effects associated with chronic exposure.

While causing fewer fatalities than machinery, contact with animals, in particular cattle, horses, sheep, and hogs, is a leading factor in total agricultural injuries. Animal handlers also face increased risk of zoonotic infection. These diseases are usually specific to certain types of animals and/or exposure circumstances and may be transmitted by bite, scratch, inhalation, ingestion, or skin contact. Certain zoonotic infections, such as brucellosis and orf, are associated with farm animals; others, such as rabies and Lyme disease, are associated simply with working outdoors (1,11,13,19).

The increased use of high-density animal confinement buildings increases risk for several of the zoonoses and also elevates the risk for other toxic exposures and allergic conditions. Both animal and crop-related organic material cause a wide spectrum of allergic conditions. The division of allergic cause by either plant or animal becomes somewhat arbitrary, as grain dust contains insect parts, animal dander, and feces, while feeds and bedding material from plant sources may cause allergies in animal handlers. Molds and bacteria in the farm environment also can be allergenic, especially in the high levels encountered in grain or animal confinement enclosed settings (7,10).

Chemical toxicity can result from animal care activities involving feeds, pesticides, animal wastes, and veterinary care. Pesticides, herbicides, fertilizers, silica, endotoxins, and decomposition gases are common crop-related chemical exposures. These exposures affect a variety of organs, especially the skin and lungs, and may result in acute and chronic diseases. Research has also begun to focus on the use of agrochemicals and possible associations with both cancer and adverse reproductive outcomes (8).

Factors affecting the health of those in agriculture extend beyond the physical, biological, and chemical hazards listed in Table 3.1. Stress remains a significant problem for rural areas in general and for farmers in particular. Strenuous working conditions, the financial uncertainty inherent in agriculture, and a relative social isolation with a lack of support services are a few of the stressors that can contribute to psychological pathology. Access to health care for farm workers can be limited by geography, cultural issues, or financial considerations. Special population groups common in agriculture—

children, the elderly, migrant workers, and others—have greater risks for certain farm-related health problems. As the multiple components of agricultural health and safety become more fully understood, modifications to current prevention efforts should improve the health of this population (4,20–22).

References

1. Center for Disease Control and Prevention. Worker Health Chartbook, 2004. Washington, DC: CDC, 2004. http://www2a.cdc.gov/niosh-Chartbook/ch3/ch2–1.asp.
2. Bureau of Labor Statistics. Census of fatal occupational injuries. Washington, DC: U.S. Department of Labor, Bureau of Labor Statistics, Safety and Health Statistics Program, 2003. www.bls.gov/iif/oshcfoi1.htm.
3. Rautianinen RH, Reynolds SJ. Mortality and morbidity in agriculture in the United States. J Agric Saf Health 2002;8:259–76.
4. Frank AL, McKnight R, Kirkhorn S, Gunderson P. Issues of agricultural safety and health. Annu Rev Public Health 2004;25:225–45.
5. Greaves I, Olson D, Shetske J, Kochevar L. An agricultural safety and health information needs assessment for rural service providers. J Agromed 1994;1:43–57.
6. Prince TS, Westneat S. Perceptions and behaviors of primary care physicians regarding farmers' occupational exposures and health. J Agromed 2001;7:79–88.
7. Kirkhorn S, Garry V. Agricultural lung disease. Env Health Perspect 2000;108:705–12.
8. Kirkhorn S, Schenker M. Current health effects of agricultural work: respiratory disease, cancer, reproductive effects, musculoskeletal injuries, and pesticide-related illnesses. J Agric Saf Health 2002;8:199–214.
9. Gehlbach S, Williams W, Perry L, Woodall J. Green tobacco sickness: an illness of tobacco harvesters. JAMA 1974;229:1880–3.
10. Seward J. Occupational allergy to animals. Occup Med 1999;14:285–303.
11. Langley R. Physical hazards of animal handlers. Occup Med 1999;14:181–94.
12. Meggs W. Chemical hazards faced by animal handlers. Occup Med 1999;14:213–24.
13. Weber D, Rutal W. Zoonotic infections. Occup Med 1999;14:247–84.
14. North American guides for children's agricultural tasks. Marshfield, WI: National Children's Center of Rural and Agricultural Health and Safety, 1999. http://www.nagcat.org.
15. National Safety Council. Injury Facts. Itasca, MN: National Safety Council, 2000.
16. Cole H, Piercy L, Struttmann T, Morgan S, Brandt V, Muehlbauer J. The Kentucky community partners for healthy farming ROPS project notebook. Lexington, KY: University of Kentucky, Southeast Center for Agricultural Health and Injury Prevention, 2000.
17. Myers J, Hendrick K. Roll-over protective structure use and the cost of retrofitting tractors in the United States, 1993. J Agric Saf Health 1995;1:185–97.
18. Canadian Agricultural Injury Surveillance Program. Fatal farm injuries in Canada, 1990–1996. Kingston, Ontario: Canadian Agricultural Injury Surveillance Program, 1998.

19. Hendricks K, Adekoya N. Nonfatal animal-related injuries to youth occurring on farms in the United States, 1998. Inj Prev 2001;7:307–11.
20. Schuman S. Farming: occupation or non-specific risk factor? J Agromed 1996;31–4.
21. Lovelace O. Stress in rural America. J Agromed 1994;2:71–8.
22. Gregoire A. The mental health of farmers. Occup Med (London) 2002;52:471–6.

4

Occupational Regulation

John E. Furman

Key words: injuries, laws, rules, regulations, prevention

The International Labor Organization (ILO) estimates that half of the world labor force is employed in agriculture and 1.3 billion workers are engaged in production agriculture worldwide, ranking it among the largest industries in the world. The agricultural labor force in the total economically active population is under 10% in developed countries and accounts for 59% of workers in less developed regions (1). Agriculture workers have a higher risk of sustaining work-related injuries and illness than most other occupations. Agriculture is ranked as one of the three most hazardous industries along with mining and construction. According to ILO estimates for 1997, out of a total of 330,000 fatal workplace accidents worldwide, there were some 170,000 casualties among agricultural workers (2).

Agriculture workers are at high risk for fatal and nonfatal injuries, work-related lung diseases, noise-induced hearing loss, skin diseases, exposure to chemicals such as pesticides, and certain cancers associated with chemical use and sun exposure (see Chapter 3). Many of these hazards are self-evident, such as traumatic injuries and fatalities caused by accidents with machinery like tractors and harvesters. Other hazards are less evident and indolent in nature. These may include neurological damage associated with prolonged pesticide exposure or chronic respiratory diseases related to organic dust exposure (3).

The United States collects some of the most comprehensive statistics on occupational injuries and illnesses in agriculture. Each year, about 100 U.S. agriculture workers are crushed to death by tractor rollovers. Every day, about 500 workers suffer disabling injuries, and about 5% of these result in permanent impairment. Production agriculture is one of the few industries in which families are also at risk for injuries, illnesses, and death (4). Agriculture industry injury and illness data are collected by a variety of agencies including the Bureau of Labor Statistics (BLS), the National Safety Council (NSC), and the National Institute of Occupational Safety and Health (NIOSH). The BLS issues annual workplace safety reports using data culled from a sample of employers reporting occupational injury and illnesses under the

Occupational Safety and Health Administration's (OSHA) record-keeping regulation (29 CFR 1904). The BLS 1999 Census of Fatal Occupational Injuries data showed that the major industry division with the highest occupational injury fatality rate was agriculture (including forestry and fishing). A major drawback with BLS data is that OSHA exempts farms with fewer than 11 paid employees and all unpaid family members working on farms from its record-keeping requirements.

In 1996 the United States recorded 710 deaths and 150,000 cases of permanent disability due to occupational accidents in the agricultural sector. The mortality rate declined from 24 per 100,000 workers in 1992 to 21 in 1996, with a peak of 27 in 1993. These figures excluded properties with fewer than 11 employees and workers under 16 years old. Other commonly reported injuries included accidents with large animals, insect stings, cuts, burns, and falls. The NSC reported the fatality rates for agricultural workers in 2000 as being 22.5 per 100,000 workers compared to 3.8 for all other industries (5).

Agriculture continues to be one of the most hazardous and least regulated major industries worldwide. The World Health Organization (WHO) and ILO are the leading international bodies working toward the establishment of universal standards for agricultural health and safety legislation. In addition to political recognition of the benefits of strong occupational safety and health legislation, countries with strong labor representation (e.g., United States, Australia, France, and Brazil) tend to have more effective occupational safety and health regulation (1). Unfortunately, the agriculture sector is still exempt from many general occupational safety and health regulations. The health of the agriculture sector is still thought of as a public health issue to a great degree and not always fully covered under occupational health and safety regulation. Occupational medicine, industrial hygiene, and safety organizations may have a strong impact on improving agricultural workers safety protections through the provision of focused educational curricula and renewed attention to the agriculture sector.

International Regulation

Internationally many different systems address agriculture safety and health. Usually, general labor laws or labor codes give no specific reference to or may not fully apply to the agricultural sector. Agriculture is given only limited attention in the occupational safety and health regulation of many countries. In other countries, such as Brazil, Kenya, and Mexico, general labor laws apply to agriculture along with other industries. In certain countries, no safety and health laws apply to the agricultural sector at all. The general labor laws of a number of countries, such as Ghana, Jordan, Morocco, Nepal, Sierra Leone, Sudan, Turkey, Yemen, and Zaire, exclude agricultural workers completely or partially (1). The WHO and ILO work together to encourage national safety and health strategies and have developed many conventions

and recommendations that relate to agriculture. Adoption of ILO conventions is voluntary on the part of member nations. Table 4.1 lists selected ILO conventions that apply to agriculture.

Effective regulation of agriculture health hazards is difficult for a variety of reasons including the lack of a mutually accepted definition of agriculture used by the international community, the unorganized nature of agriculture, the remote locations of work sites, and the lack of strong centralized occupational safety and health authorities. In many Third World countries, subsistence farming predominates. Communal farming with no direct employer–employee relationship is also common in many parts of the world. This along with a poor occupational health infrastructure lends itself to little or no regulatory enforcement (6).

The 1962 ILO/WHO Committee on Occupational Health developed a definition of *agriculture* that may be used to define a common population for coverage under occupational safety and health regulation and for reporting of occupational injury and illness incidents in agriculture:

> "Agriculture" means all forms of activities connected with growing, harvesting, and primary processing of all types of crops, with the breeding, raising, and caring for animals, and with tending gardens and nurseries (7).

Even in industrialized countries such as the United States and South Korea, small family farms make up the vast majority of agriculture workplaces (6). Many of these farms do not employ full-time employees and may rely on temporary migrant workers during high-activity periods such as planting and harvesting. These farms are generally exempt from occupational safety and health regulation. Migrant workers tend to lack power due to cultural disparities, economic and political disadvantages, and lack of union representation. Following these workers and soliciting their participation in enforcing occupational safety and health regulation is a difficult challenge. Couple this with a lack of access to medical care, no federal requirements for the provision of medical surveillance for agriculture workers, and

TABLE 4.1. Selected International Labor Organization conventions that apply to agriculture.

Convention	Overview
Minimum age C. 138	Establishes the minimum age of employment. Exempts family and small-scale farms
Working environment C. 148	Provides recommendations regarding air pollution, noise, and vibration exposure
Labor inspection C.81	Requires member nations to maintain a system of labor inspection and enforcement
Occupational cancer C. 139	Requires member nations to reduce worker exposure to carcinogenic substances
Occupational health Services C. 181	Recommends that nations adopt national policy on occupational health services for all workers

no requirements for documentation of workplace injuries and illnesses leaves the majority of agriculture workers unprotected by governmental regulation (1).

United States Regulation

In the United States, the Occupational Safety and Health Act (OSHAct) of 1970 has established specific regulations that apply to agriculture (Table 4.2) (8). The Occupational Safety and Health Administration (OSHA) enforce these regulations in states covered by the OSHAct. On the federal level the small farm exemption to the OSHAct prohibits enforcement of OSHA regulations on farms with fewer than 11 employees. State plans are not required to operate under this exemption. The health care provider must determine whether OSHA or state regulations apply in each situation.

Section 18 of the OSHAct allows states to establish their own occupational safety and health plans that are "at least as effective" as the federal plan. Currently 26 states have their own occupational safety and health plans. These states may have more stringent regulation and additional regulations that apply to agriculture. For example, the OSHA Bloodborne Pathogens Standard does not apply to agriculture operations whereas the Washington State standard does. The OSHAct applies to most federal workplaces regardless of their location. Selected federal regulations that apply to agriculture are summarized in the following paragraphs.

Required Record Keeping

Section 29 CFR 1904 of the code of federal regulations, Recording and Reporting Occupational Injuries and Illnesses, requires employers to record all work-related injuries, illnesses, and deaths on the OSHA 300 or

TABLE 4.2. Occupational Safety and Health Administration standards that apply to agriculture.

Temporary labor camps: 29 CFR 1910.142
Storage and handling of anhydrous ammonia: 29 CFR 910.111
Logging operations: 29 CFR 1910.266
Slow-moving vehicles: 29 CFR 1910.145
Hazard communication: 29 CFR 1910.1200
Retention of Department of Transportation (DOT) markings, placards, and labels: 29 CFR 1910.1201
Cadmium: 29 CFR 1910.1027
Rollover protective structures (ROPS) for tractors used in agricultural operations: 29 CFR 1928.51
Guarding of farm field equipment, farmstead equipment, and cotton gins: 29 CFR1928.57
Field sanitation: 29 CFR 1928.110

equivalent form (specified industries, such as dental clinics, are exempt from this regulation). A summary of these events must be posted in the workplace on an annual basis. In addition, the employer must report any deaths, multiple hospitalizations, or catastrophic incidents, e.g., loss of a limb, to the local OSHA office within 8 hours. Employers with fewer than 11 employees at any given time in the year are exempt from this regulation. The recording and reporting requirements do not cover unpaid family members working on farms (9).

Temporary Labor Camps

Although agriculture employers are not required to provide housing to temporary employees, 29 CFR 1910.142, Temporary Labor Camps, applies when the employer provides temporary housing to workers. This regulation seeks to ensure a safe and healthful place of living for migrant and other temporary workforces. Temporary labor camps must maintain minimum standards for site, shelter, water supply, toilet facilities, kitchen and dining facilities, pest control, first aid, and reporting of communicable diseases.

Hazard Communication

The Hazard Communication regulation, 29 CFR 1910.1200, was developed to make sure employers and employees are informed about chemical hazards in the workplace (except for pesticides, which are regulated by the Environmental Protection Agency, EPA). The regulation requires employers to obtain and maintain Material Safety Data Sheets (MSDS), inform and train employees, and label containers holding hazardous chemicals. Chemical manufacturers and importers, not employers, are required to evaluate chemicals and determine whether they are covered under 29 CFR 1910.1200.

Hazardous chemicals are any chemical, mixture of chemicals, or biological or physical agent that may cause short- or long-term health effects in exposed employees; these may include:

- Carcinogens (ethylene oxide, formaldehyde)
- Irritants (anhydrous ammonia, organic solvents)
- Corrosives (formic acid, calcium oxide)

Anhydrous Ammonia

Anhydrous ammonia is a nitrogen-rich crop fertilizer. It is a liquid when stored and becomes a gas when applied to the soil. Contact with anhydrous ammonia causes rapid dehydration resulting in severe burns of the skin and mucous membranes. Proper storage, application, and personal protective equipment use is essential when using anhydrous ammonia (3).

The Occupational Safety and Health Administration's anhydrous ammonia regulation, 29 CFR 1910.111, applies to the design, construction, location, installation, and operation of anhydrous ammonia systems including refrigerated ammonia storage systems. However, it is recommended that anyone handling anhydrous ammonia wear a face shield or goggles, rubber gloves, and a heavy-duty long-sleeved shirt as minimum protection. A full-face piece respirator with NIOSH-approved ammonia canisters is available at all fixed anhydrous ammonia storage locations and in transport vehicles (10).

Field Sanitation

The Field Sanitation regulation, 29 CFR 1928.110, was adopted to reduce the communicable disease risk among agricultural field workers. The regulation requires employers of field workers to provide potable drinking water, toilets, and hand-washing facilities to hand laborers in the field. The regulation does not cover livestock operations and hand labor operations in permanent structures (e.g., packaging and storage facilities). Employers must also inform each employee of relevant health hazards (e.g., gastrointestinal illness) and good hygiene practices that can reduce these hazards. Occupational health professionals can be instrumental in providing hygiene education resources and supporting agricultural employers in providing appropriate field sanitation programs.

Worker Protection Standard

The United States Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) gives the EPA the authority to regulate pesticides. In 1995 the EPA adopted the Pesticide Worker Protection Standard (WPS), 40 CFR 170. The WPS seeks to reduce pesticide exposure through four primary interventions: use of personal protection equipment, posted pesticide safety information, decontamination, and restricted entry intervals. The Food Quality Protection Act (FQPA) of 1996 mandated a massive re-registration of pesticides to occur over a period of years. Since the WPS requires that all pesticide label instructions be followed, the FQPA may result in increased protections afforded to agriculture pesticide handlers. The EPA is the lead enforcement agency for the WPS but has delegated much of this responsibility to the states. In most states the state Department of Agriculture administers the WPS (3).

When pesticides are used that require respiratory protection, a respiratory protection program must be in place in accordance with OSHA general respiratory protection regulation, 29 CFR 1910.134. All respirator users must undergo an initial medical evaluation regarding their fitness to use a respirator under their specific working conditions. This medical evaluation is repeated at the recommendation of the evaluating health care provider, whenever

work conditions change, or whenever a change in the employee's physical status may affect respirator use. Annual respirator fit testing and training is also required.

References

1. International Labor Organization. Safety and Health in Agriculture, Report from the 88th Session. Geneva: International Labour Conference, 2000.
2. World Health Organization. Wage Workers in Agriculture; Conditions of Employment and Work. Geneva: ILO Publications, 1996.
3. Langley RL, McLymore RL, Meggs WJ, Roberson GT. Safety and Health in Agriculture, Forestry, and Fisheries. Rockville, IL: Government Institutes, 1997.
4. National Institute of Occupational Safety and Health. Safety and Health in Agriculture. Document 705030. Washington, DC: NIOSH, 1997.
5. Sprince NL, Zwerling C, Lynch CF, et al. Risk factors for agricultural industry: a case-control analysis of Iowa farmers in the Agricultural Health Study. J Agric Saf Health 2003;9(1);5–18.
6. LaDou J. Occupational medicine in industrializing countries. In: LaDou J, et al. State of the Art Reviews, Occupational Medicine in Industrializing Countries. Philadelphia: Hanley & Belfus, 2002.
7. International Labour Organization Occupational Health Problems in Agriculture. Report of the Fourth Session at the ILO/WHO Committee on Occupational Health. Geneva: WHO, 1963.
8. United Sates Department of Labor. Occupational Safety and Health Act of 1970. Public Law 91–596.
9. Murphy DJ. Safety and Health for Production Agriculture. St. Joseph, MO: American Society of Agricultural Engineers, 1992.
10. Schutske JM. Using Anhydrous Ammonia Safely on the Farm. University of Minnesota, Minnesota Extension Service, document FO-2326-C, 2002.

5

Education and Training as Intervention Strategies

William E. Field and Roger L. Tormoehlen

Key words: injury prevention, hazards, safety, training

There is a frequently told story in Indiana of a farmer who, during corn harvest, had his arm amputated when it became entangled in the plugged husking bed of an older model corn picker. Rather than shutting off the power to the picker, he left the tractor seat with the power takeoff engaged and attempted to unplug the operating husking bed using his gloved hand. His glove became caught between the husking rolls, pulling the farmer's hand and arm into the machine up to his elbow. It was several hours before he was discovered, and he had to be cut out of the machine by local emergency rescue personnel. His injuries required a lengthy hospitalization and rehabilitation as he learned to use his newly fitted Dorrance upper limb prosthesis. A year later, however, the farmer headed back to the field with his already well-used "farmer's hook" and the same tractor and corn picker. He proceeded to lose the other hand while again unplugging the husking bed without first shutting off power to the machine.

When this story is repeated to a farm audience, the response is almost always laughter with a few expressions of disbelief. It's hard for most people to imagine that anyone could go through an entanglement in a corn picker, amputation of his arm, and months of physical rehabilitation and not learn from his mistakes.

This type of incident, documented for many types of hazards in agriculture, is sometimes used by safety and health professionals to discredit the role of education as an effective prevention strategy in reducing the frequency and severity of agricultural injuries and disease. Using anecdotal, insufficient, or poorly interpreted data, safety and health professionals undermined the traditional "milking stool" model of safety introduced by Harvey in the early part of the 20th century (Figure 5.1) (1).

As the field of agricultural safety has moved from a cadre of professionals with primarily educational and engineering training to a predominance of individuals trained in epidemiology, medicine, public health, and other basic sciences, the supporting role of education has been replaced by "research-

FIGURE 5.1. Milking-stool approach to safety and health involving the "three E's." (Copyright W.E. Field and R.L. Tormoehlen, used with permission.)

based" initiatives to change public policy, regulations, and engineering standards. Some safety and health professionals have found Harvey's model philosophically bankrupt and largely irrelevant, motivating them to pursue more aggressively coercive approaches to behavior modification such as changing public opinion and regulations (1–6).

Has some new body of knowledge determined that education and training are no longer profitable tools for injury and disease prevention, or have other influences or special interests caused the role of education to be diminished in the field of agricultural safety and health? What has changed since Whitney (7) published his 1926 article, "The Fundamental Significance of Safety Education" or since Stevenson (8) argued that "the most important single factor . . . in our accident prevention movement is education"?

In the United States each year, approximately 750 farmers, ranchers, and agricultural workers, and their family members are killed and another 130,000 are injured as the result of attitudes or behaviors that they, in most cases, knew intellectually and experientially to be unsafe. In addition, others within this population, including children and newly hired workers, are injured by hazards of which they were ignorant. It is unlikely that there is a farmer or rancher in North America who doesn't know, for example, that handling anhydrous ammonia without adequate eye protection can lead to harmful consequences or that contacting an unguarded rotating shaft can cause injury. In fact, it can be convincingly argued that the majority of injuries on farms and ranches are caused by behaviors or actions that the victim knew at the moment had a higher probability of causing injury than what would be encountered through normal daily living (9,10). Recognizing that all hazards cannot be fully mitigated, those involved in prevention need to recognize the gap that exists between what is known about the causes of agricultural injuries and disease and how agricultural workers will act in any given circumstance. Neglecting the need to effectively transfer and reinforce safety and health information to those most vulnerable allows the problem to

continue. Regardless of the advancements made in agricultural production technology, safety engineering, and safety and health regulations, education and training remain essential ingredients in the prevention of agricultural injuries and diseases (9,10).

Roots of Agricultural Safety and Health Education

The beginnings of agricultural safety and health go back to earliest recorded history. The Code of Hammurabi (1750 B.C.) and the Mosaic laws included specific rules relating to the well-being of agricultural workers. The Mosaic laws included provisions for ensuring that owners of livestock with horns knew that they had a responsibility to protect others from being gored, that those who dug pits or wells would provide a cover for them to prevent unintentional injury, and that builders would incorporate railings to prevent falls. Moses then instructed the people to teach these rules diligently to their children and to discuss them repeatedly to ensure that their children understood them (11). The United States public and nonprofit agricultural safety and health programs that exist today generally trace their roots to organizations such as the Cooperative Extension Service, American Society of Agricultural Engineers, National Safety Council, Farm Equipment Institute, and farm organizations such as Farm Bureau. In 1942 the National Safety Council held the first National Home and Farm Conference that eventually led to the declaration of National Farm Safety Week in 1944, a nationwide effort to educate farmers on the importance of reducing the number of injuries to ensure an uninterrupted flow of food during World War II (2,12).

Over the last 50 years, the primary means of disseminating agricultural safety information has been through the farm media and programs conducted by university- and school-based education programs. These programs were designed and conducted to address a wide range of health and safety issues. During that time very few resources were invested in exploring the effectiveness of the educational strategies, but the practices and technology of agriculture were changing so rapidly that cause-and-effect relationships would have been difficult to substantiate.

With the introduction of research funds in 1990, the research emphasis for many of the new professionals in the field has been surveillance and evaluation of the effectiveness of the educational and engineering methodologies. The decline in the number of fatal and nonfatal injuries associated with agriculture has reached a point where it is unlikely that any single strategy will result in additional decreases. Consequently, more energy is being invested in measuring results on a longitudinal and finite level. It can be argued that the most effective strategy has been the reduction in the number of people engaged in agricultural production due to new agricultural practices and intensive use of mechanization. Modern agriculture in North America is safer than at any time in its history (12).

Barriers to Communication

Part of the problem of effectively applying educational principles to agricultural safety and health is the lack of a common language that professionals can use to communicate among themselves and with the population they are trying to reach. Unlike the engineering, legal, and medical professionals, who generally use highly consistent terminology to communicate, educators have yet to develop a comparable means of sharing information. Even the most fundamental terms such as *education, training, competencies, school, evaluation,* and *instructor* are interpreted to mean widely different things to different people. The terms *education* and *training* by themselves can generate a long list of nondefinitive responses such as information dissemination, persuasion, development, directed teaching, instruction, discipline, and so forth. At times even the words used to define the core components of the educator's language are unhelpful in developing a broad base of understanding.

Another aspect is the lack of consistent forms of measurement to assess program effectiveness or student performance. An engineer can measure the temperature of hydraulic oil or the angle of an incline and have his findings replicated by another engineer anywhere in the world, even if he or she speaks a different language. A physician can diagnose a disease or treat a symptom using a technique developed 50 years ago by another physician and the outcomes will be highly consistent. On the other hand, an educator can apply a standard educational strategy to a group of 20 different individuals and achieve 20 extremely varied results. Knowing that a student is able to pass a written examination on a certain area of safety does not guarantee that he or she will perform safely. It is this apparent lack of consistency and confusion over the professional language that has led other professionals to view the role of education as less rigorous or scientific and therefore less effective in contributing to a reduction in agricultural injuries.

Barriers to communication also exist that are associated with the technical terms used in agricultural production. Terms such as *agricultural, farm, farm owner,* and *farm worker* are not uniformly defined and lead to considerable confusion when attempting to identify and communicate with the target population. Another example is the term *confined space* that applies appropriately to a grain storage bin used in an industrial setting but, due to U.S. federal regulations, does not apply to the same structure with the same contents located on a farm.

Geographic and enterprise differences also increase the difficulty in developing uniform agricultural safety and health educational materials. Agricultural producers in Wyoming do not want to be referred to as farmers but prefer the term *rancher*. Even certain production practices have developed terminology unique to geographic regions, countries, or continents.

The most rapidly growing barriers to communication between health and safety professionals and the agricultural community are literacy and language. The U.S. Department of Education's National Adult Literacy (NAL)

survey in 1993 found that nearly 50% of Americans over the age of 16 lacked the reading and writing skills to function effectively in the workplace. Of this functionally illiterate population, almost half were barely able to read or write at all, while the rest lacked literacy skills beyond the fifth-grade level. Forty-three percent of those with the lowest literacy skills lived in poverty, 17% received food stamps, and 70% had no job or only part-time employment such as seasonal and migrant farm work. Research to assess the pesticide safety knowledge of Hispanic migrant farm workers has found that such assessments are difficult because of the increasing number of migrant workers who speak indigenous languages and cannot understand either the English or Spanish training materials. It has been shown that even in high school-based agricultural education programs literacy skills reduce the effectiveness of computer-based education programs (13–15).

As there has been a decline in the number of seasonal and migrant agricultural workers, there has been a rapid growth in the number of Spanish-speaking workers employed in permanent positions in production agriculture. There is currently little agricultural safety and health information suitable for use with this population (12).

Role of Education in the Safety Hierarchy

In addition to the "three E's model" of achieving safety (engineering, education, and enforcement), various forms of the hierarchy of safety have been utilized by the agricultural safety and health profession. Each of these models typically includes an educational component, but most place it at the bottom of the structure or list of priorities. The steps in the hierarchy of one commonly used model are summarized as follows:

1. Remove or eliminate the hazard.
2. Guard the hazard from inadvertent contact.
3. Warn the user/operator of the potential hazard.
4. Protect the user/operator with personal protective equipment.
5. Train the user/operator to avoid contact with the hazard.

Examples of how this hierarchy of safe design applies to agricultural hazards are shown in Table 5.1. Other models of injury prevention include the application of human factors and ergonomics to the design process, a risk management approach, and the public health model. Little attention is given to education in the development of these models. There is no question that an educational component is there, but it is often buried in narrow professional language that most professional educators find uncomfortable. This includes terms such as behavioral management, acceptable risks, cost-benefit analysis, and humans being referred to as "hosts" (2).

TABLE 5.1. Applications of hierarchy of safe design to selected agricultural hazards.

Hazard	Solution based on utilizing each step in the hierarchy
Falls from upright silos	Convert feed storage to use of bunk silos or silage bagging to eliminate the need for climbing silos and the potential risk of falls from silos.
Entanglements in grain augers	Guard exposed auger flighting to meet American Society of Agricultural Engineers (ASAE) guarding standards to prevent physical contact with the rotating auger and still allow auger to function
Entanglement in power takeoff drive lines	Place "DANGER" safety messages on the drive-line shaft beneath shielding to warn operator of hazards when shield is removed
Tractor rollover injuries	Install rollover protective structure (ROPS) on tractor to provide a zone of protection for the operator in the event of overturn
Increased risk of youths being injured while operating agricultural equipment	Require youths to complete training

Source: From Murphy (2).

Efficacy of Education

There is little published work demonstrating the efficacy of agricultural safety and health education programs on reducing the frequency and severity of agricultural injuries and diseases. This lack of evidence is largely due to the lack of emphasis given to program evaluation by those organizations and agencies traditionally involved in agricultural safety and health. However, a number of studies have clearly demonstrated that educational programs, if implemented well, can enhance the safety and health of those engaged in agriculture (16,17).

Youths participating in a 4H club–sponsored tractor operator safety training program were observed to be better and safer operators than youths who had not participated but operated tractors regularly. Farmers were found to be more likely to reduce or eliminate hazards on their farms if they had been given a manual on safety and health best management practices compared to a control group that had not received the manual. High school agricultural education students were found to perform equally well using either a computer-based form of instruction or traditional instructor–based teaching methods in acquiring core competencies related to agricultural tractor and machinery operation. Farmers were found to be less likely to have been involved in a flowing grain–related incident if they had participated in training that addressed the dangers of flowing grain (18,19).

It appears that current funding criteria place greater emphasis on program evaluation, which should quickly close the current gap in definitive findings on the value of education in agricultural safety and health.

Barriers to Education

Implementing educational methodologies designed to enhance the safety and health of those engaged in agricultural production has proven to be a complex problem. The fundamental sources of complexity have little to do with the problem of knowing what hazards need to be addressed. For example, it has been known for several decades that nearly half of all agricultural tractor-related fatalities could be prevented if all tractors were equipped with rollover protective structures (ROPS) and seat belts and that as many as half of all child-related fatalities on farms could be eliminated if children were not transported as extra riders on tractors (see Chapter 6). However, transfer of this knowledge in a way that results in clear recognition of the hazards, changed attitudes about the particular hazards, and modification of risky behaviors has proven difficult. Some of the reasons for these barriers are discussed below (12).

Conflicting Traditions and Values

There has been historically more tolerance within the agricultural community for a greater incidence of farm-related fatalities, injuries, and disease than is commonly found in most other industries. This tolerance is deeply rooted in the character of agriculture and is not unique to more highly developed or mechanized countries. Farmers and ranchers around the world experience a greater loss than most of their urban counterparts and these losses have grown to be expected and accepted.

From a Western perspective, farmers tend to hold a more Calvinistic perspective on harmful events, which are often viewed as acts of God that are out of their personal control and are generally viewed as inevitable. If the audience being educated does not have the same worldview as the educator, including a common understanding that they have the collective ability to modify potentially harmful human experiences, the adoption of many prevention strategies will be unlikely (20).

Diversity of Hazards

Few occupations consist of a wider diversity of tasks, environmental conditions, and hazards than agriculture. No single educational approach can address all of the potential hazards that a worker will encounter. Consequently, current educational efforts tend to address the greatest hazards and apply the principles of cost-benefit to modify public opinion about safety procedures and policy.

Contributing to the diversity of hazards found in agriculture are rapidly changing agricultural practices and the introduction of new technology on farms and ranches. When corn pickers were introduced in the late 1940s, there was a rapid rise in the number of hand-related injuries due to exposure

to the unprotected husking bed. When combines were developed and became widely used in the 1960s, the incidences of corn picker–related hand injuries declined rapidly and became extremely rare. However, with the rapid increase in the exposure to shelled corn and on-farm storage introduced by the combine, there was a corresponding increase in entrapment and suffocations in wagons and bins used to transport and store the free-flowing grain.

Staying ahead of the rapid introduction of new practices and technology has been difficult for agricultural safety and health professionals, especially since resources have been so limited. Most of the responses have been more reactive than proactive, as in the cases of injuries caused by large round bales or exposure to anhydrous ammonia during its theft for making illegal methamphetamines. The widespread introduction of biologically modified organisms is another example of a practice and technology about which there remains uncertainty as to its potential for harm.

Diversity of the Work Force

Agricultural production is carried out by a wide range of individuals with substantially different physical characteristics, ages, educational background, and language skills. A review of farm-related fatality data will disclose cases involving tractor operators who are under the age of 10 and over the age of 90. Farmers, ranchers, and agricultural workers bring to their work everything from a minimal education in Mexico to a Ph.D. in soil science. There appears to be no research that has demonstrated a significant relationship between educational background and propensity to be involved in a fatal farm-related incident, and even less on the educational methodologies that are needed to reach such a diverse audience effectively (21).

An increasingly complex issue for agricultural safety and health educators is the growing proportion of the agricultural work force that speaks English as a second language and has limited reading comprehension skills. Traditional safety and health education methodologies are not appropriate for these audiences who will require a greater use of verbal and visually based instruction (12).

Scattered and Isolated Farm and Ranch Locations

There are approximately 10 to 12 million farms and ranches in the world, many of which are located in relatively isolated locations. Reaching these sites in a cost-effective manner has proven very difficult. Historically, the primary means of providing educational resources to the farm population has been through programs offered by government or university extension services. The United States and many other countries have an extension office that is supported by university and government specialists. Programs have included coordination of the tractor and machinery certification training for youths aged 14 to 16 seeking employment in agriculture, for pesticide applicator

training, and for technical assistance to farmers and ranchers impacted by disability. These networks of educators are being seriously eroded by budget cuts at all levels. One of the rationales provided was that the program lacked a sufficient research base (12).

Cheap Food Policy

One of the most complex and least understood influences on the safety and health of agricultural workplaces is the economic structure under which agriculture operates. Agricultural production and its associated policies are designed to give the perception to the consuming public that food is cheap when, in fact, food production, processing, and distribution are heavily subsidized through tax funds. In the United States, a loaf of bread may cost the consumer $2.00 at the supermarket, but it may actually cost another $.50 from the taxes that are directed to the farmer in the form of crop payments or other subsidies. In 2003 total farm income amounted to $59.2 billion, of which $15.9 billion or 26% came from government payments (22).

This subsidized approach to food production directly impacts agricultural safety and health and the education methodologies that can be used to effect change in agricultural workplaces. Farmers, in exchange for the subsidies they receive, give up most of their control over the price of the products they produce and therefore are prevented from passing along the cost of implementing safer agricultural production practices and technology directly to the consumer. When an automobile manufacturer incorporates an airbag into the design of a new car, the cost is added directly to the sticker price. If a farmer adds a ROPS to one of his tractors, he cannot transfer the cost of this safety device to the consumer because the price of his crop or livestock is perceived to be relatively fixed. The cost of the ROPS has to be taken from the anticipated profits, which may not be realized due to circumstances often beyond his control, such as the weather. Likewise, investment in training of agricultural workers has been viewed by many agricultural producers as an expense that cannot be passed on to the consumer. Therefore, investment in safety and health is generally viewed as optional and somewhat risky. If there is little clear evidence that such an investment will generate a return, there is little incentive to make it.

In addition, in return for “cheap” food, legislators have provided farmers with numerous exemptions from the regulations that apply to almost all other industries. In the United States, this includes the general exemption of farms with fewer than 11 employees from current workplace safety and health rules and from the provisions in the Federal Fair Labor Standards Act that allow children under 16 to be employed on farms if they are certified as having received training. Removing these exemptions would result in a substantial increase in the cost of production on most farms and ranches.

Conclusion

Education and training are essential components of a comprehensive effort to enhance the safety and health of agricultural workplaces. The transfer of knowledge using sound educational methodologies will not be replaced either by more intensive research efforts or by implementation of new safety and health regulations. As new knowledge on causative factors is acquired and new regulations are implemented, the demand for educational and training programs that are unique to agriculture and its work force will increase. There remains tremendous opportunity for educators to play a significant role in ensuring that workers in agriculture are equipped with the best knowledge and tools to perform their jobs in a safe and healthy manner.

References

1. National Safety Council. Julian Harvey dies, author of "Three E's." National Safety News 1960;81(4):1.
2. Murphy DJ. Safety and Health for Production Agriculture. St. Joseph, MO: American Society of Agricultural Engineers, 1992.
3. Aherin RR, Murphy DJ, Westby JD. Reducing Farm Injuries: Issues and Methods. St. Joseph, MO: American Society of Agricultural Engineers, 1992.
4. Donham KJ. Prologue—agricultural occupational and environmental health: policy strategies for the future. Am J Ind Med 1990;18:107–19.
5. Field WE. Editorial. J Agric Saf Health 2000;6(1):11–2.
6. Gunderson PD. Health promotion and disease prevention among farmers: revisiting the role of education. Editorial. J Agric Saf Health 1995;1(2):5–6.
7. Whitney AW. The fundamental significance of safety education. In: Whipple GM, ed. The Present Status of Safety Education. Bloomington, IL: Public School Publishing Company, 1926.
8. Stevenson I. Safety Education. New York: A.S. Barney, 1931.
9. National Safety Council. Injury Facts, 2003. Chicago: National Safety Council, 2003.
10. Injuries among farm workers in the United States. 1993. DHHS/NIOSH publication No. 97–115. Cincinnati, OH: National Institute for Occupational Safety and Health, 1997.
11. New American Standard Bible. Deuteronomy 6:12. Grand Rapids, MI: Zondervan Publishing House, 1995.
12. United States Department of Agriculture. National Land Grant Research and Extension Agenda for Agricultural Safety and Health. Washington, DC: Government Printing Office, 2003.
13. Rural Clearinghouse Digest on Rural Literacy. National Adult Literacy Survey. Manhattan, KS: Kansas State University, 1993.
14. Ortega RR, Tormoehlen RL, Field WE, Balschwied MA Machtmes KL. Determining critical subject matter content for a safety certification program for youth employed in production agriculture. J Agric Ed 2003;44(4):67–78.
15. McCauley LA, Shapiro SE, Scherer JA, Lasarew MR. Assessing pesticide safety knowledge among Hispanic migrant farm workers in Oregon. J Agric Saf Health 2004;10(3):177–86.

16. DeRoo LA, Rautiainen RH. A systematic review of farm safety interventions. Am J Prev Med 2000;18(45):51–62.
17. Shutske JM. An educator's perspective on childhood agricultural injury. J Agromed 1994;1(4):31–46.
18. Carrabba JJ, Field WE, Tormoehlen RL, Talbert BA. Effectiveness of the Indiana 4–H tractor program of instilling safe tractor operating behaviors and attitudes in youth. J Agric Saf Health 2000;6(3):179–89.
19. Legault ML, Murphy DJ. Evaluation of the agricultural safety and health best management practices manual. J Agric Saf Health 2000;6(2):141–53.
20. Jones PJ, Field WE. Farm safety issues in old order Anabaptist communities: unique aspects and innovation intervention strategies. J Agric Saf Health 2002;8(1):67–81.
21. Purschwitz MA. Farm and agricultural injury statistics. In: Murphy DJ, ed. Safety and Health in Production Agriculture. St. Joseph, MO: American Society of Agricultural Engineers, 1997.
22. Economic Research Service. Farm Income and Costs: Farm Income Forecasts. Washington, DC: United States Department of Agriculture, 2004

6

Personal Protective Equipment and Safety Engineering of Machinery

MARK A. PURSCHWITZ

Key words: protection, design, hazards, guards, interlocks

Personal Protective Equipment

Preventing injuries may involve providing personal equipment to individual workers to protect them against hazards. Decisions about personal protective equipment (PPE) should be made based on knowledge of the hazards for any particular task and the PPE available to protect against such hazards. Agricultural chemicals have both detailed labels and Material Safety Data Sheets (MSDS) that provide recommendations for appropriate PPE to protect workers from specific chemicals. Reputable suppliers are knowledgeable about the capabilities of various types and variations of PPE and should be consulted in the selection process (Table 6.1).

Eye Protection

Eye protection is critical for protecting an incredibly valuable yet vulnerable organ from traumatic injury. Flying particles, objects, or chemicals can instantly cause blindness. A variety of safety glasses, goggles, and face shields are available to protect against such hazards.

Safety glasses to protect against impact should meet the recognized American National Standards Institute (ANSI) standard for eye protection (ANSI Z87.1-2003). A variety of stylish safety glasses are available to meet the comfort and appearance desires of any user. Safety glasses generally offer wraparound protection or folding side shields. Prescription safety glasses are also available through opticians. Goggles also provide impact protection, including fitting over glasses. Face shields meeting the standard provide impact protection to the entire face (1).

Eye protection from chemicals involves protecting against direct splash, although in some situations protection against vapor is also needed. To protect against direct splash, chemical goggles or a face shield is needed. Chemical goggles differ from other goggles by having indirect venting—

TABLE 6.1. Personal protective equipment.

Eye protection	Safety glasses, goggles, chemical goggles
Hearing protection	Earplugs, earmuffs, noise-reduction rating (NRR)
Respirators	Particulate, chemical (half-mask, full-face), powered air-purifying, supplied-air
Coveralls and aprons	Disposable, liquid-resistant, liquid-proof
Gloves, shoes, boots	Chemical protective, other
Fall arrest systems	Body harness, lanyard, anchor point

instead of holes along the side, which could allow liquid to splash through, chemical goggles have vents that allow air movement but do not provide a direct path for splash. Anhydrous ammonia is a common agricultural chemical for which protection is needed against the vapor as well as splash, so non-vented rather than regular chemical goggles should be used. If a face shield is used to protect the face against anhydrous ammonia splashes, non-vented goggles must still be worn.

Hearing Protection

To protect the ears against noise, hearing protection PPE is available in two common forms: earplugs and earmuffs. Earplugs are commonly made from high-density foam that can be compressed for insertion into the ear, after which the foam expands to block the ear canal. Some earplugs are made from a very soft plastic. Earplugs are typically disposable, but reusable types are available.

Earmuffs fit over the ears to provide hearing protection. They are designed for that purpose and should not be confused with music headphones. Some earmuff-type hearing protectors are available with built-in radios.

Hearing protectors are rated with a noise reduction rating number (NRR), which is in decibels (dB). The NRR is determined by the manufacturer, using Environmental Protection Agency (EPA)-mandated laboratory procedures. A rating of NRR 28 means that under ideal conditions the equipment reduces noise levels by 28 dB. However, to reflect real-life experience, the United States Occupational Safety and Hazard Administration (OSHA) derates the NRR by half, and the National Institute of Occupational Safety and Health (NIOSH) recommends different correction factors based on the type of hearing protector (2).

Pulmonary Protection

Respirators are devices that fit on the face or head to provide protection against hazards from dusts, mists, fumes, and vapors. Respirators are designed for specific hazards. Testing any respirator to obtain a good fit of the mask to the individual user's face (fit testing) is important. The vendor or respirator manufacturer can provide instructions on how this should be done. Many companies have a trained individual to do fit testing using

special equipment or procedures, but for many agricultural operations it is up to each worker to follow the instructions and ensure the mask fits properly. Beards interfere with sealing and are generally not compatible with respirators.

Particulate Respirators

To prevent respiratory exposure to dusts, mists, and vapors, respirators are available in a variety of models. Particulate respirators, also known as dust and mist respirators, are intended for dusts from hay, silage, molds, soil particles, and the environment inside livestock buildings, which can consist of manure particles, feed particles, and animal dander. Mists are composed of relatively large suspended liquid particles and thus can be filtered by particulate respirators, as opposed to vapors that must be filtered by other means. Particulate respirators should never be used when hazardous vapors will be present.

A particulate respirator is not the same as the simple dust mask often found at hardware or discount stores. An approved particulate respirator has been tested and approved by the National Institute for Occupational Safety and Health (NIOSH) or the Mine Safety and Health Administration (MSHA) and has an approval number, starting with the letters "TC." It can filter out small toxic particles like mold spores and is very useful in agricultural applications. It typically has two straps appearing relatively thick compared to those on a dust mask and covering the nose, mouth, and chin (3).

Dust masks are for nuisance dusts like sawdust or pollen, are relatively thin, and typically have one strap. They have not been tested and do not carry a TC approval number. Dust masks costs much less than true particulate respirators, perhaps one tenth as much, but they are not recommended. An unapproved dust mask should never be called a "respirator."

Particulate respirators are rated for protection against oil-based chemicals and overall filtering efficiency. To follow these ratings, manufacturers' recommendations should always be followed regarding proper duration and conditions of use (Table 6.2).

Particulate respirators may have special features. Some have exhaust valves that make breathing easier and also enable a better seal to be maintained with the face. Without an exhaust valve, exhalation tends to push the respirator away from the face. Some contain a layer of activated carbon to

TABLE 6.2. Rating system for particulate respirators.

Overall efficiency at filtering particles	Rating letter	Rated as
95%	N	Not resistant to oils
99%	R	Resistant to oils (≤8 hours)
100%	P	Oil proof

remove nuisance odors, not to be mistaken for true chemical respirators. Still others are designed specifically to protect against welding fumes (a fume is an aerosol of small particles from condensation of molten metals, such as from welding).

Some chemical respirators can be fitted with particulate filters, either for particulates alone or in series with a vapor cartridge as a pre-filter ahead of the particulate cartridge. These particulate filters are approved respirators and as such carry NIOSH approval numbers.

Chemical Respirators

Chemical respirators filter out vapors that are the gaseous form of a liquid or solid, such as gasoline. They also carry TC approval numbers. These respirators typically have cartridges of activated carbon and are color-coded for easy identification. Standard cartridges are black for organic vapors (pesticides and paints), green (ammonia), yellow (acid gases), and white (chlorine). Although color coding of cartridges is standardized, the shape and fit of cartridges among different manufacturers are not requiring use of cartridges specific to a given brand of respirator (1).

The cartridge instructions, along with chemical labels or MSDS for specific chemicals, should always be consulted to determine the correct cartridge. As mentioned earlier, particulate pre-filters can be used ahead of the chemical cartridge to prevent particulates from clogging the cartridges.

Cartridges are used on several types of chemical respirators. These include the half-mask with a replaceable cartridge, the disposable half-mask with fixed cartridges, and the full-face respirator. The half-mask respirator covers the nose, mouth, and chin, and seals against the top of the nose, cheeks, and chin. It is held in place by a pair of straps. Most have replaceable cartridges, allowing replacement when a cartridge's filtering ability is depleted and also allowing use of different cartridges in different applications. Some have fixed cartridges and must be discarded when the filtering ability is depleted.

The full-face respirator has a large clear face shield and seals around the entire face, so it protects the eyes as well as the respiratory system. Beneath the face shield is an inner seal that seals around the nose, cheeks, and chin like a half-mask respirator. Full-face respirators have replaceable canisters. A full-face respirator with a very large canister for increased duration of protection is sometimes referred to as a "gas mask."

Some tractor cabs are specifically constructed to provide respiratory protection against chemicals during pesticide spraying. Operators in these cabs may not be required to wear respiratory PPE. Replacement filters are available for some "ordinary" tractor cabs. These filters contain activated charcoal to filter vapors, but they are not approved as replacements for PPE and do not offer the protection of cabs designed and constructed for that purpose (1).

Powered Air-Purifying and Supplied-Air Respirators

Powered air-purifying respirators (PAPRs) are a helmet or hood with a fan that pumps filtered air into it. The filter generally consists of one or two cartridges for protection against chemicals and/or particulates, typically connected to the helmet by a flexible hose. Approved particulate filters for PAPR units carry a high-efficiency particulate air (HEPA) rating. Because a PAPR only filters air, it must not be used where inadequate oxygen concentrations are present (1).

For protection against atmospheres that are immediately dangerous to life or health (IDLH) due to lack of oxygen or the presence of toxic chemicals that cannot be adequately filtered, a supplied-air respirator is required. These respirators provide breathing air from portable tanks carried by the wearer, or by an air hose extending to a fixed air supply. Respirators with tanks are known as self-contained breathing apparatus (SCBA) and are commonly used by firefighters. They require special training and maintenance, and should only be used by trained personnel. Underwater SCBA for divers, known as self-contained underwater breathing apparatus (SCUBA), is not the same and should not be used as a substitute.

Coveralls and Aprons

Coveralls are used as protective outer garments, particularly against chemicals. The chemical label or MSDS should be consulted to determine the proper type of coverall. Disposable coveralls are common and come in various grades depending on the level of protection needed. The most common material for disposable coveralls is Tyvek, a fabric made by DuPont. Ordinary Tyvek or its equivalent will normally protect against dry chemicals. Tyvek is not considered waterproof and therefore offers limited spray or splash protection. Coated or laminated Tyvek or its equivalent or polyvinyl chloride (PVC) is needed when more hazardous chemicals are used. Some circumstances require a complete protective suit, including a hood and gloves (1).

There is a difference between a coverall that is liquid resistant and one that is liquid-proof. Coveralls made from liquid-resistant materials can still allow liquids to enter through the seams. A liquid-proof coverall has sealed seams to prevent penetration (1).

Aprons are generally used when mixing chemicals to guard against direct splashes of concentrate against the torso. Aprons are commonly made of nitrile, PVC, or other resistant materials and are less likely to be considered a disposable item, although some disposable aprons are available.

Gloves, Shoes, and Boots

Protection of extremities, specifically hands and feet, may require special gloves, shoes, or boots, depending on the hazard.

For protection against chemicals, gloves are available in several types of materials. Nitrile is commonly used for protection against pesticides. The chemical label or MSDS should be consulted for the recommended type. To protect against absorption of chemicals into a soft inner lining, unlined gloves are generally used. One exception is gloves used for handling anhydrous ammonia, which is extremely cold upon vaporization at ambient temperatures. A soft inner lining is provided as insulation.

Gloves also protect against cuts or abrasions, protect against constant exposure to or immersion in water, provide increased gripping ability, or provide increased sanitation when handing food products. Many different types of gloves are available for virtually any application.

Protective shoes and boots include steel-toed shoes to protect against dropped objects and boots of various materials to protect against water and chemicals. For chemicals, the chemical label or MSDS should be consulted for recommendations. Disposable booties are available in a variety of materials for a variety of applications. Boots or booties should always be worn if there is risk of direct splash of chemical concentrate onto leather shoes, since the leather absorbs the chemical and cannot be cleaned.

Fall Arrest Systems

A "personal fall arrest system" is a type of PPE that works in conjunction with a fixed structure. It consists of a purpose-designed full-body harness tied off to a fall-limiting device, which in turn is connected to the structure. All connections use locking snap hooks or D-rings to prevent separation. The goal is to provide freedom of movement yet prevent or limit falls.

The fall-limiting device typically consists of an elastic shock-absorbing lanyard, or a retractable lanyard with a braking mechanism, to limit the fall and the shock to the worker's body. In all cases the lanyard must be designed for fall protection and must meet ANSI and/or OSHA standards for strength and function. Properly designed lanyards and anchorage points should support 5000 pounds of force per worker (1,4).

One type of fall protection for permanently installed vertical ladders involves connecting the body harness to a braking mechanism riding on a vertical cable installed alongside the ladder. The connection allows the person to travel up and down the ladder, but if the person falls the mechanism grabs the cable and instantly arrests the fall.

Safety Engineering of Machinery

Agricultural machines cut, pick, lift, load, move, carry, unload, strip, thresh, grind, mix, chop, spread, spray, discharge, and otherwise process many types of agricultural materials, including crops, soils, chemicals, and wastes. They also include tractors and other units that provide the power necessary to pull

and actuate the machines that actually process the materials. This processing requires machine components of two types:

1. Functional components that perform the desired function on the materials
2. Power transmission components that transmit the power from the engine or motor to the functional components

Operation of machines can result in acute or chronic injury if they are not designed with ergonomics and human factors in mind.

Machine Components Presenting Hazards

Types of functional components include:

1. Rotating, oscillating, swinging, or stationary knives
2. Rolls and rollers, including pairs that press tightly together
3. Plungers
4. Rotating bars or cylinders carrying rasps
5. Teeth or blades
6. Augers
7. Swinging hammers
8. Fans
9. Chains and conveyors
10. Large spikes
11. Pinch and crush points

Types of power transmission components that present hazards include:

1. Rotating shafts
2. Gears, chains, and sprockets
3. Belts and pulleys

If an engine is present, there are additional hazards of related chemicals (e.g., fuel, battery acid), and heat, which can lead to contact burns, fires, or heat exhaustion.

Hydraulics (high-pressure oil that flows from power unit to machine to perform tasks) is commonly found on agricultural machines. Components include:

1. Cylinders that extend under pressure to lift or move loads or other machine components
2. Motors that turn the energy of flowing oil into rotary motion
3. Hoses and tubing that carry the oil

Leaks, ruptures, or failures in the system can expose the operator to hot oil of 2500 psi or more, resulting in injection injury or burns, or resulting in cylinders retracting suddenly and dropping loads on unsuspecting people below.

Machines that are transported on public roads risk collisions with other vehicles. Any machine can be involved in a "runover," where the machine runs over a victim. These two hazards, plus the hazard of overturns with the operator beneath are particularly applicable to operators of tractors and self-propelled machines.

There are additional hazards specific to certain types of machines. For example, a gravity-unloading grain wagon, which has a slanted floor and can unload grain by gravity flow, has the hazard of entrapping a person who is standing on top of the grain when the unloading door is opened.

Safety Hierarchy and Machine Safety Design Protocol

The consensus safety hierarchy for prevention of agricultural injuries follows five steps, in priority order:

1. Eliminate the hazards, if possible. Observe American Society of Agricultural Engineers (ASAE) and OSHA safety standards.
2. Guard the hazard. Use shield, casing, enclosure, barrier, or interlock.
3. Warn about the hazard.
4. Train the user about the hazard.
5. Protect the user with personal protective equipment.

Often a combination of methods is used. Design engineers have control over the first three steps; therefore, these steps comprise a machine safety design protocol (5).

Eliminating the hazard means using a mechanism that does not include the hazard, if feasible. Guarding the hazard is done when the hazard cannot be eliminated; the hazard may be guarded by a purpose-designed shield or cover, or by location, for example, positioning the hazard in a place inaccessible to the operator. Warning about the hazard is done even for hazards that are guarded if there is any chance that the guard might be removed, but is the primary prevention method where the hazard cannot be guarded. A typical example of the latter is the crop intake of a harvesting machine, where an opening must be provided for the crop to enter the machine. Such an opening might also be used to reach into the machine.

Research has been conducted on presence-sensing devices, such as using infrared or sonic waves, that would shield hazards from personal contact by sensing when a person is present and responding by shutting off the machine. Challenges include prevention of false triggering for mobile machines, shutting off high-inertia machines rapidly, reliability in harsh environments over many years of service, cost, and risk of providing a false sense of security (inviting operators into dangerous areas they would normally avoid because they assume the device will protect them). Because of these challenges, such devices are not currently found on farm machines (6).

Agricultural machine designs evolve, and increasing attention has been paid to safety in recent years, as is true for automobiles. However, unlike

automobiles, agricultural machines last for decades, and thus hazards that have been eliminated or guarded in newer machines continue to cause injuries as operators use machines that may be decades old.

Safety Standards

Agricultural machines sold and used in the U.S. and Canadian markets are designed in accordance with ASAE standards, which are voluntary consensus documents. These standards do not carry the force of law, but they are followed by machinery manufacturers. Not following such standards is generally looked upon negatively in any product-related litigation. There are numerous ASAE standards relating to the safety of machines. While new standards and revisions of older standards have improved safety of machines designed and manufactured in accordance with such standards, older machines in use may not meet such standards, and there is no requirement to modify or retrofit older machines to newer standards (7).

Two OSHA agricultural standards apply specifically to mobile agricultural machines:

1. 1928.51, "Rollover Protective Structures (ROPS) for Tractors Used in Agricultural Operations"
2. 1928.57, "Guarding of Farm Field Equipment, Farmstead Equipment, and Cotton Gins"

In addition, two OSHA general industry standards also have application to agricultural machines:

1. 1910.145(d)(10), "Slow-Moving Vehicles"
2. 910.111(a)and(b), "Storage and Handling of Anhydrous Ammonia"

It is incumbent on the employer, not the manufacturer, to ensure that machines used by employees meet OSHA standards. Machines designed and manufactured to ASAE standards are generally considered to meet OSHA standards. At present, federal OSHA standards are enforceable only on farms with 11 or more employees, so most farms are exempt. States that have their own OSHA or equivalent can apply their regulations differently (8,9).

Other countries have their own standards, often in the form of government regulations, although they may be lacking in developing nations. Some countries strictly regulate farm machines themselves, either requiring government approval of new designs or establishing requirements for all machines, new or old, whereas the United States relies on a voluntary system. The International Standards Organization (ISO) develops voluntary standards involving representatives from many countries, including the United States, but typically national regulations (which may or may not be based on ISO standards) still take precedence. Harmonization of national regulations or standards, including ASAE standards, with international standards is an ongoing process.

Guards

A guard is "a protective device designed and fitted to reasonably minimize the possibility of inadvertent contact with machinery hazards, as well as to restrict access to other hazardous areas" (7). The same standard goes on to define four types of guards:

1. Shield or cover
2. Casing
3. Enclosure
4. Barrier

Guards are necessary to the prevention of traumatic injury and must always remain in place during machine operation. Removal of guards, either intentionally or forgetting to replace them following service or repairs, is a common factor in machine-related injuries (7).

Guards must allow routine maintenance, such as lubrication or cleaning, and still remain on the machine. Guards may also need to allow movement and flexibility of the guarded component if the component must move relative to other components. An example is the guarding system for the implement input driveline (IID), commonly known as the power takeoff (PTO) driveline. The driveline connects tractor to trailing machine and must move laterally, vertically, and telescopically. The guarding system made of three separate guards must maintain integrity while accommodating all movements. The guarding system must also allow a machine to be hooked up to a variety of different tractors.

Guards must maintain structural integrity while operating or being stored in harsh environments including weather, soil, manure, or physical abuse, over a period of decades. Guards must not be so difficult to remove and replace that operators find it simpler to leave them off after maintenance or repairs, yet not be so easily removed that they will fall off or be easily separated (intentionally or unintentionally) from the machines. Figure 6.1 shows a hinged shield on a new machine, in the raised position for access.

Openings that allow crops or other materials to enter may also be a path of entry for a hand, foot, or entire body. Increasing capacity of larger machines means larger and faster material intake. Guards that inhibit material intake are disliked and removed by owners. Augers, for example, are often guarded by cage-type guards that allow grain to pass through, yet prevent inadvertent contact with hands or feet. Yet some operators remove the guards because they feel the guard slows down grain flow. Also, such guards can be defeated by unsupervised small children where they are not designed to prevent small hands from reaching through, and would be restrictive if they did.

Replacement guards for older machines may be available from the manufacturer, but given the age of many machines and the fact that many smaller manufacturers have gone out of business, such guards may be difficult if not impossible to locate.

FIGURE 6.1. Hinged shield in raised (open) position for access.

Interlocks

Interlocks, devices that require the presence or positioning of a guard or control in order for a machine to function, are common in many industries but not in agriculture. While some interlocks have been used for years, such as clutch and transmission interlocks on tractors that require the clutch to be disengaged and the transmission to be in neutral prior to starting, interlocks have historically not been used with machine component guards. They have been considered vulnerable to the rugged use and environments found in agriculture, require maintenance, add complexity, and require the operator not bypass them by removal or electrically wiring around them. Unlike factories, where workers are supervised and cannot modify machines at will, farms often have machines operated by owners who wish to maximize production and minimize costs. Interlocks on guards could complicate troubleshooting, since it is sometimes necessary to operate the machine with the shield open to see the problem.

Some interlocks are now being used, such as seat interlocks that shut off the crop intake of certain machines if the operator leaves the seat for maintenance purposes. Other interlocks are specifically intended to facilitate maintenance and repairs, such as tethered controls on silo unloaders and cotton pickers, which enable an operator to control the machine while standing near functional components.

Warnings

Warnings are used when a hazard cannot be eliminated or guarded, meaning it is up to the operator to take proper actions to prevent injury. Warnings are also used when hazards are guarded, both to inform the operator and to provide a reason not to remove a guard or take actions that could result in injury. Additionally, warnings educate the operator about proper procedures and additional hazards that a machine operator could encounter during the course of operation; for example, an operator of a machine that can be raised to considerable heights would be warned to stay away from overhead power lines.

Warnings are found both on the machine itself, in the form of safety signs, and in the operator's manual, in the form of safety signs and additional text. Safety signs, sometimes called "warning labels," should follow ASAE standards that spells out the design, format, wording, colors, placement, and pictorials for such signs. Properly designed safety signs follow a strict protocol, using a standardized safety alert symbol, a standard "signal word" that "designates a degree or level of hazard seriousness," and a message text panel. They may optionally contain a pictorial panel to overcome language barriers, and example pictorials are provided in the standard to improve consistency across the industry (7).

Three signal words, which appear boldly at the top of a safety sign, have been standardized and are not used indiscriminately. The three words, standard colors, and definitions are as follows:

DANGER: Printed in white letters on a red background, this "indicates an imminently hazardous situation that, if not avoided, will result in death or serious injury. This signal word is to be limited to the most extreme situations, typically for machine components that, for functional purposes, cannot be guarded" (7).

WARNING: Printed in black letters on an orange background, this "indicates a potentially hazardous situation that, if not avoided, could result in death or serious injury, and includes hazards that are exposed when guards are removed. It may also be used to alert against unsafe practices" (7).

CAUTION: Printed in black letters on a yellow background, this "indicates a potentially hazardous situation that, if not avoided, may result in minor or moderate injury. It may also be used to alert against unsafe practices" (7).

Safety signs on machines may fade or be damaged over time. Older machines may lack safety signs or have signs that do not follow current standards. Older machines may have operator's manuals with less safety information than would be currently provided. Many operators of older machines purchased second-hand do not have the operator's manual. A secure location for the operator manual is now often provided right on the machine to minimize the chance of loss and promote keeping it with the machine at resale.

Replacement safety signs and operator's manuals may be available from the manufacturer, but given the age of many machines and the disappearance of

companies, such signs and manuals may be difficult if not impossible to locate. Due to the interest in restoring older tractors, there are independent suppliers of manuals and some safety signs for old tractors and other machines.

Tractors and Self-Propelled Machines

Operators of tractors and self-propelled machines face risk of overturns, runovers, and roadway collisions. Tractors and self-propelled machines also have operator stations that must be engineered with human factors in mind for safe and comfortable operation.

Overturns

To minimize or prevent injury during an overturn, either caused by operator practice or situations beyond control of the operator, ROPS have been developed. They are not ordinarily found on self-propelled machines other than tractors, since the risk of overturn is considered by the industry to be minimal.

The ROPS are crush-proof structures designed to create a zone of protection around the operator during an overturn; ASAE standard S383.1 FEB04, "Rollover Protective Structures (ROPS) for Wheeled Agricultural Tractors," is the current standard for ROPS design. The ROPS may be in the form of a two-post structure (two nearly vertical steel posts located behind the operator connected by a crossbar on top), a four-post structure, or a cab with a crush-proof frame. Some ROPS are designed to fold to allow entrance through low doors or use in low-clearance situations. Seat belts must be worn to prevent the operator from being thrown outside the zone of protection during an overturn. Figure 6.2 shows a two-post folding ROPS in the upright position (7).

Tractor manufacturers have provided ROPS as standard equipment on all tractors in the U.S. and Canadian market since 1985. Retrofits are available for many U.S. tractors going back to the mid-to-late 1960s, but availability for tractors older than that is more limited. Federal OSHA standard 1928.51 requires ROPS only on tractors that were manufactured after October 25, 1976, and operated by employees. Farmers historically have not voluntarily clamored to purchase retrofit ROPS. A guide to retrofit ROPS is available (8,10).

Other countries have varying requirements for ROPS. Contacts should be made with the minister of agriculture or equivalent in countries of interest to determine such requirements.

Runovers

Runovers can result from three primary causes:

1. Operators or extra riders falling from the operator platform during operation
2. Operators attempting to start the tractor from the ground while standing alongside it
3. Unseen bystanders being in the path of travel

FIGURE 6.2. Two-post folding rollover protective structure (ROPS) in upright position.

Seat belts help prevent operators from falling from the platform, but only tractors with ROPS have seat belts, and it is common knowledge that relatively few operators wear them. Cabs offer an additional safety factor but people (particularly extra riders) have been known to fall against doors or windows and fall out of the cab. Extra riders should not be allowed, but recognizing the desire of operators to bring along a second person for training purposes, manufacturers have provided training seats with seat belts in some newer tractor cabs. Backup alarms are not generally found on agricultural tractors and machines.

Roadway Collisions

Engineering to prevent roadway collisions involves providing lighting and marking to improve visibility of the machine by other motorists and identification as a slow-moving vehicle. Lighting and marking on tractors and self-propelled machines can consist of headlights, amber flashing lights (combination flashers and turn signals), and conspicuity tape (amber reflective strips) located on the front of the machine, and red taillights, amber flashing lights, and conspicuity tape (fluorescent orange strips for daytime visibility and red reflective strips) located on the rear of the machine. Trailing machines pulled behind a tractor can have much or all of the same lighting and marking, except for headlights. Newer tractors and machines have extremity lighting and marking with flashers and conspicuity tape located to mark the outer extremities of wide components.

In the United States and Canada, a slow-moving vehicle (SMV) emblem is located on the rear of vehicles normally traveling 25 mph or less on public roads. The emblem is a standard triangular sign, 350 mm high, consisting of a fluorescent orange triangle outlined with red reflective material. Other countries have different markings for road travel. As tractors are manufactured that exceed 25 mph, standards are being developed calling for additional markings to identify the additional speeds (7).

In the United States, state requirements for other lighting and markings are variable and often lag well behind the state of the art. Most states require the SMV emblem. During hours of darkness, some states require only two headlights and a single red taillight in addition to the SMV emblem. As ASAE standards have evolved, manufacturers have provided increased lighting and marking. In general, the older the machine, the less lighting and marking it will have. Retrofitting is possible but not widespread. Lighting and marking must be maintained, and it is not uncommon on older machines to see nonoperational lights or faded markings.

Compatibility of lighting systems between tractors and trailing machines of different ages is a problem. In the mid-1970s, tractor manufacturers began providing turn signals on their tractors along with a standard seven-pin connector in the rear to activate lighting on trailed machines. Some trailing machines, particularly those manufactured by tractor manufacturers, had optional lighting packages, but these were not widely purchased. Conversely, while these lighting packages became standard on trailing machines in the 1990s, many of these machines are pulled by older tractors that lack the requisite seven-pin connector. Retrofitting of tractors and trailed machines is possible but not widely done.

Human Factors

Manufacturers of tractors and self-propelled machines have devoted much time to ergonomics and human factors in the design of operator stations, including cabs, seats, and controls. Ingress and egress, seating, controls, noise, and general operator comfort are some of the factors covered. Seat design has evolved into seats with complex suspensions, some of which have computerized active vibration cancellation to counteract movement by the tractor and to maintain a steady ride for the operator. Controls are placed logically and within easy reach, and colors and activation motions have been standardized. Adjustments must meet a wide range of physically small and large operators. Improvements in noise reduction inside cabs have brought sound levels well below 80 dB, as compared with 100 dB that operators may be exposed to on old tractors and below OSHA's 90-dB, 8-hour permissible exposure limit. Climate control, including dust filtration and air conditioning, is common in newer tractors with cabs. Other features like drink holders and even coolers are being incorporated. To help fight fatigue and at the same time improve accuracy, steering systems that follow existing rows or use global positioning satellites (GPSs) are available that allow the operator to let

the machine follow the row without constant close attention. As with all other engineering improvements, the newer the machine, the more likely these improved features will be found.

Other Machines and Systems

Engineering design and the incorporation of safety features goes beyond field and farmstead machines. Engineering safety standards can be followed in the design or installation of such machines and systems as crop handling and processing equipment, livestock structures, livestock handling and related equipment, crop storage structures, waste (manure) storage structures, irrigation systems, ventilation systems, fencing, chemical containment, and others. Since in the United States such standards are voluntary, following such standards is up to the designer, manufacturer, construction contractor, or owner/operator of such systems (7).

Ergonomics

For many years quick-hitch attachments have been available from tractor manufacturers to enable hitching of three-point-hitch mounted equipment right from the tractor seat. After-market manufacturers have developed automatic hitching systems for drawbar-attached machines that make up the majority of machines pulled behind tractors. However, these systems still require manual hookup of the PTO driveline and hydraulic couplers and are not widely found on farms.

Engineering work is being conducted to investigate and improve ergonomic conditions in agricultural tasks requiring hand labor, although there is still a great deal of work to be done. Examples of work involving crops include intensive movement and handling of plants at nurseries; picking, carrying, and loading of tree fruits; hand cultivating of field crops; and harvest and handling of fresh-market berries and vegetables. Examples involving livestock include feeding of calves, handling of cattle, and improved lighting in dairy barns. In certain cases, specialized tools or practices have been developed to improve ergonomic conditions, although acceptance of these tools and practices will depend on such factors as cost, compatibility with existing systems, and effect on productivity (11–15).

References

1. Gempler's Division of Lab Safety Supply. 2004 Master Catalog. Madison, WI: Gempler's, 2004.
2. National Institute for Occupational Safety and Health. Criteria for a recommended standard: occupational noise exposure, revised criteria 1998. DHHS (NIOSH) publication No. 98–126. Cincinnati, OH: NIOSH, 1998.

3. National Institute for Occupational Safety and Health. NIOSH guide to selection and use of particulate respirators certified under 42 CFR 84. DHHS (NIOSH) publication No. 96–101. Cincinnati, OH: NIOSH, 1996.
4. Occupational Safety and Health Administration. Personal Fall Arrest System (Section I—Mandatory; Sections II and III—Nonmandatory) 1910.66 App C. Appendix C of OSHA Standard 29 CFR 1910.66, Powered Platforms for Building Maintenance. Washington, DC: OSHA, 2004.
5. Murphy D, Anderson K. Strategy: engineering for hazard and injury prevention and control. In: Murphy D. Safety and Health for Production Agriculture. St. Joseph, MO: American Society of Agricultural Engineers, 1992.
6. Shutske J, Gilbert W, Chaplin J. Evaluation of a microwave and infrared human-presence sensing system for agricultural equipment. J Agric Saf Health 2001;7:253–64.
7. American Society of Agricultural Engineers. ASAE Standards 2004, 51st ed. St. Joseph, MO: ASAE, 2004.
8. Occupational Safety and Health Administration. Occupational Safety and Health Standards for Agriculture. 29 CFR Part 1928. Washington, DC: OSHA, 2004.
9. Occupational Safety and Health Administration. Enforcement Exemptions and Limitations Under the Appropriations Act. Directive CPL 02-00-051–CPL 2-0.51j, May 28, 1998, as amended January 7, 2003. Washington, DC: OSHA, 2004.
10. National Farm Medicine Center, Marshfield, WI. A guide to agricultural tractor rollover protective structures. Marshfield, WI: NFMC, 2002. http://research.marshfieldclinic.org/nfmc/.
11. Estill C, Baron S, Steege A. Research and dissemination needs for ergonomics in agriculture. Public Health Rep 2002;117:440–5.
12. National Institute for Occupational Safety and Health. Simple solutions: ergonomics for farm workers. DHHS (NIOSH) publication No. 2001-111. Cincinnati, OH: NIOSH, 1996.
13. University of California, Davis. Agricultural Ergonomics Research Center. http://ag-ergo.ucdavis.edu/.
14. University of California, Davis. Western Center for Agricultural Health and Safety. http://agcenter.ucdavis.edu/.
15. University of Wisconsin, Madison. Healthy farmers, healthy profits project. http://bse.wisc.edu/HFHP/.

7

Disability in Agriculture

William E. Field and Paul Jones

Key words: prosthesis, return-to-work, rehabilitation, alternative employment, assistive technology

There are few occupations in which the evidence of disabling injuries is more apparent than agriculture. A casual assessment of any group of farm or ranch workers will often detect missing digits and limbs, impaired mobility, or a wide range of scars from accidents with both animals and machines. In fact, the common name used for many years for the Dorrance hook, an upper limb prosthetic device, was the farmer's hook. Over a 25-year period in Indiana beginning in the late 1940s, more than 100 farmers per year lost one or more upper extremities due to entanglements in corn pickers. The widespread prevalence of disability within the agricultural community has historically provided support for an unfounded assumption that since many in this population of workers with disabilities continued to be productive, they generally had few if any special needs. Consequently, many of the benefits associated with recent advance in rehabilitation practices and assistive technology have been slow in being realized by many of these people.

Over the past two decades, momentum has grown for ensuring that the rehabilitation needs of rural people, including farmers, ranchers, and agricultural workers with serious disabilities, are being met at a comparable level of enthusiasm, efficiency, expertise, and resources as is found in most urban settings. The disparities, however, are still substantial, and there is still much to be done to assist rural and agricultural communities in becoming more inclusive and accommodating of those with disabilities.

Prevalence of Disability Within Agriculture

Even though considerable attention has been given to the size of the disability community in the United States, few data sources definitively capture either the prevalence or nature of disability, especially within rural areas. There is also considerable ambiguity over the terminology used. One data

source, for example, defines a disability as being off work for at least 1 day, while other sources use vague terms such as "total" and "partial" to categorize disability types. Terms such as "rural," "farm," and "agricultural worker" are also not uniformly defined. Consequently, estimating the prevalence of disability within the agricultural work force becomes more of an art form than a science.

Approximately 2.13 million farms and ranches in the United States are responsible for the production of most of the food and fiber consumed and utilized in the United States. These farms and ranches are primarily operated by families that consist of 3.12 million operators and 3.49 million operator household members, many of whom provide both paid and unpaid labor to the operation. In addition, approximately 1.2 million hired agricultural workers are employed in agricultural production on a full-time or seasonal basis. This relatively small proportion of the population has a significant responsibility given the dependency of the entire population on the agricultural products they produce (1,2).

Farm-related injury data have shown that those engaged in agriculture-related activities are especially susceptible to disabling injuries. The National Safety Council has historically classified agriculture as one of the three most hazardous occupations. If injuries involving children in the agricultural workplace were included, agriculture's injury rate would be even higher. Approximately 5% of nonfatal farm injuries that occur each year are severe enough to prevent the farmer from continuing to farm due to a serious permanent disability. Approximately 1300 individuals sustained such injuries in 2003. A greater, though undocumented, number of farmers and ranchers continue to farm following a serious injury in spite of their inability to perform essential work-related tasks due to a permanent disabling condition. Approximately 2% of the full-time farm operators and workers who participated in the National Safety Council's multistate agricultural injury survey had suffered permanent disabling injuries while performing farm-related work (3–5).

According to the United States Bureau of Labor Statistics, as reported by the National Safety Council, for agriculture, fishing, and forestry (not including logging), approximately 130,000 disabling injuries occurred per year in 2000 and 2001. Although frequently used to represent the number of disabling farm-related injuries each year, the definition for disabling injury in these reports included any workers requiring medical treatment or having lost work for more than half a day. The National Institute for Occupational Safety and Health (NIOSH) estimated that the rate of disabling injuries for agricultural workers to be 500 per day and stated that approximately 5% of these injuries result in permanent disability (2,5,6).

For example, farm-related amputations accounted for 2.6% of all reported workplace amputations in 1999 and 11% of all serious farm-related injuries. For the period 1992 to 1999, 344 farm-related amputations were reported per year, which included only those documented by the state departments of labor and reported to the Bureau of Labor Statistics (7,8).

Farmers and agricultural workers are also disabled as the result of non–farm-related or non–work-related injuries. Of the severely disabled farmers and ranchers who contacted the Breaking New Ground Resource Center at Purdue University over the period 1990 to 2000, motor vehicle and recreational-related injuries each accounted for more disabilities than farm-related mishaps.

In addition to disabilities caused by injuries, farmers, ranchers, and other agricultural workers are also affected by health-related disabilities or a combination of disabilities that restrict their ability to perform their jobs and participate fully in daily living activities. A study of Indiana farm operators completed at Purdue University in 1981 revealed that 66% were affected by at least one physical impairment. Over 30% cited musculoskeletal impairments; 25% indicated hearing impairments; 24% cited cardiovascular impairments; and 22% reported respiratory impairments. Over 17% responded that there were work-related tasks on their farms that they were no longer able to perform due to their disabilities, and over 19% said that they were hindered or limited in their ability to perform necessary tasks. Nineteen percent also stated that they required assistance from a neighbor, employee, or family member to perform necessary tasks in their farm operations (9).

A comparison of general and farm population data concerning the nature and scope of physical disabilities suggested that rural and farm populations have a greater proportion of persons with disabilities. Early studies by the National Center for Health Statistics reported that 16.4% of the farm population had experienced some limitation of activity due to chronic conditions, whereas only 10.5% of the total labor force encountered such problems. Back problems were more prevalent among the farm population: 17.7 people per 1000 had displaced intervertebral disks compared to 13.5 people per 1000 for the nonfarm population. The farm population was more severely plagued by arthritis with 130.7 cases per 1000 as compared with 109.2 cases per 1000 for nonfarm people. The Missouri Farmers and Arthritis Project confirmed the earlier findings when it found that one third of farmers surveyed reported that arthritis inhibits some of their activities, and one third said they had reduced their physical level of labor due to arthritis. The Arthritis Foundation–Indiana Chapter stated that farmers are at an increased risk for arthritis-related disability and that the impact can be quite profound in regard to reducing physical strength and ability to perform routine chores (10–12).

Kirkhorn and Schenker (13) noted that the reporting system for occupational illnesses is still inadequate, which makes it almost impossible to accurately track trends in chronic illnesses that are a consequence of agricultural occupational exposure. Despite lower rates of smoking, farmers have an increased prevalence of several acute or chronic respiratory diseases, and there is increasing evidence that endotoxins, which are found in organic dusts from both grain storage and confined animal feeding operations, are significant contributors to these conditions (see Chapter 19). The authors reported

that over 700,000 workers spent part of each day working in confined animal feeding operations. The impact of long-term disability due to respiratory diseases is largely undocumented within the agricultural work force, especially with respect to the ability of those affected to continue engaging in productive agricultural work (13).

Apart from injuries and occupation-related diseases, many farm and rural families are affected by congenital or birth defects at levels comparable to the general populations. Farmers and ranchers are diagnosed with such diseases as multiple sclerosis and retinitis pigmentosa, and thousands of rural children are also born each year with developmental disabilities such as cerebral palsy and Down syndrome.

Previous rough estimates of the total number of workers with disabilities participating in agricultural work in the United States range from an unpublished figure of 288,000 to 500,000 reported by the U.S. Department of Agriculture's AgrAbility Program. The U.S. Department of Agriculture (USDA) also reported that over 13 million Americans living in rural areas have chronic or permanent disabilities. These data are considered conservative considering the increased risk of injury for those employed in agriculture (14).

Using the most recent Census of Agriculture data (2002) and applying a conservative value of 20% of the farm and ranch population having a disability that restricts daily living, it is currently estimated that approximately 1.36 million individuals who own, operate, live on, or work on United States farms and ranches are impacted by disability (1,2,9).

Availability of Disability-Related Resources

Prior to the 1980s few published reports or resources were available to agricultural workers or rehabilitation professionals for solving disability-related problems within farm or ranch settings. The one well-documented exception was the Vermont Farm Family and Rural Rehabilitation Program that was established in 1967 as a cooperative effort between the Vermont Office of Vocational Rehabilitation and the University of Vermont extension service. Few forms of rehabilitation or assistive technology appropriate for farmers or ranchers had been documented, and little effort had been made to define the unique needs of individuals with severe disabilities who desired to remain involved in production agriculture in spite of their limitations. Over the past two decades, several initiatives were undertaken to address this void of knowledge and skills within the field of vocational rehabilitation (15). These initiatives included:

1. The establishment in 1979 of Purdue University's Breaking New Ground (BNG) Resource Center and Outreach Program and the subsequent preparation of various resource materials including four editions of

Agricultural Tools, Equipment, Machinery, and Buildings for Farmers and Ranchers with Physical Disabilities. This program was initially supported by Deere and Company and by the U.S. Department of Education's National Institute on Disability and Rehabilitation Research (16).
2. Technical material generated by the two international conferences in 1979 and 1982 on rural rehabilitation technologies hosted by the University of North Dakota, Grand Forks. These were the first events that were designed to focus attention on the unique assistive technology needs of rural residents with disabilities.
3. Service delivery experience gained by the FaRM Program in Iowa and the Breaking New Ground Outreach program in Indiana, both established in the mid-1980s. These programs used a community-based approach to the delivery of rehabilitation technology services to rural and farm families and became models for the establishment of the U.S. Department of Agriculture's AgrAbility Program (14).
4. The establishment in 1985 of the Rural Rehabilitation Research and Training Center at the University of Montana, Missoula by the National Institute for Disability and Rehabilitation Research. This center has provided researchers the opportunity to identify and respond to long-term research priorities on issues related to rural rehabilitation.
5. The establishment of Life Essentials of Lafayette, Indiana, in the late 1980s. Life Essentials was one of the first manufacturers to design, fabricate, and market assistive technology specifically for use by farmers and ranchers with disabilities. One example is a tractor-mounted lift designed to enable farmers with severe mobility impairments to gain access to the operator's seat.
6. Passage of the 1990 Farm Bill that established the USDA AgrAbility Program. This program began providing funds through land grant universities to support technical assistance training and information dissemination activities for farmers and ranchers through agreements between the Cooperative Extension Services in selected states and nonprofit disability organizations such as Easter Seal affiliates and centers for independent living. At present 24 funded projects serve farmers and ranchers with disabilities in 26 states.

Barriers and Opportunities in Returning to Work

The most significant barriers that many individuals with disabilities face when attempting to return to work in production agriculture are the attitudes of those in their family and on the rehabilitation team. The general perception held by many rehabilitation professionals that there has to be something easier, safer, and more profitable than farming or ranching has proven to be a significant hurdle for many farmers and ranchers involved in the vocational rehabilitation process. Family members may also discourage return to

farming or ranching due to fear of another injury or the uncertainty of success. On the other hand, a supportive family and rehabilitation team have been shown to be important indicators of a successful transition back to farming or ranching following a disabling injury or illness.

The economics associated with production agriculture has also proven to be a critical factor in determining whether a person can successfully return to the farm or ranch. If there is substantial long-term indebtedness, returning to agriculture may be very difficult, especially if there are substantial medical and rehabilitation expenses. A disproportionate number of farm and ranch families are uninsured or underinsured, which can be catastrophic to the business following a serious injury or disease, especially if the medical bills become personal liabilities (9).

The lack of alternative employment opportunities in most rural communities often leaves the farmer or rancher with few choices concerning potential career changes. Some have moved into related occupations following a disability that have allowed them to use their knowledge of agriculture to remain employed. In some cases such career shifts have resulted in substantially better income and health care benefits, which are especially important to a person with a disability. The potential for succeeding in agricultural production following the acquisition of a disability is extremely low if the individual was not actively engaged in some agricultural enterprise prior to the disability.

In most cases, however, the message from the farmer or rancher following a disabling injury or illness is clear: his or her goal is to return to the farm or ranch and be productive. In some cases, work-site modifications are needed, while in other cases individuals explore alternative agricultural enterprises that better suit their limitations.

Other barriers regularly identified during the rehabilitation process include:

1. Lack of local specialized health care and rehabilitation services
2. Limited educational opportunities that would provide alternative career training
3. Nonexistent public or accessible transportation that allows independent access to needed services
4. Lack of access to information on appropriate and affordable forms of assistive technology that could be used to accommodate disability within agricultural workplaces

Assistive Technology

Through the work over the past 25 years of the Breaking New Ground Resource Center, a large database of information on assistive technology appropriate for use in agricultural work sites has been developed. Portions of the database have been made available in printed form and distributed to

farmers, ranchers, and rehabilitation professionals throughout North America. The most recent release is available in CD format and includes extensive information on enhancing accessibility to agricultural work sites. Figures 7.1 and 7.2 provide examples of the type of technologies included in the database (16). Additional information on resources available on assistive technology can be found at the Breaking New Ground Web site (www.breakingnewground.org).

Secondary Injuries Associated with Disability

One of the most frequent concerns raised about the decision by a farmer or rancher to return to work in agriculture following a disabling injury or illness is the fear of additional or secondary injuries caused by physical limitations associated with the disability. Individuals with considerable experience in production agricultural prior to their disability are often encouraged by physicians or rehabilitation professions to consider other safer or healthier forms of employment. These fears, generally based on the perceptions of

FIGURE 7.1. Ventrac-powered mobility aid for users of wheelchairs wanting access to rough terrain. Courtesy of Venture Products Inc., Orrville, Ohio.

FIGURE 7.2. Modified hand tool for upper limb prosthetic user. Photo courtesy of Texas Assistive Devices, LLC, Brazoria, Texas.

individuals not experienced with modern agricultural practices, have proven to be significant and in most cases unnecessary barriers to individuals who desire to return to doing what they know best and enjoy most. In reality, there is little evidence to support excessive caution about returning to agriculture if appropriate safeguards are taken (17).

Clay et al. (18), in their study of secondary injuries among Native Americans, concluded that surprisingly little is known about the incidence or prevalence of secondary disability in any population. A review of the literature identified only a handful of references to secondary injuries or the effect that disability may have on the risk of farm- or ranch-related injuries.

Allen et al. (19), in their survey of farmers and ranchers with serious permanent disabilities, found that 81% reported that there were necessary work-related tasks on their farms and ranches that they could no longer perform or were seriously hindered from performing because of their disability. The authors noted that as many as 25% of the participants believed that they had experienced a secondary injury that they attributed to their disability. The most frequently reported injuries were related to exposure to livestock and falls. Of the reported injuries, 43% required medical attention. A high proportion of the Allen study involved farmers and ranchers with spinal cord injuries, a factor that was concluded to have contributed to the high incidence of secondary injury.

Gruver et al. (17), in a bulletin published by the Breaking New Ground Resource Center at Purdue University, identified the following hazards associated with farming with a disability:

1. Risks to caregivers, family members, and coworkers providing assistance to the person with the disability. This included children asked to assist with tasks that exceeded their maturity or physical strength.
2. Risks associated with farm equipment operation. Issues raised included the increased potential of injury due to vision and hearing impairments that may prevent an individual from recognizing the presence of hazards or responding to them appropriately.
3. Risks related to the handling of livestock, which can be extremely large and highly unpredictable. Workers with mobility impairments would have more difficulty responding quickly and avoiding contact with unruly animals.
4. Risks associated with fires in equipment and buildings. Several cases of fires on self-propelled equipment have been documented that resulted in injury to operators with impaired mobility.
5. Exposure to excessive vibration and motion that could lead to deterioration of existing disabling conditions. This phenomenon has been documented in cases where loss of feeling had occurred due to spinal cord injury.
6. Potential for falls when climbing with missing limbs or with impaired coordination and balance.
7. Respiratory hazards that are nearly impossible to eliminate due to environmental conditions and may result in more severe symptoms over time.
8. Added risk to some workers from temperature extremes that may not be tolerated well. This includes risks to those with spinal cord injuries who have lost some of their ability to regulate body temperature and to amputees who have highly sensitive stumps.
9. Hazards associated with the use of assistive technology that may not be designed or installed properly or may be unfamiliar to the user. Currently, there is no process in place to test the safety or efficacy of assistive technology used by farmers or ranchers (17).

The potential for farm-related injuries is present for both the able-bodied and workers with disabilities involved in agricultural production. There is evidence to suggest that some disabling conditions may increase the risk of injury if preventative steps are not taken. Anyone involved with assisting a farmer's or rancher's efforts to return to work needs to understand both the potential hazards that the worker may face and the influence of the disabling conditions on safety and health. This is not, however, justification for discouraging or prohibiting a person with a disability from pursuing a career in agriculture. The use of more mechanized agricultural practices and the incorporation of appropriate forms of assistive technology have enabled thousands of individuals with severe disabilities to return to productive and safe engagement in agriculture.

Conclusion

As society, especially in rural communities, becomes increasingly inclusive and access to technology becomes more affordable and reliable, the uniqueness of seeing a person with a severe disability working in agricultural production will likely disappear. Vigorous, labor intensive-tasks that a few years ago required two strong arms and legs and a strong back are being rapidly taken over by highly automated machines or replaced entirely by changing agricultural practices, such as the introduction of new herbicides to control weeds. Farmers with missing limbs are compensating with specialized devices that are finding their way into the toolboxes of able-bodied farmers because they make tasks easier to accomplish for everyone. Ranchers with spinal cord injuries are gaining access to and operating large self-propelled pieces of agricultural equipment with the same ease they have in accessing and operating their modified vans. The question is no longer, "Is it possible?" but rather, "How much does it cost and when will it be available?"

If the trend continues toward an increasingly older rural and farm population, the issues of disability within this work force will become even more significant. There will be a need for changes in public policy to ensure adequate funding along with innovative ways to ensure that the rehabilitation needs of this population are not neglected.

References

1. United States Department of Agriculture. 2001 Census of Agriculture. Washington, DC: U.S. Department of Agriculture, 2003. http://www.nass.usda.gov/census/.
2. Farm Labor Department. Washington, DC: National Agricultural Statistics Service, Agricultural Statistics Board, 2002. http://usda.mannlib.cornell.edu/reports/nassr/other/ptl-66/2002/fmla1102.txt.
3. National Safety Council. Injury Facts, 2003. Chicago, IL: National Safety Council, 2003.
4. Hoskin AF, Miller TA. Farm accident surveys: A 21-state summary with emphasis on animal-related injuries. J Saf Res 1979;11(1):23–36.
5. Purschwitz MA, Field WE. Scope and magnitude of injuries in the agricultural workplace. Am J Ind Med 1990;18:1797–192.
6. Injuries Among Farm Workers in the United States 1993. DHHS (NIOSH) publication No. 97–115. Cincinnati, OH: National Institute for Occupational Safety and Health, 1997.
7. Brown JD. Amputations: A Continuing Workplace Hazard. Washington, DC: Bureau of Labor Statistics, 2003.
8. Zhou C, Roseman JM. Agricultural injuries among a population-based sample of farm operators in Alabama. Am J of Ind Med 1994;25:285–402.
9. Tormoehlen RL, Field WE. Projecting economic losses associated with farm-related permanent disabilities. J Agric Saf Health 1995;1(1):27–36.
10. Prevalence of chronic skin and musculoskeletal conditions (Series 10, No. 124). Washington, DC: U.S. Department of Health, Education and Welfare, 1976.

11. Selected health characteristics by occupation (Series 10, No 133). Washington, DC: U.S. Department of Health, Education and Welfare, 1976.
12. United States National Arthritis Foundation. Arthritis and Agriculture: A Guide to Understanding and Living with Arthritis. Indianapolis, IN: National Arthritis Foundation, 2004.
13. Kirkhorn SR, Schenker MB. Current health effects of agricultural work: Respiratory disease, cancer, reproductive effects, musculoskeletal injuries and pesticide-related illnesses. J Agric Saf Health 2002;8(2):199–214.
14. Breaking New Ground Resource Center. Ten Year AgrAbility Report. West Lafayette, IN: Purdue University/US Department of Agriculture-CSREES, 2002.
15. Tomkpkins EH. Vermont rural and farm family rehabilitation project. Report No. RR-MP-73. Burlington, VT: University of Vermont Agricultural Experiment Station, 1973.
16. Breaking New Ground Resource Center. The Toolbox, Agricultural Tools, Equipment, Machinery and Buildings for Farmers and Ranchers with Physical Disabilities (CD version). West Lafayette, IN: Breaking New Ground Resource Center, Purdue University, 2003.
17. Gruver ML, Allen PR, Field WE, Schweitzer JJ. Potential health and safety risks of farming and ranching with a disability (Plowshares technical article #27). West Lafayette, IN: Breaking New Ground Resource Center, Purdue University, 1997.
18. Clay JA, Seekins T, Cowie C. Secondary Disabilities Among American Indians on Three Reservations in Montana. Missoula, MT: Research and Training Center Rural Rehabilitation Services, University of Montana, 1990.
19. Allen PB, Field WE, Frick MJ. Assessment of work-related injury risk for farmers and ranchers with physical disabilities. J Agric Saf Health 1995;1(2):71–81.

8

Physical Monitoring

James M. Daniels

Key words: pre-placement, drivers, respiratory monitoring, hearing

This chapter focuses on Occupational Safety and Health Administration (OSHA) regulations, physical examinations, hearing monitoring and protection, respiratory protection programs, and hazardous substance monitoring.

OSHA Regulations

The U.S. Occupational Safety and Health Act of 1970 requires private sector employees to prepare and maintain records of work-related injuries and illness. Employers with 11 or more employees in the following industries must keep records: agriculture, forestry, fishing, construction, manufacturing, transportation, public utilities, and wholesale trade. Employers with 11 or more workers also must maintain an OSHA 200 log and report all accidents resulting in work-related death or 5 days of hospitalization or longer. In addition, employers are advised to follow general standards that include the evaluation and monitoring of physical hazards in the workplace. This requirement includes providing hazardous material training, establishing a respiratory protection program, and providing a hearing protection program (1,2).

The legislation that created OSHA applies to all eligible workplaces. However, an agricultural worker may be employed by a large multinational conglomerate that employs a staff of full-time professionals to administer safety programs or by a small family-owned farm that is not bound by federal OSHA regulations. Twenty-five U.S. states and territories operate their own "OSHAs." Employers in the following states and territories should contact their local agencies for regulatory statutes: Alaska, Arizona, California, Connecticut (covers state and local government employees only), Hawaii, Indiana, Iowa, Kentucky, Maryland, Michigan, Minnesota, Nevada, New Mexico, New York (covers state and local government employees only), North Carolina, Oregon, Puerto Rico, South Carolina, Tennessee, Utah, Vermont, Virginia, Virgin Islands, Washington, and Wyoming. Individuals

who are self-employed or are not directly covered by these regulations should still evaluate their work site for physical hazards.

Around the world, various countries have their own work injury reporting and prevention programs. The strongest are in Europe and Japan. Lack of consistency in rules and regulations between countries are a problem in companies with operations in the new global economy.

Physical Examinations

Preplacement Physical Examinations

The basis of any physical hazards program is the preplacement evaluation. In the 1980s, the American Disability Act described the rationale for preplacement evaluations. They are meant to ascertain whether the worker has any medical condition that might put the worker or someone else at risk for injury in the workplace. To put it another way: Does the applicant meet the minimum physical requirements for the job? In generating reports, physicians must give to supervisors and managers only the work restrictions or accommodations to allow the prospective employee to complete his or her job safely.

Preplacement evaluations may be done by a physician, physician assistant, or nurse practitioner. Evaluations can vary in price from around $30 (for a review of a health questionnaire) to hundreds of dollars for an exhaustive examination with testing. Most small businesses do not offer preplacement evaluations, so the agricultural worker would be well served to discuss the occupational hazards in their workplace with their physician (1).

Drivers' Physical Examinations (DOT or DMV Physicals)

There are certain circumstances in which preplacement evaluations are mandated. The United States Department of Transportation (DOT) and various state Departments of Motor Vehicles (DMVs) designate that workers who operate a vehicle on a public highway are required to undergo a medical evaluation by a licensed health care professional if they drive any of the vehicle types listed in Table 8.1. Many other countries have similar requirements (3).

Respiratory Examinations and Monitoring

Although respiratory protections is specifically covered by OSHA, the United States Environmental Protection Agency (EPA) Worker Protection Standard 40 USC part 170 states that workers should wear respiratory protection in certain agricultural areas. Federal Regulation 39 CFR 1910.134 requires employers to designate a program administrator to implement a respiratory protection program. This requires workers to complete an OSHA respirator medical evaluation questionnaire and have this reviewed by a

TABLE 8.1. Criteria to decide if drivers must have physical examinations (must meet only one).

If the vehicle:

1. Has a gross vehicle weight rating or gross combination weight rating, gross vehicle weight, or gross combination weight, of 4537 kg (10,001 lb) or more, whichever is greater
2. Is designed or used to transport more than eight passengers (including the driver) for compensation
3. Is designed or used to transport more than 15 passengers (including the driver) and is not used to transport passengers for compensation
4. Is used in transporting material found by the Secretary of Transportation to be hazardous under 49 USC 5103 and transported in a quantity requiring placarding under regulations prescribed by the Secretary under 49 CFR, subtitle B, Chapter 1, subchapter C

Data from Hartenbaum (3).

qualified health care worker. Depending on the circumstances, the worker may be required to undergo a complete physical examination and, if indicated by circumstances, pulmonary function test, tuberculosis testing, and chest x-ray (4).

Hazardous Chemicals Worker Monitoring

Workers exposed to certain hazardous chemicals (a list can be found in the Federal Regulation CFR, part 1910, subpart z. 29 CFR 1910 or by contacting local or federal agencies as outlined above) must undergo preplacement screening, ongoing evaluations, and an exit evaluation when leaving employment by transfer, retirement, or termination. The examination must be completed by a licensed physician and includes a medical history and physical examination of the patient and may include other laboratory testing (Table 8.2).

If a formal medical surveillance program is implemented, some thought must be given to this process, as once a program is started, employees may question the circumstances if it is somehow discontinued or changed. Most primary care physicians are more than willing to assist in starting a medical

TABLE 8.2. Resources.

American Conference of Governmental Industrial Hygienists, 1330 Kemper Meadow Drive, Cincinnati, Ohio 45240; phone (513) 742-2020; Web site: www.acgih.org

NIOSH (National Institute for Occupational Safety and Health), Building 1, Room 3007, D-35; Center for Disease Control, Atlanta, Georgia 30333; phone (404) 639-3061; Web site: www.cdc.gov/niosh/homepage

Occupational Safety and Health Administration Department of Labor, 200 Constitution Avenue NW, Washington, DC 20210; phone (202) 523-8151; Web site: www.osha.gov

National Agriculture Safety Data Base, Web site: www.cdc.gov/nasd

American College of Occupational and Environmental Medicine, Web site: www.acoem.org

monitoring program. Local hospitals and health departments may have occupational nurses, audiologists, and industrial hygienists to assist with this process.

Hearing Conservation Programs

A complete hearing conservation program can be divided into four parts: (1) noise monitoring, (2) audiometric testing, (3) hearing protection devices, and (4) employee training.

Noise Monitoring

The program starts with workplace noise monitoring. To do this a sound dosimeter can be purchased fairly inexpensively. Local health departments, hospital occupational health programs, or industrial hygienists can also be consulted to complete workplace sound monitoring. Sound monitoring must be repeated whenever there is a change in the production process, and the employees must all be informed of the results.

Audiometric Testing

A baseline audiogram needs to be obtained on every worker exposed to an 85-dB time-weighted average or greater. Employees must be tested within 6 months of hire and then at least annually thereafter. Testing procedures must meet OSHA standards, and the test must include frequencies in the 500-, 1000-, 2000-, 3000-, 4000-, and 6000-Hz range. (The 8000-Hz range must be added in Kentucky and certain countries in Europe.) The standard requires audiometry analysis and follow up with the program manager (an audiologist or nurse), who must review the audiograms and determine if there is a need for further evaluation (5).

If there is an average change of 10 dB or more from baseline audiogram test at 2000, 3000, or 4000 Hz, it is considered a standard threshold shift. The law requires that the employee be counseled within 21 days of this determination. If the employee is currently wearing a hearing protector that does not offer adequate protection, then a different device should be used. The hearing protection device fit should be checked. Appropriate records of follow-up and testing should be retained, and it is the employer's responsibility to pay for the testing and equipment.

Hearing Protection Devices

Hearing protection devices must be made available to all employees exposed to 85-dB time-weighted average or greater. The employee must have the opportunity to select hearing protectors from a variety of suitable subtypes.

Suitable variety is usually considered to be one earplug type and one muff type. The employee must receive training on the care and the use of the hearing protectors (see Chapter 35).

Employee Training

Employees exposed to 85-dB time-weighted average must receive annual training on hearing conservation. The following topics must be covered during this training program: effects of noise on hearing; the purpose of hearing protectors; the advantages and disadvantages of various types of hearing protection; instruction on hearing protection selection, fitting, use, and care; and the purpose of audiometric testing (see Chapter 5) (6).

Hearing protection is only a small part of an overall conservation program. Loud noises in the workplace should be engineered out. Worker noise exposure can easily be decreased by a simple rotation of jobs. The use of mufflers on equipment and even moving farm equipment away from shops are simple but effective ways to accomplish this. Agricultural workers are exposed to noise not only at work, but also recreationally by hunting, trapshooting, or snowmobiling, or by the use of a chainsaw (see Chapter 35, Table 35.1) (1,2).

Respiratory Protection Program

The EPA worker protection standards (40 USC Part 170) cover the respiratory protection regulations in the agricultural industry. The program requires at minimum that workers complete an OSHA Respirator Medical Evaluation Questionnaire, which can be found at the OSHA Web site.

The United States National Institute of Occupational Safety and Health (NIOSH) recommends that an industrial hygienist should be consulted during any production process when respirators are considered. General engineering standards are the best way to take care of respiratory problems (4).

In general, whenever there is enough particulate matter in the air that the worker's view is obstructed, it is probably a good idea to consider the use of either an engineering practice to cut down on the amount of particulate matter or a respirator. Chapter 6 prescribes general parameters for the types of respirators required for certain environments. Since regulations create nine classes for particulate filters, the original NIOSH decision logic must be supplemented with an algorithm for selecting the correct particulate filter. The ultimate responsibility for determining the employee's ability to wear a respirator lies with the employer.

If a respirator is needed in the workplace, the employer is required to produce a written respiratory protection program. This program must be administered by a suitably trained program administrator or it may be outsourced. Small company compliance guidelines are available from OSHA by accessing their Web site. The employer must include the following:

1. Procedures for selecting respirators
2. Medical evaluation of workers required to use respirators
3. Fit-testing procedures for tight-fitting respirators
4. Respirator use procedures for both routine and foreseeable emergency activities
5. Respirator maintenance procedures and schedules (cleaning, disinfecting, storage, repair, and discarding)
6. Procedures for ensuring the adequacy of air quality, quantity, and flow for atmosphere-supplying respirators
7. Training for employees regarding the respiratory hazards in the workplace
8. Training for employees on the limitations of the assigned respirator and its proper fit, use, and maintenance
9. Procedures for evaluating the effectiveness of the company's respiratory protection program.

Employees must be trained in the use, maintenance, and care of the respirator. The cleaning procedure should only be done for reusable respirators. There are some respirators that are one-use, throwaways that should not be reused.

Hazardous Substance Monitoring

In agriculture many workers are exposed to hazardous substances on a daily basis. In addition to this, the best way to protect against any type of hazardous substances is with the proper protective gear. This could include gloves, coveralls, etc. It is important, however, that the equipment and clothing be cared for properly; otherwise they may cause cross-contamination affecting other workers or the worker's family. The proper laundering of work clothing can greatly reduce exposure of toxic chemicals.

The first step in worker protection is compliance with applicable local and national laws and regulations. The employers must obtain a Material Safety Data Sheet (MSDS) for any substance that is used in the workplace. It can be obtained from the manufacturers of the substance and should be available to workers for their review. The MSDSs give detailed information about the toxicity of the product and the proper precautions that must be taken while using the substances. If the substance lacks a specific OSHA standard exposure guideline, the one proposed by the American Conference of Governmental Industrial Hygienists should be met.

Implementing a Medical Surveillance Program

Once a decision has been made to develop a medical surveillance program, its components must be organized. A physician must be selected and employees must be informed of the program. The surveillance program must be

provided at no cost to the employee, including proper equipment. Some hazardous substances have specific OSHA standards. One example would be cotton dust, often used as a standard for other harmful dust exposures (CFR Part 191R, part Z). Medical surveillance physicals must be conducted by a licensed physician. The health care provider must be given the employee's job description, what type of personal protective equipment is to be used, chemical exposures on the job including exposure levels for each substance, the MSDS, and ergonomic exposures to the job. The examination, depending on the substance involved, may also include x-rays, pulmonary testing, blood tests, and even cardiac testing.

Conclusion

This chapter consolidates a compliance strategy for the main physical hazards of the workplace. One should not forget, however, that the main reason for implementing such programs should not be to avoid fines, but to safeguard workers, some of whom may be friends or family members.

References

1. Cordes DH, Rea DF. Occupational Medicine: State of the Art Reviews, volume 6, number 3. Philadelphia: Hanley & Belfus, 1991.
2. DiBenedetto DV, Harris JS, McCunney RJ. Occupational Health and Safety Manual. Beverly, MA: OEM Press, 1996.
3. Hartenbaum NP. The DOT Medical Examination: A Guide to Commercial Drivers' Medical Certification. Beverly Farms, MA: OEM Press, 2000.
4. McLellan RK, Schusler KM. Guide to the Medical Evaluation for Respirator Use. Beverly Farms, MA: OEM Press, 2000.
5. Royster JD, Royster LH. Hearing Conservation Programs: Practical Guidelines for Success. Chelsea, MI: Lewis Publishers, 1990.
6. Sataloff RT, Sataloff J. Occupational Hearing Loss. New York: Marcel Dekker, 1993.

9

Biological Monitoring

James B. Becker and James E. Lessenger

Key words: cholinesterase testing, organophosphates, carbamates, lead

Within agriculture there are two principal substances for which biological monitoring are effective: cholinesterase and lead. Biological testing is the monitoring of the body's physiology to detect early changes so that corrective action such as removal from exposure and safety training can be implemented. Respiratory monitoring is discussed in Chapter 19, and hearing monitoring is discussed in Chapter 35. Reproductive function monitoring such as sperm counts, are performed in certain chemical formulation processes, but not in agriculture.

Cholinesterase Testing

Thousands of tons of acetylcholinesterase-inhibiting carbamate and organophosphate pesticides are used throughout the world for agricultural applications as insecticides, acaricides, aphicides, larvicides, and nematocides. Several are used as herbicides (see Chapters 13 and 16).

The direct measurement of carbamate (CM) or organophosphate (OP) pesticide levels in the blood or urine is cumbersome, time consuming, and expensive. Each pesticide requires a separate assay, and the serum level of the chemical might not be directly related to the degree of enzyme poisoning. In some parts of the world, it may take weeks for laboratory results to be returned. Even in witnessed exposures, blood chemical levels may be too low for detection. In addition, self-reported symptoms are inconsistent, vague, and unreliable. Cholinesterase activity testing has the advantage of measuring the degree of physiological response of the neuromuscular junction in a quantifiable manner (1).

Physiology

Acetylcholinesterase (AChE) inhibitors act on the enzyme AChE, which deactivates acetylcholine at the neuromuscular junction. The system also

includes butyrylcholinesterase (BChE), which inactivates butyrylcholine in plasma. For purposes of this chapter, AChE and BChE are considered together and referred to as AChE (2).

Acetylcholine transmits electrochemical impulses across neuronal synapses and neuromuscular junctions and is hydrolyzed by the action of the enzyme acetylcholinesterase. The toxic effects of CM and OP agents result from their ability to inhibit the catalytic activity of AChE in the nervous system by forming covalent bonds to acetylcholine receptors and preventing hydrolysis of acetylcholine by the enzyme (2,3).

The complexes formed between these poisons and the enzymes are hydrolyzed slowly in the case of the carbamoylated enzymes (deactivated by carbamates) or not at all with some phosphorylated enzymes (deactivated by organophosphates), thereby prolonging the action of acetylcholine. Enzyme activity returns only after a period of days or weeks, when new AChE molecules are synthesized.

Acetylcholinesterase activity depression is dose dependent, and there are differences in rates of inactivation and recovery between the plasma and red blood cell (RBC) enzymes (2).

Genetic influences not related to gender, race, or age account for a 23% variation in AChE activity levels among humans. Two types of AChE receptors exist: nicotinic, which are excitatory, and muscarinic, which produce either an excitatory or inhibitory postsynaptic potential.

The 23% variation of AChE activity levels among humans mandates that a baseline be obtained before OP or CM exposure and ongoing AChE testing. AChE activity levels can also be affected by cocaine, pharmaceuticals, and illness (2–4).

Laboratory Methods

Six methods of determining AChE activity have been developed; of these the electrometric method, which measures a pH change, and the colorimetric method are most often used. Both methods are effective for serum and erythrocyte testing and are relatively simple, inexpensive, and reproducible. The methods are highly dependent on skill, and their reporting units are not standardized between kits, so that a testing program should select one kit and continue using it. A field testing kit has been tested and released on the market (3,5).

The Testing Process

When evaluating AChE tests clinically, three factors must be kept in mind:

1. Anticholinesterase agents *depress* AChE levels.
2. Baseline levels may vary 23% among individuals.
3. The testing results can be affected by extraneous health problems, medications, and illegal drugs.

It is common for consultants to encounter patients who have been diagnosed with pesticide poisoning and removed from duty for extended periods of time as a result of *elevated* AChE levels. It must be kept in mind that organophosphates and carbamates *depress* AChE activity levels, and the tests measure an enzyme activity and not the concentration of a chemical (5,6).

Any monitoring program that does not take into consideration the genetic variation in AChE levels is invalid. Because of the 23% variation, there is a wide range of "normal." If AChE levels are determined only after an alleged exposure, the possibility of low but normal AChE activity levels could lead to a false-positive finding.

Acetylcholinesterase activity levels are affected by illness, medications, and illegal drugs. Hepatorenal and neuromuscular diseases, wasting, and alcoholism can affect the levels by altering AChE metabolism. Medications, especially those affecting the neuromuscular junction such as physostigmine and Aricept, can alter the activity levels; cocaine can alter levels (5).

There are two modes in which AChE testing is utilized: preexposure testing and monitoring and exposure testing.

Preexposure Testing

Beginning in 1974, California has required the testing of pesticide applicators, mixer-loaders, flagmen, maintenance personnel, supervisors, and others who come in daily contact with class I or II OPs and CMs. The program includes criteria for testing, testing protocols, and actions to be taken given various levels of AChE activity depression. These are summarized in Table 9.1 (7–9).

TABLE 9.1. The California cholinesterase monitoring protocol baseline.

Indication: if an employee is handling class I or II organophosphate or carbamate pesticides more than 6 days in a 30-day period.

Testing: average of two tests not closer than 3 days and not further apart than 15 days from each other. If the tests are not within 15% of each other, a third test is performed and the two closest to each other are averaged.

Periodic testing

Timing: if spraying 6 days in a 30-day period

Three tests at 30-day intervals

Then testing at 60-day intervals

More often as determined by the medical supervisor if the values are inconsistent or low or if the employee has been involved in an exposure.

Action: plasma or RBC activity levels falls to 80% of baseline: report to employer advising an investigation into the work practices of the handler.

Plasma falls to 60% of baseline or RBC falls to 70% of baseline: remove employee from exposure.

Employee must remain away from exposure but may work at another job task not requiring exposure until both the serum and RBC cholinesterase activity levels return to 80% of baseline.

Source: Adapted from the California Environmental Protection Agency guidelines (7).

Participants in the program include:

1. Employers who select the employees who need to be tested and send them to the clinic
2. Employees who are tested and often miss their appointments
3. Physicians who interpret the tests and send the results and recommendations to the employer
4. County agricultural officials who monitor the employers for compliance
5. State researchers who monitor the program for effectiveness

Surveys have demonstrated that most monitoring is done incorrectly. Ames and Associates (7) have found four categories of problems with AChE monitoring:

1. Employers fail to refer employees for baseline measurements and monitoring.
2. Laboratories use the wrong methods or fail to conduct the tests appropriately.
3. Physicians fail to interpret test results properly and to make the appropriate recommendations.
4. There are insufficient numbers of county employees to monitor the employers effectively.
5. The state is unable to monitor physicians because training and certification is not required.

Proposed solutions include employer and physicians training, physician training, and the standardization of laboratory kits and procedures (7).

Exposure Testing

Acetylcholinesterase testing is beneficial only for carbamate and organophosphate poisoning, and these agents comprise the minority of compounds used as pesticides. He and Associates (10), writing in China, found the problem of incorrect diagnosis of carbamate and organophosphate poisoning based on low but normal AChE levels measured in cholinesterase testing. Several patients died as a result of injudicious use of atropine (a cholinergic antagonist) as treatment for poisoning with pyrethroids, which have no effect on AChE levels.

Currently two testing procedures are used to document carbamate or organophosphate exposure and recovery: testing for exposure with ongoing monitoring and testing without ongoing monitoring (5,11).

Ongoing Monitoring

A dip in AChE activity levels is expected in a person who is subject to ongoing monitoring and who has been exposed to carbamate or organophosphate pesticides. Because the patient may not be symptomatic, the decrease in AChE monitoring levels may be the only finding. A dip of greater than 20% is considered evidence of overexposure.

Without Monitoring

Workers might be exposed to a substantial amount of an organophosphate or carbamate and have immediate signs and symptoms of poisoning. Depression of AChE values can be variable and might not correspond to the severity of the clinical findings. The decision to treat should be based on clinical, not laboratory, considerations (5,11).

In Japan more than 600 persons were treated for sarin poisoning caused by terrorists. The decision to treat was based on clinical findings. Acetylcholinesterase testing was useful in follow-up of the exposed persons, and it took up to 3 months before levels stabilized at presumably normal levels (12).

In patients with documented carbamate or organophosphate poisoning and with depressed or normal AChE levels, overexposure can be reflected in a 20% *increase* after the exposure, representing recovery of the activity levels. Plasma levels can be expected to increase first, followed by the RBC levels (1).

Lead Testing

Though the consequences of lead exposure in the occupational setting and in pediatric preventive health have been extensively reported, the issue of agricultural exposure to lead has likely been underappreciated. Lead exposure on farms has been recognized for decades, but few scientific studies have focused on this health risk factor (see Chapter 23).

Occupational exposures have been attributed to work in smelters and with paint, storage batteries, pigments, solder, ammunition, and gasoline additives. Greater than 100 occupational activities and job titles have been associated with risk of lead exposure.

Agricultural activities can include many of the same lead exposure scenarios. Farm equipment maintenance may involve exposure because of lead-based paint on older equipment. Many farmers perform cutting, welding, soldering, and brazing without the benefit of personal protective equipment or even minimal environmental controls. In some farm settings, water systems are soldered with lead-based solder, which may leach into water supplies. Older buildings may contain lead-based paint. Melting of lead to produce weights, sinkers, and ammunition can pose a threat of lead exposure. Despite the potential risks, family farms and most agricultural activities are not subject to monitoring. Table 9.2 provides a summary of United States regulations and standards for lead.

Farm environments can expose certain at-risk populations, including pregnant women and children, to higher-than-acceptable lead concentrations. A report by the Institute of Medicine described a “glaring and significant gap

TABLE 9.2. Summary of standards and regulations for lead.

Agency	Media	Level	Comments
Centers for Disease Control and Prevention	Blood	10 µg/dL	Advisory; level of concern for children
Occupational Safety and Health Administration	Blood	40 µg/dL	Regulation; cause for written notification and medical exam
		50 µg/dL	Regulation; cause for medical removal from exposure
	Air (workplace)	50 µg/m^3	Regulation; permissible exposure limit (8-hr average) (general industry)
		30 µg/m^3	Regulation; action level
National Institute for Occupational Safety and Health	Air (workplace)	50 µg/m^3	Advisory; recommended exposure limit (nonenforceable)
		100 mg/m^3	Advisory; immediately dangerous to life and health
American Conference of Governmental Industrial Hygienists	Air (workplace)	150 µg/m^3	TLV/TWA guideline for lead arsenate
		50 µg lead/m^3	TLV/TWA guideline for other forms of lead
	Blood	30 µg/dL	Advisory; biological exposure index
U.S. Environmental Protection Agency	Air (ambient)	1.5 µg/m^3	Regulation; National Ambient Air Quality Standard; 3-month average
	Soil (residential)	400 mg/kg	Soil screening guidance
	Water (drinking)	15 µg/L	Action level for public supplies
		0 µg/L	Nonenforceable goal; maximum contaminant level goal
Food and Drug Administration	Food	Various	Action levels for various foods; example: lead-soldered food cans now banned
Consumer Product Safety Commission	Paint	600 ppm (0.06%)	Regulation; by dry weight

TLV/TWA, threshold limit value/time-weighted average; ppm: parts per million.
Source: Data from Center for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry (13).

in the scientific literature" for research on health hazards to the children of migrant workers (14,15).

The clinical risks associated with lead have been abundantly documented. Low-level exposures in pediatric populations have been associated with abnormalities of neural development, cognitive development, and behavior. Chronic low-level exposure in adults has recently been associated with all-cause mortality (16,17).

Physiology of Lead

Lead is absorbed through both the lungs and the gastrointestinal tract. When it enters the systemic circulation, it is bound to erythrocytes (99%). Three compartments comprise the lead body burden:

1. The blood and other rapidly exchanging tissues
2. The soft tissues
3. Bone, which stores 90% of the body burden and has a half-life of 20 years (18)

Lead is excreted primarily through the kidneys (75%) but can also be identified in bile, sweat, hair, and nails. Table 9.2 summarizes the lowest observable effects of inorganic lead in pediatric and adult populations (19).

Biological Monitoring

Biological monitoring of lead exposure is performed utilizing three types of tests:

1. Direct measurements of lead concentration in tissues (blood, hair, bone)
2. Urine test following the administration of a chelating agent
3. Screening for early biological effects of lead exposure as reflected in changes in hemoglobin, free erythrocyte protoporphyrin, zinc protoporphyrin, basophilic stippling, or measurement of porphyrins in the urine (18)

Lead Concentration Monitoring

Periodic measurement of the blood lead level forms the cornerstone of biological monitoring of lead-exposed workers. Measurements are quickly and reliably performed using atomic absorption techniques. Blood lead concentration is the best available indicator of current lead exposure.

It has been estimated that with an exposure level of 1 μg lead/m^3 in air, an increase of 1 to 2 μg lead/100 g whole blood will occur. Blood lead does not correlate well with body burden of lead. In experiments with increasing dietary lead in volunteers it has been shown that a plateau of the blood level is reached while body burden continues to increase (18,19).

Lead in urine reflects lead recently absorbed. Urine levels usually average 50 μg/g creatinine for a blood lead level of 40 μg/100 g whole blood.

Because lead excretion varies from one individual to another, and recognizing the low correlation between levels of lead in blood and urine, most authors agree that urine lead levels should not be used for the routine assessment of exposure.

Urine lead levels can be measured following administration of a single dose of chelating agent (usually 1 g of ethylenediaminetetraacetic acid, EDTA). This testing can be used to confirm past exposure in individuals who are not currently exposed to the metal. An excretion of lead exceeding 600 μg/24 h after EDTA administration in currently unexposed individuals suggests increased body burden (18,19).

Biological Effects Monitoring

Zinc protoporphyrin (ZPP) and free erythrocyte protoporphyrin are the most commonly performed assessments of lead-related biochemical effects. Determinations of these levels are recommended for screening purposes. Zinc protoporphyrin levels can be conveniently tested with a hematofluorometer, still found in use in some rural clinics. Most commercial laboratories perform both blood lead and ZPP on all samples submitted for screening.

Zinc protoporphyrin levels are typically less than 40 μg/100 mL whole blood. Biological exposure indices are indicated above 100 μg ZPP/100 mL blood. Elevated ZPP levels must be confirmed and correlated with lead levels, which are a more specific indictor of lead exposure (18–20).

Management of Lead Exposure in Agriculture

Under the U.S. Occupational Safety and Hazard Administration (OSHA) Lead Standard, medical surveillance is required if workplace lead levels exceed 30 $\mu g/m^3$ for more than 30 days per year. Many farm environments are exempt from OSHA oversight; however, the strategy for biological monitoring is still broadly applicable though it may not be mandatory (21).

For workers in environments exceeding the action level (30 $\mu g/m^3$ for 30 days per year) the OSHA standard recommendations are given in Table 9.3. The World Health Organization (WHO) in 1980 specified a time weighted

TABLE 9.3. Duty action levels in lead monitoring.

For workers in environments exceeding the action level (30 $\mu g/m^3$ for 30 days per year) the U.S. OSHA Standard recommends:

1. Blood lead levels:
   a. Every 6 months if the level is less than 40 μg/dL
   b. Every 2 months if the level is less than 40 μg/dL, until two consecutive levels are found to be <40 μg/dL
   c. Monthly in workers removed from exposure
2. Medical examinations:
   a. Yearly for any exposed worker if the blood lead level has exceeded 40 μg/dL
   b. Prior to assignment to a work area in which the action level has been exceeded
   c. If signs or symptoms of possible lead intoxication develop (see Chapter 17)
3. Removal from exposure of:
   a. Workers whose lead levels exceeds 60 μg/dL, unless the last lead level tested was under 40 μg/dL
   b. Workers whose last three lead levels exceeded 50 μg/dL
   c. Workers judged to be at increased risk of impairment of health from exposure to lead such as during pregnancy and lactation
4. Return to duty:
   a. A worker who has been removed from exposure because of elevated lead level may be returned to work if two consecutive lead levels measure <40 μg/dL

Source: Data from National Institute for Occupational Safety and Health (21), Occupational Safety and Health Administration (22).

action blood lead level (TWL) for removal from duty of 40 µg/dL in the general population and a level of 30 µg/dL in women of childbearing age. Baseline blood levels (nonanthropogenic or causing changes in the body) are 10 to 30 µg/dL based on the observation that normal life in an industrialized city will produce levels in that range. Above 30 µg/dL is considered toxic (21–24).

Where required, medical examinations include a detailed work history (with special attention to all toxic exposure potential), medical history, and a thorough medical examination, with special attention to the neurological system, kidneys, teeth, gums, blood, blood pressure, heart, gastrointestinal system, lungs, and fingernails (looking for Mees lines) (21–24).

Germany, Canada, Australia, and Switzerland have each developed lead standards for their general populations. In addition, many states within the United States and provinces within Canada have elected to implement their own guidelines (23,24).

References

1. Coye MJ, Lowe JA, Maddy KT. Biological monitoring of agricultural workers exposed to pesticides: I. Cholinesterase activity determinations. J Occup Med 1986;28:619–27.
2. Lessenger JE, Reese BJ. The pathophysiology of acetylcholinesterase inhibiting pesticides. J Agromed 2000;7:5–19.
3. Chu S. Depression of serum cholinesterase activity as an indicator for insecticide exposure—consideration of the analytical and biological variations. Clin Biochem 1985;18:323–26.
4. Mason HJ, Lewis PJ. Intra-individual variation in plasma and erythrocyte cholinesterase activities and the monitoring of uptake of organophosphate pesticides. Occup Med 1989;29:121–4.
5. Lessenger JE, Reese BJ. Rational use of cholinesterase activity testing in pesticide poisoning. J Am Board Fam Pract 1999;12:307–14.
6. Fillmore CM, Lessenger JE. A cholinesterase testing program for pesticide applicators. J Occup Med 1993;35:61–70.
7. Ames, RG, Brown SK, Mengle DC, Kahn E, Stratton JW, Jackson RJ. Cholinesterase activity depression among California agricultural pesticide applicators. Am J Ind Med 1989;15:143–50.
8. Ames, RG, Brown SK, Mengle DC, Kahn E, Stratton JW, Jackson RJ. Protecting agricultural applicators from over-exposure to cholinesterase-inhibiting pesticides: perspectives from the California programme. J Soc Occup Med 1989;39:85–92.
9. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Guidelines for physicians who supervise workers exposed to cholinesterase-inhibiting pesticides, 3rd ed. Sacramento, Pesticide and Environmental Toxicology Section, 1995.
10. He F, Wang S, Liu L, Chen S, Zhang Z, Sun J. Clinical manifestations and diagnosis of acute pyrethroid poisoning. Arch Toxicol 1989;63:54–8.

11. Gage JC. The significance of blood cholinesterase activity measurements. Residue Rev 1967;18:159–73.
12. Morita H, Yanagishawa N, Makajima T, Shimizu M. Sarin poisoning in Matsumoto, Japan. Lancet 1995;346:290–3.
13. Center for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry. Case Studies in Environmental Medicine; Case Study 19—Lead Toxicity, Course SS3059. Atlanta, GA: Center for Disease Control and Prevention, 2000.
14. Perrin JM, Merkens MJ. Blood lead levels in a rural population: relative elevations among migrant farmworker children. Pediatrics 1979;64:540–2.
15. Hernandez D, Charney E ed. From Generation to Generation: The Health and Well-Being of Children in Immigrant Families. Washington, DC: National Academy Press, 1998.
16. Lustberg M, Silbergeld E. Blood lead levels and mortality. Arch Intern Med 2002;162(21):2443–9.
17. Lanphear B. Cognitive deficits associated with blood lead concentrations <10 mg/dL in US children and adolescents. Public Health Rep 2000;521–9.
18. Rabinowitz M, Wang J, Soong W. Kinetic analysis of lead metabolism in healthy humans. J Clin Invest 1976;58:260.
19. Kehoe R. The metabolism of lead in man in health and disease. Lecture II. J R Inst Public Health Hyg 1961;24:120.
20. Center for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry. Toxicological profile for lead. ATSDR publication TP-88/17. Atlanta, GA: Center for Disease Control and Prevention, 1997.
21. National Institute for Occupational Safety and Health. Protecting Workers Exposed to Lead-based Paint Hazards: A Report to Congress. Publication No. 98–112. Washington, DC: DHHS (NIOSH), 1997.
22. Occupational Safety and Health Administration. Medical Surveillance Guidelines, 1926.62. Washington, DC: U.S. Department of Labor, 1997.
23. World Health Organization, Regional Office for Europe. Air Quality Guidelines, 2nd ed. Copenhagen: World Health Organization, 2001.
24. World Health Organization, Regional Office for the Eastern Mediterranean. Occupational Health: A Manual for Primary Health Care Workers. Cairo: World Health Organization, 2001.

10

Drug Programs and Testing

James E. Lessenger

Key words: intoxication, withdrawal, addiction, drug testing, substance abuse

In the United States and many Western countries, drug testing and drug programs have become necessary to control drug use in agriculture and decrease accompanying injuries and illnesses. As drug use spreads and more countries add mechanization to agriculture, more drug programs will be necessary.

Drug abuse has become an endemic in all phases of agriculture as in other industries. Research by the United States Substance Abuse and Mental Health Services Administration (SAMHSA) reveals that substance use or dependence among full-time workers aged 18 to 49 in 2000 was 8.1% for alcohol use and 7.8% for illicit drug use. The most recent data indicated that 19.7% of farm workers had used illicit drugs in the year prior to the study. This figure had increased from 10.8% from the previous year (1,2).

Workplace drug use and intoxication has been demonstrated to decrease productivity and increase absenteeism and injuries. Studies performed by the United States Postal Service demonstrated that positive preemployment screens for marijuana and cocaine were associated with increased adverse employment outcomes such as accidents, injuries, and employee behavior discipline. A study performed in a major teaching hospital documented that, as a consequence of preemployment drug testing, the incidence of drug use declines and that drug screening can serve as a deterrent for drug-using persons in applying for employment (3,4).

Studies comparing two manufacturing plants, one that did preemployment drug testing and another that didn't, demonstrated a decreased rate of employee turnover, accidents, and unauthorized absence in the company that did preemployment drug testing (5).

Basics of Drug Abuse

Addiction and Abuse

The term *chemical dependency* is often used synonymously with terms such as *addiction, drug dependence, alcoholism, polysubstance abuse, substance abuse, substance dependence,* and *drug abuse*. Seymour and Smith (6) provide what is probably the best definition of chemical dependency: "Addictive disease is a pathological state with characteristic signs and symptoms as well as a predictable outcome if not treated. Dependency is characterized by a compulsive desire for the drug, loss of control when exposed to the drug, and continued use in spite of adverse consequences" (Table 10.1).

The *Diagnostic and Statistical Manual of Mental Disorders* (7) defines substance abuse as a maladaptive pattern of substance use. One of the criteria listed for the diagnosis of substance abuse is a failure to fulfill the major role obligations of work as well as other social situations (Table 10.2).

Abused Drugs

Drugs of addiction are a complicated group of stimulants, depressants, hallucinogenic substances, and sedative-hypnotics (Tables 10.3 to 10.6). These substances can be taken orally, by nasal insufflation (snorting), placed rectally, inhaled, injected under the skin (skin popping), injected in mucous membranes, injected intravenously (mainlining), or applied by a skin patch as

TABLE 10.1. Criteria for substance dependence (DSM IV).

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more of the following, occurring at any time in the same 12–month period:

1. Tolerance, as defined by either of the following:
   a. A need for markedly increased amounts of the substance to achieve intoxication or desired effect
   b. Markedly diminished effect with continued use of the same amount of the substance
2. Withdrawal, as manifested by either of the following:
   a. The characteristic withdrawal syndrome for the substance
   b. The same or closely related substance is taken to relieve or avoid withdrawal symptoms
3. The substance is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful effort to cut down or control substance use
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects
6. Important social, occupational, or recreational activities are given up or reduced because of substance use
7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance

Source: Data from American Psychiatric Association (7).

TABLE 10.2. Criteria for substance abuse (DSM-IV).

A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12–month period:

1. Recurrent use resulting in a failure to fulfill major role obligations at work, school, or home
2. Recurrent substance use in situations in which it is physically hazardous
3. Recurrent substance-related legal problems
4. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the consequences of the substance

Source: Data from American Psychiatric Association (7).

in the case of Fentanyl addiction. Several substances, such as the opiates and methamphetamines, have medical uses so that any drug testing program must allow for a review to determine if the substance is being taken legally. Some substances, such as PCP, once had a legal use in the United States and are still used in some countries. Legality of the substances varies by country; for example, heroin, illegal in the United States, is used as an analgesic in treatment of cancer in Great Britain and other countries (8,9).

Usage Patterns

There are four common usage patterns of illicit drug use: experimental, recreational, circumstantial, and compulsive. Experimental use involves short-term trials of drugs motivated by curiosity and is common among teenagers, young adults, and others naive about the effects of the drugs (8,9,11).

Recreational drug users use drugs in social settings with friends or acquaintances who desire to share the experience. Use is patterned and voluntary depending on the social situation, and the impact on the workplace may vary by its use. For example, an after-work drink may be acceptable for relaxation and socialization, but drinks taken during the lunch break by mechanized combine drivers who are harvesting wheat may be deadly. Any alcohol use in workers who apply the growth regulator hydrogen cyanamide is dangerous because it triggers a potentially fatal Antabuse reaction (see Chapters 13 and 15) (10).

TABLE 10.3. Stimulants.

Example	Intoxication	Withdrawal	Overdose
Cocaine	Increased alertness	Apathy	Agitation
Methamphetamines	Excitation	Hypersomnia	Hyperpyrexia
Amphetamines	Euphoria	Irritability	Hallucinations
Nicotine	Tachycardia	Depression	Seizures
Caffeine	Hypertension	Disorientation	Death
Ephedrine	Insomnia		
	Anorexia		
	Paranoia		

Source: Data from Graham and Schultz (8), Lowinson et al. (9), and Coleman and Kay (10).

TABLE 10.4. Depressants.

Examples	Intoxication	Withdrawal	Overdose
Heroin	Euphoria	Watery eyes	Slow breathing
Morphine	Drowsiness	Rhinorrhea	Shock
Opium	Respiratory depression	Yawning	Seizures
Codeine	Constricted pupils	Irritability	Coma
Methadone	Nausea	Tremor	
Propoxyphene		Anxiety	
Talwin		Muscle cramps	
Dilaudid		Chills	
Percodan		Diaphoresis	
Fentanyl		Picking at skin	
Tramadol		Piloerection (cold turkey)	
Oxycodone			
Demerol			
Butorphanol			
Pentazocine			

Source: Data from Graham and Schultz (8), Lowinson et al. (9), and Coleman and Kay (10).

TABLE 10.5. Hallucinogens.

Example	Intoxication	Withdrawal	Overdose
LSD	Hallucinations	No symptoms reported	Intense hallucinations
Psilocybin	Nystagmus		Respiratory depression
Mescaline (peyote)	Reactions: Psychosis Depression		Death
THC	Flashbacks		
Marijuana	Emotional detachment		
PCP			
Jimson weed			
Ergot alkaloids			
MDA			
MDMA (ecstasy)			
MDE			

Source: Data from Graham and Schultz (8), Lowinson et al. (9), and Coleman and Kay (10).

TABLE 10.6. Sedative-hypnotics.

Examples	Intoxication	Withdrawal	Overdose
Alcohol	Mood swings	Tremors	Somnolence
Barbiturates	Aggressiveness	Hallucinations	Respiratory depression
Benzodiazepines	Impaired motor control	Agitation	Coma
Antianxiety medicines	Unsteady gait	Delirium tremors (alcohol)	Death
	Slurred speech		
	Impaired judgment		

Source: Data from Graham and Schultz (8), Lowinson et al. (9), and Coleman and Kay (10).

Circumstantial use is common in workers who require an anticipated drug effect to cope with a specific problem, situation, or condition at work or home. Examples of this are workers spraying pesticides at night who use stimulants to keep awake, truckers who use stimulants for long-haul drives, or farm managers who use benzodiazepines to cope with stress (6,8,9).

Compulsive drug use is defined by Seymour and Smith (6) as "drug use that is patterned behavior of high frequency and a high level of intensity, characterized by a high degree of psychological dependence and perhaps physical dependence. The drug use dominates the individuals' existence, and preoccupation with drug-taking precludes other social functioning." This person is likely to use various behaviors and excuses to avoid drug tests and will deny use if caught. This person may use the agricultural workplace as a source of funds for addiction and as a place to buy, sell, or store drugs (6,8,9).

Nature of Addiction

Biological, psychological, and sociological factors contribute to the propagation of drug addiction and abuse.

Biological Factors of Addiction

Evidence suggests that drug-seeking behavior may be caused by genetically determined abnormalities in central nervous system neurotransmitters. Depressants such as heroin or stimulants such as cocaine mimic the structure of neurotransmitters at synaptic junctions of the brain. Stimulants such as amphetamines and cocaine mimic neurotransmitters that cause a stimulant reaction; heroin, other natural and synthetic opiates, and alcohol mimic neurotransmitters with a depressant effect. Dopamine has been suggested as a positive reinforcer, and drugs such as amphetamine, cocaine, and nicotine act by increasing the amount of dopamine in the synapse. Tetrahydrocannabinol (THC, marijuana) acts like dopamine in the brain and reinforces the stimulant effects of the neurotransmitter. Alcohol also stimulates the release of dopamine (12).

Illicit drugs may also act at the level of the axon. Phencyclidine hydrochloride (PCP), alcohol, and inhalants interfere with cell membrane function to influence cell transmission along the axon (12).

Despite superficial differences, all drugs activate the limbic system composed of the temporal lobes, amygdala, and hippocampus. The nucleus accumbens within the limbic system is involved in the perception of pleasure and may be the common site of action of all drugs. The limbic system has connections throughout the brain, especially those areas involving voluntary control and cognition (12).

Alcohol addiction may be caused by abnormalities in several central neurotransmitters, including serotonin and dopamine. Changes in serotonergic and dopaminergic systems are associated with states of alcohol intoxication and withdrawal (12).

Cocaine is thought to cause a surge of dopamine and serotonin in the brain that triggers the cocaine "high." Dopamine activation had been described as essential in drug reinforcement and is associated with pleasure and elation. Some authorities suggested it is the master molecule of addiction and the nucleus accumbens is the master organ. Reinforcement theory in drug use proposes that compulsive substance abusers use drugs because these same drugs have been positive reinforcers on previous occasions. Dopamine exercises power over learning and memory, creating a neurochemical support for addiction so powerful that the people, places, and thoughts associated with drug taking are also imprinted on the brain (12).

Psychological Factors of Addiction

Psychological factors that contribute to addiction include extroversion, lack of conscientiousness, and openness to experience. Dependent personality disorders (easily led by others), anxiety disorders, and depression are commonly associated with drug abuse. In adolescents, when most drug abuse starts, low affect and lack of behavior self-regulation when interacting with family and peers predisposes them to substance experimentation. In addition, immaturity may exacerbate the natural low psychological self-regulation in childhood to promote initiation of alcohol, tobacco, and other drug consumption (12–16).

Sociological Factors of Drug Abuse Causation

Social factors include peer pressure and the availability of drugs in the community, school, or workplace. Experimentation with drugs is common among youths, but only a small number develop habituation and addiction. Drug addicts need to have other users around them to validate their behavior and to use in transport (mules), sales (pushers), or purchases of drugs. In this manner, drug use is a socially contagious disease. The workplace, whether it is a farm, packing house, or veterinary supply depot, becomes the location where drugs are bartered, used, and sometimes grown or manufactured (17).

Occupational and agricultural risk factors for drug and alcohol use include poor job performance; safety hazards while intoxicated or during withdrawal; drug-seeking behavior at work such as buying, manufacturing, stealing, or selling; and poor health. Drug users often try to recruit fellow employees to validate their own drug behavior and to use them as a source of buyers for income. An employer may find a stockroom or production line has been turned into a drug distribution point by drug-using employees (6).

Diagnosis of Drug Dependence

Intoxication, withdrawal, and tolerance are the most prevalent substance-related disorders. Intoxication is the development of a substance-specific syndrome that disturbs perceptions and develops immediately after ingestion. Intoxication is also manifested by socially maladaptive behavior such as impaired judgment, cognitive impairment, loss of impulse control, and impaired social and occupational control. Withdrawal is a substance-specific condition resulting from the cessation or reduction of the substance causing intoxication (9).

Tolerance is the requirement of ever-increasing amounts of the drug to deliver the same pharmacological effect. Eventually, the abuser develops tolerance to the substance's effects and a cross-tolerance to effects of substances in the same class (3,8).

To make the diagnosis of substance dependence requires three symptoms from a list of seven, present during the same 12-month period: intoxication; withdrawal; tolerance; a personal desire or unsuccessful effort to cut down; drug-seeking behavior; social, occupational, or recreational consequences; and persistent substance use despite knowledge that it is making the user's health worse (see Tables 10.1 and 10.2) (7).

The history may not be useful in making the diagnosis as the patient may deny drug use or lie about its extent. In addition, the classic signs and symptoms of intoxication and withdrawal may be clouded by polydrug abuse and the concurrent presence of psychosis, depression, or anxiety (16).

Secondary signs of drug use may also be helpful in making a diagnosis. These may include track marks (the scars caused by injecting drugs), distinctive tattoos (especially on the arms to hide track marks), jewelry, and drugs on the person or at the workplace. Paraphernalia found on the worker's person or at the workplace may include roach clips (used to hold marijuana cigarettes), cigarette papers, bongs for smoking hashish, syringes for injecting drugs such as heroin and "crack," and spoons for "cooking" heroin before injection. However, care must be exercised not to become overzealous and make a diagnosis based on misinterpretation of secondary signs. Drug-related jewelry may be worn innocently, diabetics may carry syringes, and former drug users, bikers, and almost anybody may have tattoos.

Management

Basic treatment regimens consist of one or more combinations of the following modalities: pharmacological treatments, behavioral modification, aversion therapy, a 12-step abstinence-based approach, individual psychotherapy, counseling, drug education, controlled drinking, broad-spectrum approaches, and relapse prevention (17).

Pharmacological Treatments

Pharmacotherapies for alcohol and drug addiction have been shown to be effective during the acute or subacute withdrawal periods and with methadone maintenance. Studies have examined antidipsotropics (disulfiram, calcium carbamide, metronidazole), antianxiety agents (diazepam), antipsychotics (thiothixene, trifluoperazine), antidepressants (imipramine, desipramine, fluoxetine, lithium), and hallucinogens (lysergic acid diethylamide). Methadone maintenance for heroin addicts has also demonstrated benefit (18).

Behavioral Modification

Operant methods and aversion therapy are found in this class. Reinforcement and punishment contingencies can be used to enhance program compliance, but the ultimate impact on addictive behavior depends on the effectiveness of the program itself (16).

The principle of aversion therapy is to produce an aversive reaction to alcohol by establishing a conditioned response in an individual. Ingestion of alcohol is paired with a negative stimulus to produce an automatic negative response when exposed to alcohol alone. The four major types of aversive stimuli are nausea, apnea, electric shock, and imagery. A large body of research demonstrates effectiveness for several months but not in the long run (17).

Twelve-Step Abstinence-Based Approach

Pioneered by Alcohol Anonymous (AA) and Narcotics Anonymous (NA), the 12-step approach features abstinence and a self-help program of rehabilitation. While not a religion, a significant part of the program is calling upon a Supreme Being for help and guidance. Results of multiple studies have been summarized by Miller (17) as follows:

1. Of those sober less than a year, about 41% will remain in the AA Fellowship another year.
2. Of those sober less than 5 years, about 83% will remain in the Fellowship another year.
3. Of those sober 5 years or more, 91% will remain in the Fellowship another year

Individual and Group Psychotherapy and Counseling

Studies quoted by Miller (17) did not reveal consistently positive results from psychotherapy despite clinical intuition that individual attention to the alcoholic or addict was valuable. Confrontation, a subset of group psychotherapy, where the addict or alcoholic is confronted by other addicts with his or her addiction, also hasn't produced data demonstrating its effectiveness.

Drug Education

Education programs (called "scare school" by the participants) teach the addict about the drugs they are using, their health effects, and what one can expect in detoxification. No data documenting the effectiveness of this approach exist (17).

Broad-Spectrum Approaches

These approaches include social skills training (called "charm school" by the participants), stress management, anger management, and community-based reinforcement such as education and job placement. Tattoo and scar removal is also an important facet of drug treatment as gang and drug-related tattoos serve to identify a drug user to other drug users and to alienate potential employers. Tattoo removal can serve to improve a former drug abuser's reentry into the workplace. As people detoxify from opiates, they often experience debilitating dental pain. The chances are high that they will return to opiate use unless the dental conditions are treated. Drug abusers may have other drug-related health problems such as infectious hepatitis, HIV, and skin infections. These problems require aggressive diagnosis and treatment. Finally, the dual diagnosis of drug addiction with psychiatric disease such as depression, bipolar disorder, anxiety, or schizophrenia must be diagnosed and treated concomitantly using psychotherapy and pharmaceuticals during drug withdrawal (16–18).

Relapse Prevention

The goal is to remove the triggers that may precipitate the relapse to alcohol and drugs. Twelve-step programs serve to change the people, places, and things that trigger drug use and to make fundamental changes in attitudes and behaviors. Medication support for withdrawal, treatment of psychological issues, and intense alteration of the social context may be necessary to keep people clean and sober.

Drug Use Prevention in the Workplace

Any drug treatment or rehabilitation program must take into consideration the biological, psychological, and societal causes and consequences of drug abuse. A policy begins with the employer's recognition of the problem, which may be triggered by government requirements, an insurance company's or subcontractor's contractual requirements, by an injury or accident, by discovery of drugs or drug use on the work premises by law enforcement, or by the confrontation of a drug- or alcohol-intoxicated employee (Table 10.7).

TABLE 10.7. Industrial Drug Program.

- Employer's recognition for a need of a drug program triggered by:
  - Government requirement
  - Insurance company requirement
  - Injury or accidents
  - Discovery of drugs or drug use
  - Confrontation with an intoxicated employee
- Decision for action:
  - Recognize the costs and consequences
  - Select consultants
- Creation of a company policy:
  - Use attorneys and consultants
  - Decide which modes of testing will be conducted: preemployment, for-cause, random, postaccident, return-to-duty, follow-up
  - Short and easily understandable policy transmitted to the employees in writing
  - Must be fair and applicable to all employees
  - Selection of collection company, testing lab, medical review officer (MRO), and counselors; have this arranged ahead of time
- Education:
  - Employees:
    - About drugs
    - About the company policy
  - Supervisors:
    - About drugs
    - About the company policy
    - Recognition of drug syndromes and what to do when noticed
- Testing process (variations of this process may be used from company to company and situation to situation):
  - Employee (or applicant) is informed of the need for a test; a written request form is issued.
  - Collection point:
    - Chain-of-custody and identification forms completed
    - The employee is positively identified through a driver's license, passport or other form
  - Specimen is provided by the employee:
    - Witnessed if there is reason to believe the individual is trying to fake a test
    - Bottle is sealed and marked in the presence of the donor
    - Specimen is stored in a secure location and chain-of-custody forms completed
  - Transportation:
    - By secure courier and using chain-of-custody forms
  - Testing:
    - Secure, reliable laboratory
    - Maintain chain-of-custody
    - Confirmation of positive results with a second, alternative method
    - Written reports
- Medical review officer (MRO):
  - Reviews all positives in regulated testing
  - May be asked to review all positives in nonregulated testing
  - Provides written report to employer
- Employer:
  - Action according to stated company policy:
    - Do nothing
    - Remove the employee from duty until rehabilitation is completed
    - Keep the employee on duty until rehabilitation is completed
    - Terminate employment

Once the problem is recognized, the supervisors and managers of the company must be willing to engage in a detection and prevention program. Through research, education, or consultation with a specialist, the company management makes a decision for action, knowing there will be an expense for testing and that employees may have to be terminated from employment. Management must be prepared to litigate if challenged and take their policy as far in the courts as is needed to protect their program.

When the company management has demonstrated willingness to proceed, a short, understandable, and blunt policy is formulated in lay language. Consultants or attorneys will usually have input in the policy that lays out the forbidden conditions or actions and resultant discipline. The policy needs to be communicated to the employees with documentation. In 2000 in the United States 76% of full-time workers aged 18 to 49 (more than 66 million workers) were aware of written policies on substance use at their workplace. Awareness was greatest in administrative support personnel and smallest in precision production crafts and repair. Government employees were more aware of alcohol- and drug-use policies than any other industry. While not specifically studied, agriculture, which has a mix of workers in different categories, seems to be in the middle (19).

Utilizing consultants, the company will typically conduct an education program on drug abuse for employees and an additional class on the recognition of drug use behavior for supervisors. Once the policy is in place, the company can begin testing, typically using a third party such as a physician, laboratory, clinic or collection company.

Drug Testing

Testing for drugs can be preemployment, routine, random, for reasonable cause, postaccident, return-to-duty, and follow-up. Preemployment tests are conducted before the applicant is accepted for a position. Routine testing may be performed at the time of an annual physical assessment or upon the anniversary of employment but is less productive because it gives the employee a chance to stop drug use in anticipation of a test. Random testing typically follows a formula to trigger the test, such as a number drawn from a hat or extracted from a random number table and matched to the year of a person's birthday or another identifier. Reasonable cause applies to situations where a supervisor, through observation and comparison to guidelines, has determined that there is reasonable cause to suspect the employee is using drugs or alcohol. Postaccident testing is done after an accident or injury and may be limited to certain levels of damage, for example, drug tests done if there is more than $10,000 in damages. Return-to-duty tests are performed when the employee returns after long absences due to health, disciplinary, or other causes. Follow-up tests are typically performed after an employee has a

positive test and has entered a rehabilitation program. Testing in this mode may last for over 1 year.

Drug Testing Process

The drug testing process depends on whether the testing is nonregulated or regulated.

Nonregulated Testing

These tests are usually performed by private companies where there is no government requirement for testing. The standards for nonregulated testing are minimal to nonexistent.

Regulated Testing

These drug tests are required by one of six United States federal agencies and follow strict protocols for collection and evaluation. Most testing protocols use the urine drug test, although some forensic testing for criminal prosecution uses blood testing and various companies use hair analysis. Federal and many company protocols call for the use of breath analysis for alcohol testing because the results are instantaneous.

Common Components

Regardless of whether the testing protocol is regulated or nonregulated, there are common components. Collection and consent forms are necessary to document the identity of the donor using a driver's license or similar identification and to maintain a chain of custody. Proper collection procedures, either witnessed or nonwitnessed, are required to ensure the donor is actually providing the urine sample. It may be necessary to turn off water to sinks and to use bluing agents in the toilet water in the collection room to prevent the donor from using water from the sink or toilet. In addition, measuring urine temperature, creatinine, and specific gravity can help to assure the substance in the collection bottle is urine from the individual being tested.

Circumstances also dictate whether the donation of the specimen is witnessed or not witnessed. The only way to effectively prevent the use of specimens hidden on the donor's person is to witness the collection, yet this invades the person's privacy and takes more time. Many drug protocols call for a witnessed sample only if there is a specific indication that the person is using drugs or might hide the specimen in a container on his or her person (Figure 10.1).

Specimen security is important in ensuring the specimen is not tampered with between collection and testing. Measures may include secured refrigerators and the use of forensic containers and security sealing tape. All regulated and most unregulated testing requires a two-step laboratory

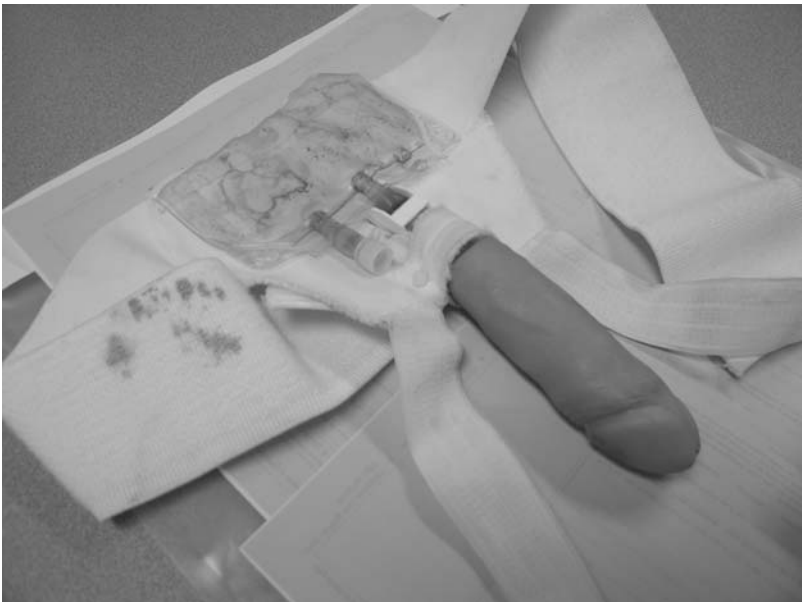


FIGURE 10.1. This artificial penis and bladder apparatus was used by an agricultural worker to provide a specimen for drug testing.

process of screening with an inexpensive kit and confirmation of positive results with the more expensive, but highly accurate, gas chromatography and mass spectrometry units.

The choices of illicit drugs to be tested vary from the five plus alcohol required by SAMHSA (the so-called SAMHSA Five: cocaine, amphetamines, opiates, marijuana, and PCP) for regulated testing, to 15 drug panels provided for nonregulated testing. Some companies, disappointed at the small number of drugs being tested for in the regulated testing program, test an expanded panel at the same time.

All regulated and many nonregulated programs require that laboratory reports be sent to a physician acting as a medical review officer (MRO). It is the MRO's responsibility to ensure that the process was done properly and to call the donor to make sure none of the substances are being taken by prescription for a legitimate medical reason. Medical review officer qualifications include training and certification through the Medical Review Officer Coordinating Council (www.ACOEM.org).

The American College of Occupational and Environmental Medicine teaches in its MRO course that the responsibilities of the MRO include:

1. Receive the results either by mail or secure fax.
2. Review the results.

3. Investigate, inquire, or interview the donor if there is an unexplained positive.
4. Record the findings.
5. Record the donor's excuses for a positive response (and do not be tricked by them).
6. Order a reanalysis or retest if appropriate.
7. Refer the donor for a medical evaluation if necessary.
8. Interpret the findings.
9. Report the results to the employer.
10. Release the medical information appropriately.
11. Keep appropriate records.

The MRO must be aware of scams used by drug users to falsify drug test results and the sources of false positives (20).

When positive reports of drug or alcohol testing are transmitted to the employer, the employer has four choices, depending on whether the testing is regulated or unregulated and what the company drug policy says:

1. Do nothing.
2. Remove the employee from duty until rehabilitation is completed.
3. Keep the employee on duty until rehabilitation is completed.
4. Terminate the person's employment.

Each of the six federally regulated programs has different requirements for removal from duty and rehabilitation. All require input from a substance abuse professional (SAP) to organize and supervise the rehabilitation and repeat negative testing. Requirements for rehabilitation in nonregulated testing depend on the company policy, state law, and union agreements. While programs vary, rehabilitation typically includes 12-step groups, counseling, group therapy, education, and repeat drug testing. In regulated and most nonregulated programs, repeated drug tests and ongoing participation in 12-step groups and counseling are required for the employee to remain at work.

References

1. Office of Applied Studies, Substance Abuse and Mental Health Administration. Drug use among U.S. workers: prevalence and trends by occupation and industry. DHHS Publication No. (SMA)96–3089, May 1996.
2. Office of Applied Studies, Substance Abuse and Mental Health Services Administration. The NHDSDA Report, September 6, 2002. Substance use, dependence or abuse among full-time workers, pp. 1–3.
3. Zwerling C, Ryan J, Orav EJ. The efficacy of preemployment drug screening for marijuana and cocaine in predicting employment outcome. JAMA 1990;264(20): 2639–43.
4. Lange WR, Cabanilla BR, Moler G, Bernacki EJ, Frankenfield DL, Fudala PJ. Preemployment drug screening at the Johns Hopkins Hospital, 1989 and 1991. Am J Drug Alcohol Abuse 1994;20(1):35–46.

5. Borofsky GL, Bielema M, Hoffman J. Accidents, turnover, and use of a preemployment screening inventory. Psychol Rep 1993;73(3 pt 2):1067–76.
6. Seymour, RB, Smith DE. Identifying and responding to drug abuse in the workplace: an overview. J Psychoactive Drugs 1990;22:383–405.
7. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV). Washington: American Psychiatric Association, 1994.
8. Graham AW, Schultz TK, eds. Principles of Addiction Medicine. Chevy Chase, MD: American Society of Addiction Medicine, 1998.
9. Lowinson JH, Ruiz P, Millman RB, Langrod JG. Substance Abuse: A Comprehensive Textbook. Baltimore: Williams and Wilkins, 1997.
10. Coleman FS, Kay J. Biology of addiction. Obstet Gynecol Clin North Am 1998;25(1):1–19.
11. Tarter RE. Etiology of adolescent substance abuse: a developmental perspective. Am J Addictions 2002;11:171–91.
12. Zimmermann P, Wittchen H-U, Hofler M, Kessler RC, Lieb R. Primary anxiety disorders and the development of subsequent alcohol use disorders: a 4–year community study of adolescents and young adults. Psychol Med 2002;33:1211–22.
13. Lessenger JE. Case study: hypotension, nausea and vertigo linked to hydrogen cyanamide exposure. J Agromed 1998;5(3):5–11.
14. Flory K, Lynam D, Milich R, Leukefeld C, Clayton R. The relations among personality, symptoms of alcohol and marijuana abuse, and symptoms of co-morbid psychopathology: results from a community sample. Exp Clin Psychopharmacol 2002;10:425–34.
15. McDowell DM, Clodfelter, RC. Depression and substance abuse: considerations of etiology, co-morbidity, evaluation, and treatment. Psychiatr Ann 2002;31:244–51.
16. Phillips P, Johnson S. How does drug and alcohol misuse develop among people with psychotic illness? A literature review. Soc Psychiatry Psychiatr Epidemiol 2001;36(6):269–76.
17. Miller NS. History and review of contemporary addiction treatment. Alcohol Treat Q 1995;12(2):1–22.
18. Mee-Lee D. Matching in addictions treatment: How do we get there from here? Alcohol Treat Q 1995;12(2):113–27.
19. Miller NS. Pharmacotherapy in alcoholism. Alcohol Treat Q 1995:12(2):129–52.
20. American College of Occupational and Environmental Medicine. Medical review officer drug and alcohol testing comprehensive/fast track course, 2003 course syllabus. Arlington Heights, IL: American College of Occupational and Environmental Medicine, 2003.

11

Work Site Visits

Victor Duraj

Key words: modified duty, hazards, return to work, injury prevention

A better understanding of the health hazards of the workplace can be gained by work site visits. Physicians can use their observational skills to increase their understanding of work processes, hazardous exposures, potential adverse health effects, preventive principles, and control measures during inspection of work sites. This chapter focuses on previsit preparations, the site visit, and postvisit responses (1,2).

Previsit Preparations

Permission and Appointments

Unless the physician is making an unannounced visit as part of a government or insurance company safety survey, it is always preferable to call ahead and make an appointment with the manager or owner. The physician will seldom be turned down (a cause for suspicion), and most owners are proud to show off their animals, crops, and machines. The manager or owner will want to know the reason for the visit and may advise the physician on basic hazards and safety rules (3).

Proper Attire and Safety Rules

Any physician who visits the agricultural workplace must dress appropriately, using proper shoes, clothing, and protection against the elements. He or she should observe all safety rules requiring personal protective equipment for the ears, eyes, skin, and hair. Long hair should be pinned up to avoid catching it in rollers with the resultant scalp avulsion injuries. Women should not wear high or open-toe shoes. It is important for the physician to set an example in the use of safety equipment and following the safety rules.

The Site Visit

The reasons why a physician should sometimes leave the confines of the hospital or clinic and venture out into the agricultural workplace are summarized in Table 11.1.

Understanding the Workplace

A physician not familiar with the agricultural workplace may approach the patient's injuries without knowing the mechanism or agent of injury (see Chapter 25). Some injured workers may not be able to adequately explain how they were injured. A physician who visits the workplace has a greater understanding of the conditions under which the employee works and how the injury occurred (4).

Developing a Working Relationship

The work site visit is also an opportunity for the physician to establish a working relationship of mutual respect with the owner or management, the union, and the employees. Employees are especially impressed to see a physician who will come out to the farm to see what they actually do (5).

Establishing the Tasks for Preplacement Physicals

It is important for physicians who do preplacement or fitness-for-duty examinations to know the details of the job for which the employee is being considered. The workplace visit serves to educate the physician regarding the tasks that the prospective employee will be required to perform.

Coordinating Modified Duty and Return to Work

Even workers with serious injuries can be returned to work as long as precautions are taken to ensure that the environment is conducive to the mental and physical healing of the patient. For a physician who sees many injured employees from a particular agricultural work environment, such as a packing shed or processing plant, there is an advantage to going to the workplace

TABLE 11.1. Reasons and goals for a workplace visit.

To obtain a working understanding of the work the employee is doing so the physician can understand what the employee is talking about when he or she comes into the office
To coordinate a modified duty and early return to work program
To assist in creating a first-aid or rescue program for injured workers
To observe workplace hazards and how the employees are being protected from them
To evaluate the veracity of a worker's claim for injury or disability

and determining in advance which jobs employees with limitations can perform. The job placements and modifications may be short term or permanent, but the goal is to return the worker to a productive capacity and, at the same time, to cut down on the long-term costs of rehabilitation and temporary disability (6).

The mental well-being of the patient may be more important than the physical injuries, and a rapid return to work restores to the injured employee a sense that he or she is once again a breadwinner and is useful to society.

Because low back pain is the most common injury in agriculture, multidisciplinary teams have been developed to expedite the patient's recovery and return to work. A work site visit by a physician or another trained health professional has been found to be an effective component of such a team approach (7).

Creation of First-Aid and Rescue Programs

Particularly in rural areas remote from cities and city emergency departments, physician visits can be productive in initiating, funding, overseeing, and evaluating first-aid programs. In some countries, a lone physician or clinic is all that is available for injured workers from the fields. In those cases, physician visits to the workplace can help to coordinate first aid, evacuation protocols, and equipment (see Chapter 25).

Migrant Housing

Agricultural health hazards affect not only persons performing the fieldwork but also persons who live in the immediate environment. Migrant workers may live in on-site temporary or dilapidated housing without the basic hygienic requirements dictated by governmental regulations. What might be considered dilapidated temporary housing in some parts of the world might represent the norm in other parts. A useful checklist for assessing the safety and hygienic conditions of worker housing can be found at the U.S. Department of Labor Web site (http://fortress.wa.gov/esd/portal/employment/ag/etahousingcheck.pdf).

Workplace Hazards

The agricultural work site is replete with hazards that result in fatal and nonfatal debilitating injuries or illnesses (see Chapter 3). Proven methods can eliminate or reduce many types of hazards and help identify the causes of an existing health problem (see Chapters 4, 5, and 6). An inspection of the work site by a person who is familiar with the types of work, the work environment, the social environment of agriculture, and the associated risk factors can identify health hazards (8).

A productive agricultural site visit requires fundamental understanding of the potential factors for both chronic and acute injuries. Preprinted checklists provide a comprehensive group of questions to prepare for evaluating a particular work site or injury. You can find appropriate checklists by searching the Internet for "farm and ranch safety audit."

In addition to typical field and farm activities, agricultural work includes jobs in processing facilities such as canneries and packing sheds. These environments include aspects that more closely resemble typical industrial and manufacturing environments, except that the various pressures are often different, driven in part by maturity of the crop, the impending weather conditions, lack of a stable work force, and processing equipment that remains idle for most of the year and draws less maintenance attention than it should (9).

There usually are multiple causes or factors leading to an injury incident. Often the absence of one factor in the series could have prevented the particular incident from occurring. However, correcting all of the contributing factors will further reduce the likelihood of a repeated or similar injury (9).

Many insurance underwriters and workers compensation insurance carriers have safety information that they utilize and make available to the public. Organizations such as AgSafe (www.agsafe.org) provide certificate programs and materials that prepare persons to perform hazard identification and control activities as well as other injury and illness prevention plan (IIPP) development. Enforcement inspections are significantly associated with decreasing compensable workers compensation claims rates (10).

Evaluating the Veracity of Claims

Employers and employees may decide to falsify injuries for their own financial gain. Alternatively, attorneys, government agencies, and insurance carriers may have doubts that an injury actually occurred. The treating physician is in a unique position to answer the question of causation by making a work site visit.

Determining how an injury occurred involves asking open-ended questions to elicit more detailed responses in the form of thoughts, observations, and history. The physician should keep in mind the principle of multiple causal factors and should avoid drawing conclusions until after conflicting or incomplete information is resolved as best as possible. However, because much farm work involves lone workers, the specific cause may be difficult to ascertain, especially with deceased or memory-blocked victims. Ascertaining the cause of an agricultural injury depends on finding one of several possibilities summarized in Table 11.2 (9).

To determine the veracity of a claim, the physician may best serve the patient by going to the workplace and actually seeing the circumstances of the accident. Sometimes the injury can be reenacted to see if the history related by the patient is plausible (11,12).

TABLE 11.2. Factors to consider when determining causation of a work-related injury.

A cause-and-effect relationship
Consistency of the mechanism and agents of injury with the description of the injury itself (see Chapter 25)
Internal consistency of the employee's history
External consistency with the history as related by coworkers
Consistency with what is medically known about the offending substance, machine, animal, infectious agent, or job task

Post-visit Actions

The physician needs to write up details of health problems observed in the work-site visit. Appropriate reports, action reports, and memorandums of understanding should record recommendations for hazard abatement, return to duty programs, and modified duty programs. In certain countries and states, specific hazardous conditions, epidemics, infectious diseases, and other problems must be reported to local authorities.

References

1. Cordes DH, Rea DF. Work-site risk assessment. Prim Care 1994;21:267–74.
2. Cordes DH, Rea DF. Workplace visits: an important place in family practice. Am Fam Physician 1994;49:733, 736, 741.
3. Tong DW. Conducting a factory or plant visit. Australas J Dermatol 1995;36:129–32.
4. Gillies RR, Zuckerman HS, Burns LR, et al. Physician-system relationships: stumbling blocks and promising practices. Medcare 2001; 39(7 suppl): I92–106
5. Kushnir T, Melamed S, Ribak J. Occupational physicians in Israel: work structure, job and personal characteristics, and job satisfaction. J Occup Environ Med 1997;39:874–81.
6. Noel B, Boillat MA. Reasons for consultation in occupational medicine. Rev Med Suisse Romand. 1994;114:633–41.
7. Karjalainen K, Malmivaara A, van Tulder M, et al. Multidisciplinary biopsychosocial rehabilitation for sub acute low back pain among working age adults. Cochrane Database Syst Rev 2003;(2)CD002193.
8. Wesdock JC, Sokas RK. Medical surveillance in work-site safety and health programs. Am Fam Physician 2000;61:2785–90.
9. Murphy D. Safety and Health for Production Agriculture. St Joseph, MI: American Society of Agricultural Engineers, 1992.
10. Baggs J, Silverstein B, Foley M. Workplace health and safety regulations: impact of enforcement and consultation on workers' compensation claims rates in Washington State. Am J Ind Med 2003;43:483–94.
11. Larsen ME, Schuman SH, Hainer BL. Workplace observation: key to a meaningful office history. J Fam Pract 1983;16:1179–84.
12. Lessenger JE. Case Report: Fraudulent pesticide injury: value of a work site visit. J Agromed 1996;3:27–32.

12

Children in Agriculture

Lorann Stallones and Huiyun Xiang

Key words: children, communicable diseases, disabilities, injuries, farm tasks

Children who live, play, and work on farms are exposed to agricultural hazards that include biological, physical, and chemical agents. The agricultural environment includes animals, insect vectors, machinery, structures, bodies of water, and extreme climates, both hot and cold. Exposures to agricultural hazards among children vary greatly based on the environment and the cultural conditions that guide farming activities. The type of agriculture in a region, the climatic conditions, and the agricultural practices, both current and historical, are important considerations in evaluating the nature of hazardous or salubrious exposures for children. While some children who live on farms may not participate in farm chores, others may be actively involved and more highly exposed. Further, children may be exposed to hazards of farming as bystanders in the workplace.

The definition of *child* is relative and varies across cultures and periods of time. Categories of children used by international labor conventions are the following:

1. Children are under 15 years of age (although in some places this age would vary by a year, making it 14 or 16)
2. Adolescents are 15 to 18 years of age (or in some places this category starts at 14 or 16).

In many countries, children's involvement in agriculture is viewed as a normal part of living on farms or as a useful part of their socialization and life skills development (1,2).

Agricultural work performed by children varies from short periods of light work after school to long hours of arduous work involving dangerous chemicals and work processes in subsistence or commercial production (1,2).

Children working in agriculture comprise 70.4% of all working children. Among working boys, 68.9% are involved in agriculture, and among working girls, 75.3% are involved in agriculture. Millions of people are involved in agriculture worldwide; in many countries children begin working on farms at

a very young age. Agriculture encompasses the bulk of the world's poor, who work long hours for meager returns and under hazardous and difficult conditions. In India, the combination of poor nutrition and agricultural work in childhood has resulted in decreased stature, which impairs earning ability later in life. Children working on family-based vegetable farms in the Philippines have been exposed to infections from biohazards and chemicals in soil and water, and back problems from the heavy lifting of watering cans. They often work without protective clothing. Children working in South America peeling, cutting, and grading cashew nuts are exposed to cuts, skin irritation, and back pain from sitting or standing for long hours (2,3).

Children's work in agriculture often goes hand in hand with debt bondage, where the poorest families have no land or too little land to meet subsistence needs and become trapped in debt to their landlord or another person. Parents may have little choice but to bond their children into agriculture or domestic work to help their families repay the debt. In commercial agriculture, children comprise a substantial portion of the work force associated with global markets for coca, coffee, cotton, rubber, sisal, tea, and other commodities. Studies in Brazil, Kenya, and Mexico have shown that children under 15 years of age make up 25% to 30% of the total work force in various agricultural commodities (4,5).

Studies using rapid assessment techniques have suggested there are common characteristics of children in the plantation work force in a number of countries:

1. Parents have low levels of education.
2. Most children attend school but work after school, on weekends, or during vacations.
3. Children's wages are included with those of a working parent.
4. Children do not like the work but are expected to help with household expenses and/or school fees (4–6).

In some former Eastern Bloc countries, the transition of collective farms into private, family-owned farms has increased the need for unpaid family labor. However, in the Russian Federation, the same changes in farm structure have resulted in less forced involvement of children in crop harvesting, as the children are no longer harvesting crops as part of their school activities (2).

In developed countries, the majority of working children are found in agriculture. Three distinct groups of youth work on farms:

1. Children who live and work on farms owned or operated by their parents
2. Adolescents who are hired to work on farms not owned or operated by parents and whose parents are not farm employees
3. Children who accompany their migrant farm-worker parents (6,7)

A trend of increased percentage of hired farm workers between the ages 14 and 17 has been reported, with that age group comprising 7% of all hired farm

workers. In the United States, an estimated 2 million children and adolescents under the age of 20 years lived or worked on farms in 1998. Protection under the Fair Labor Standards Act differs for children working in agriculture than for children working in other industries. In other industries, children must be 14 years of age before they can legally work, but children as young as 10 years old can legally participate in some aspects of farm work. Family farms are exempt from minimum age restrictions, and children may be employed by their parents on any farm owned or operated by the parents (7,8).

Epidemiology of Pediatric Illnesses, Injuries, and Disabilities in Agriculture

Although the hazards in agriculture have long been recognized among adults, there is less information available regarding children who live and work on farms. Chronic effects on children of farm work conditions such as extended hours, adverse weather conditions, repetitive work methods, and exposure to infectious agents and farm chemicals have been addressed sporadically in the literature (7,8).

Allergies and Allergic Sensitization

In European studies, children of farmers are at decreased risk of developing allergic sensitization. Factors explaining this decrease include early exposure to animals, including livestock and pets. In a study conducted in New Zealand, children living on farms were found to have an increased prevalence of allergic symptoms but not of skin-prick positivity. Weekly consumption of yogurt was associated with decreased risk of hay fever and allergic rhinitis, and consumption of unpasteurized milk was associated with decreased risk of atopic dermatitis and eczema (9–13).

Farm Chemicals

Parental occupational and nonoccupational exposures to pesticides have been associated with childhood cases of neuroblastoma, retinoblastoma, non-Hodgkin's lymphoma, Wilms' tumor, astrocytoma, and primitive neuroectodermal tumors. Not all studies have shown a positive association between parental exposures in agricultural work and diseases in the offspring. However, larger studies have reported a positive association between parental occupation in agriculture and childhood brain tumors. Children of mothers who were employed as farmers or farm workers or were exposed to fertilizers, pesticides, animal manure, or unprocessed wool were more likely to have childhood brain tumors. In addition, children exposed to pigs, horses, and cats in combination with living on a farm had a threefold risk for childhood brain tumors (14–18).

Congenital anomalies associated with farm chemicals are a hazard for children whose parents live and work in agricultural areas. While most of the research has focused on the causal association between congenital anomalies and agricultural chemicals, one must also note that children with the long-term disabilities associated with these defects may be living in rural areas, giving rise to a special-needs population in remote areas. An increase in limb reduction defects, hypospadias, and epispadias was reported in an area in New Zealand where 2,4,5-T (an herbicide) was sprayed for 4 to 6 months a year. Women who resided in Imperial County, California, a highly agricultural community, were more likely to have infants with limb reduction defects than women who resided in urban areas. Malathion, an organophosphate insecticide and acaricide, has been reported to be associated with an increase in rates of gastrointestinal, limb, and orofacial defects, but these associations were not supported in a later study in which only tracheoesophageal fistulas were reported to be elevated (19–22).

In Colombia, Captan, a fungicide with structural similarities to thalidomide, was reported to be associated with a moderate increased risk of congenital malformations among occupationally exposed mothers. In an ecological study in Colorado, chromosomal defects were significantly elevated in counties with high fungicide and herbicide use, and with intensively irrigated pastureland. Heart defects were elevated in counties with intensive irrigation of pastures and cropland. Some investigators have suggested that the solvents used in the pesticide application mixture play a significant role in the teratogenic activity associated with agricultural activities. Despite substantial evidence indicating birth defects associated with pesticide exposures as an important health problem, there is virtually no published literature assessing disabilities among children on farms (23–25).

Children may have enhanced susceptibility to pesticide exposures because of their size, increased metabolism, and rapid growth. As a result, studies of adult pesticide exposure and associated adverse health effects cannot be extrapolated to children. In a qualitative study among farm-worker mothers and their children, the potential sources of exposure to pesticides were described among those aged 8 to 16 years in Colorado and Texas. The following farm activities increased the chance of exposure of children to pesticides:

1. Playing in farm fields
2. Playing in dirt near fields
3. Swimming in irrigation ditches (a *big* risk)
4. Being outside when fields were being sprayed with chemicals
5. Eating fruits and vegetables without washing them
6. Eating food while working in a field
7. Picking crops
8. Spraying weeds and insects (Figure 12.1)
9. Driving tractors to cut wheat and corn or to pick up trash (Figure 12.2)
10. Helping to move or feed cattle

FIGURE 12.1. A young man in China using a backpack sprayer to apply pesticide. Note that he is not wearing gloves, goggles, or a mask. Dermal exposure and inhalation are significant routes of exposure to pesticides. In addition, he is spraying over his head, which allows drift that can cover his body in the pesticide. His long-sleeved shirt and long pants provide some protection. However, cotton can absorb the compounds and keep them next to his skin for long periods of time if he is out spraying for several hours, thereby increasing his exposure. (Photograph by Huiling Xiang.)

Many of these activities clearly also may put the children at risk of an acute illness or injury (26,27).

Due to the intense use of synthetic fertilizers and livestock manure in agriculture, levels of nitrate in water may be elevated. This waterborne chemical hazard for very young children on farms results in a potential for overexposure to nitrates through drinking water. Nitrate contamination in shallow wells may lead to methemoglobinemia in infants. Nitrate is converted to nitrite by commensal bacteria in the gut and absorbed primarily in the small intestine. Levels of nitrate that are safe for adults pose a significant hazard for infants, due to the inability of the infant to process the nitrate and excrete it in the nontoxic form (28–30).

Communicable Diseases

In low-income countries, waterborne diseases remain a major public health problem. Drinking water can be the direct cause of enteric infections, bacillary dysentery, and cholera. Standing water can also serve as the indirect cause through transmission of mosquito-borne diseases such as malaria and

FIGURE 12.2. Driving equipment is one of the serious hazards for children on farms. This girl is driving a tractor without rollover protection. One concern is how much training she has received about operating the tractor and whether she would be able to respond to an emergency. Judgment can play a significant role in appropriate responses in emergency situations; many researchers have questioned which tasks are the age-appropriate for children working on farms. (Photograph by William Bennett, Jr.)

filariasis. Water can also be the indirect cause of transmission of schistosomiasis, brucellosis, tularemia, hemorrhagic jaundice, and several other protozoal, bacterial, and viral infections (31,32).

Schistosomiasis affects individuals in rural areas who work either in irrigation ditches or freshwater fishing ponds. It is a blood fluke infection with adult male and female worms living within mesenteric or vesical veins of the host. Symptoms can be diarrhea, abdominal pain, hepatosplenomegaly, dysuria, urinary frequency, and hematuria. This parasitic disease is caused by infection with blood flukes belonging to the genus *Schistosoma*. The larval stages of the parasite develop in aquatic snails, emerge and penetrate the skin of anyone in contact with the water. Untreated, schistosomiasis causes considerable pathology and can be fatal in chronic advanced cases (31–33).

As children in agricultural areas have daily contact with water in summer either through helping parents in agricultural work or playing (e.g., swimming) in the water, the risk of infection with schistosomiasis is extremely high. In many areas, a high proportion of children between the ages 10 and 14 are infected. An estimated 66 million children throughout 54 countries are

affected by urinary schistosomiasis. Unfortunately, some environment modifications by human beings spread schistosomiasis rapidly. An extreme example is that in some villages around Lake Volta in Ghana the prevalence of the schistosomiasis among schoolchildren increased by more than 400% after the completion of the dam (31–33).

Between 1961 and 1964, the Akosombo Dam was constructed on the Volta River in Ghana, creating Lake Volta, one of the largest artificial lakes in the world. The Akosombo Dam and a nearby dam built in 1981 have dramatically changed the existing physical, biological, and socioeconomic environment of the people living above and below them. The construction of the dams and Lake Volta has created conditions suitable for explosive outbreaks of waterborne diseases, especially urinary schistosomiasis (31).

An epidemiological survey conducted before Lake Volta was constructed found that the prevalence of urinary schistosomiasis in schoolchildren in the riparian villages was 5.0%. A 1982 postconstruction survey at eight schools near Lake Volta revealed urinary schistosomiasis prevalence rates of 74.5% to 88.0% in schoolchildren, a substantial increase in schistosomiasis prevalence since the two dams were built. In addition to the infection of local children, several schistosomiasis cases have been identified among tourists who swam in Lake Volta (31).

Many regions in the world use raw wastewater for agricultural purposes. Raw wastewater has been associated with increased prevalence of helminthic infections among children in Morocco. In central Mexico there is a higher risk of diarrheal disease and a fivefold increase in risk of *Ascaris lumbricoides* infection among children as compared to areas where raw wastewater was not used. In Mexico, no association was found between raw wastewater use and *Giardia intestinalis,* even though children were found to have the highest prevalence of infection. The benefits of wastewater reuse in agriculture are limited by the hazards associated with the risk of transmission of pathogenic organisms from irrigated soil to crops, grazing animals, and humans (32–35).

Development of infrastructure for increased agricultural production in dry areas may lead to changes in the ecosystem that increase mosquito populations. Large-scale irrigation has often resulted in increased human malaria incidence, which leads to a need to aggressively address mosquito control. In studies of malaria prevalence in Laos during the dry season, 28% of villagers were infected with malaria. During the rainy season, 16% of villagers were infected with consistently high prevalence (40% among boys and 20% among girls) during the dry season among children under the age of 10 years (36,37).

Zoonotic Diseases

With intensification of animal husbandry practices and international trade in animals and animal products, the importance of animal-borne diseases is increasingly recognized (see Chapter 29). Transmission of bacterial and parasitological zoonoses can occur through the following:

1. Ticks, fleas, and sand flies (Chapter 30)
2. Ingestion of contaminated animal or plant products and water
3. Contact with contaminated soil

Young children on farms may be uniquely susceptible to specific zoonotic diseases due to their hand-to-mouth practices and proximity to fields, irrigation ditches, herds, and flocks (38).

Disabilities and Musculoskeletal Disorders

Hearing loss was studied in high school students by researchers at the Marshfield Clinic in Wisconsin. Children who lived and worked on farms were found to have excess hearing loss in the left ear compared with children who neither lived nor worked on farms and children who lived but did not work on farms. The investigators suggested that the excess left ear hearing loss that has been observed in adult farmers begins during childhood (39).

Musculoskeletal disorders can result from excessive physical demands or repetitive movements related to work. Few studies have evaluated the physical demands associated with jobs performed by children and adolescents. These work-related health problems may contribute significantly to long-term problems among youth and need to be addressed in future research (40).

Injuries

A number of studies have reported trauma-related mortality and morbidity on farms. In the United States the annual rate of death was 13.2 per 100,000 farm population between 1979 and 1981 and declined to 8 per 100,000 farm population between 1991 and 1993. Based on the observation that the in-hospital death rate increased significantly between the two periods, the decline was attributed to improvements in emergency medical services in rural areas. The annual morbidity rate for farm injuries reported between 1979 and 1983 was 1,551 per 100,000 and increased to 1,717 per 100,000 between 1990 and 1993. Myers (8) estimated that children aged 10 and under suffered nearly 13,000 agricultural work-related injuries in 1993, with nearly two thirds of these injuries occurring during the summer months when children were out of school. Children working in fields may

1. be near or in the way of machinery, including tractors and trucks;
2. fall from ladders while picking fruit; or
3. become dehydrated due to lack of drinking water.

Common agents of minor injuries to children are animal bites and falls, while the common agents of serious injury in North America involve tractors and moving machinery. Hauling and driving equipment including tractors

are common activities for children on farms, particularly when harvesting and planting needs to get done quickly. Frequently the children are driving older tractors and doing routine maintenance around a farm such as mowing. Older tractors, such as the one in Figure 12.2, are less likely to have rollover protection structures and therefore present a significant hazard in the event that there is a rollover. These older tractors tend to be those that are used for routine maintenance such as mowing on hillsides (41–51).

Farm Tasks of Children

Children working on farms are involved in a wide array of farm tasks. In Kentucky, 82% of children studied were involved in the feeding and care of animals and 70% performed work related to the production of tobacco. In Colorado, children reported working with feeding animals and collecting eggs as early as 18 months, driving four wheelers or three wheelers between the ages of 4 and 7, driving tractors as early as 7 years, with many driving tractors by age 10 (Fig. 12.2). Children and parents reported that parents and grandparents decide when children are old enough to perform chores and that they learn how to perform chores by assisting under supervision and then performing independently. Safety information was learned from observation of parents and other workers on the farms, with the children being aware of inconsistencies between what they were told was safe and what safety practices they observed in others. The children also viewed being injured as a normal part of growing up and working on a farm. The attitude of children and adolescents toward safety equipment was that it was inconvenient, uncomfortable, and frequently unavailable. Further, since much of the equipment available, such as hearing protection, serves to protect injuries that will affect the children later in life, the use of such protection was not seen as immediately relevant (44,52–55).

Considerable attention and financial resources have been devoted to educational efforts to promote childhood farm safety, in part because education is the most acceptable prevention strategy among farm populations. A recent educational approach is the North American Guidelines for Children's Agricultural Tasks (NAGCAT) (http://www.nagcat.com), which assists parents in assigning developmentally appropriate and safe work for children aged 7 to 16 years. In 2003, Safe Kids Canada commissioned a systematic review to synthesize evidence about the application of NAGCAT and the efficacy or effectiveness of other strategies aimed at farm injuries to children (http://www.safekidscanada.ca/ENGLISH/IP_PROFESSIONALS/RuralSafetyProgram/SafeKidsFullRuralReport.pdf) (56–58).

The NAGCAT authors concluded:

1. Few studies have evaluated structural changes on farms to make them safer.
2. Prevention efforts were limited for toddlers and preschool children.
3. There are no evaluations of child care for farm children.

4. NAGCAT dissemination efforts were improved when accompanied by a visit to the farm by a safety professional or when child development principles were provided in conjunction with the guidelines.
5. School-based programs and safety day camps were effective in increasing short-term knowledge, but none addressed reduction of injuries as an outcome.
6. The results of tractor training programs and community-based interventions involving youth were inconsistent.

In a study among Hmong children involved in agricultural work, the authors concluded that NAGCAT could not be literally translated and disseminated due to cultural differences in task assignment, level of responsibility compared with North American children, more authoritarian parenting practices among Hmong parents, and the shorter stature of Hmong children. More information on farm task assignments among children and adolescents from other cultural groups, including migrant and seasonal farm workers, is needed to evaluate the relevance of the NAGCAT program. In addition, studies assessing injury outcomes are also needed for all prevention and intervention programs that are currently being used (58).

Conclusion

Worldwide, children and adolescents continue to make significant contributions to the agricultural work force, but the farm as a place for work and for play can be hazardous for them. Technology has altered the hazards in many developing economies, from increased potential for vectors of disease to increased exposure to pesticides. The increased used of heavy equipment will similarly shift the risks associated with farm work among children and adolescents. Progress toward recognition of hazards inherent in child labor has reduced the risks of farm injury in developed countries; that recognition needs to be applied in developing economies. Strategies need to be devised that address the different farm tasks and cultures in order to have a significant impact on health.

References

1. International Labour Office. Sustainable agricultural in a globalized economy. Report for discussion at the tripartite meeting on moving to sustainable agricultural development through the modernization of agriculture and employment in a globalized economy. Geneva: ILO Sectoral Activities Programme, 2000. www.ilo.org/public/english/dialogue/sector/techmeet/tmad00/tmadr.htm.
2. International Labour Office. A future without child labour. Report to the Director-General, International Labour Conference 90th Session. Geneva, International Labour Office, 2002. www.ilo.org/dyn/declaris/DECLARATIONWEB.INDEXPAGE.

3. Stellman, J.M., ed. Encyclopedia of Occupational Health and Safety, 4th ed. Geneva: International Labour Office, 1998.
4. International Labour Office. Stopping forced labour. Report to the Director-General, International Labour Conference, 89th session, International Labour Office, Geneva, Switzerland, 2001.
5. IPEC. Child labour in commercial agriculture in Africa. Technical Report. Geneva: International Labour Organization, 1997.
6. Pearson M, Jensen RT. Investigating the worst forms of child labour: rapid assessment synthesis report. Geneva: International Labour Organization, 2001.
7. National Academy of Sciences. Protecting Youth at Work: Health, Safety and Development of Working Children and Adolescents in the United States. Washington: National Academy Press, 1998.
8. Myers J. Special analysis of data from the National Institute and Health (NIOSH Traumatic Injury Surveillance of Farmer survey). Morgantown: National Institute for Occupational Safety and Health, 1995.
9. Lauener RP, Birchler T, Adamski J, et al. Expression of CD14 and Toll-like receptor 2 in farmers' and non-farmers' children. Lancet 2002;360:465–6.
10. Horak F, Studnicka M, Gartner C, et al. Parental farming protects children against atopy: longitudinal evidence involving skin-prick tests. Clin Exp Allergy 2002;32:1155–59.
11. Portengen L, Sigsgaard T, Omland O, Hjort C, Heedrik D, Doekes G. Low prevalence of atopy in young Danish farmers and farming students born and raised on a farm. Clin Exp Allergy 2002;32:247–53.
12. Remes ST, Iivanainen K, Koskela H, Pekkannen J. Which factors explain the lower prevalence of atopy amongst farmers' children? Clin Exp Allergy 2003;33:409–11.
13. Wickens K, Lane JM, Fitzharris P, et al. Farm residence and exposure and the risk of allergic diseases in New Zealand children. Allergy 2002;57:1171–9.
14. Van Wijngaarden E, Stewart PA, Olshan AF, Savitz DA, Buinn GR. Parental occupational exposure to pesticides and childhood brain cancer. Am J Epidemiol 2003;157:989–97.
15. Efird JT, Holly EA, Preston-Martin S, et al. Farm-related exposures and childhood brain tumours in seven countries: results from the SEARCH International Brain Tumour Study. Paediatr Perinatol Epidemiol 2003;17:201–11.
16. Cordier S, Ha M, Ayme S, Goujard J. Maternal occupational exposure and congenital malformations. Scand J Work Environ Health 1992;18:11–7.
17. Cordier S, Mandereau L, Preston-Marin S, et al. Parental occupation and childhood brain tumors: results from an international case-control study. Cancer Cause Control 2001;12:865–74.
18. Daniels J, Olshan A, Savitz D. Pesticides and childhood cancers. Environ Health Perspect 1997;105:1068–77.
19. Hanify J, Metcalf C, Nobbs L, Worsley K. Aerial spraying of 2,4,5–T and human birth malformations: an epidemiological investigation. Science 1981;212:349–76.
20. Schwartz D, LoGerfo. Congenital limb reduction defects in the agricultural setting. Am J Public Health 1988;78:654–7.
21. Thomas D, Petitti D, Goldhaber M, Swan S, Rappaport E, Hertz-Picciotto I. Reproductive outcomes in relation to malathion spraying in the San Francisco Bay area. Epidemiol 1992;3:32–9.

22. Grether J, Harris R, Neutra R, Kizer K. Exposure to aerial malathion application and the occurrence of congenital anomalies and low birth weight. Am J Public Health 1987;77:1009–10.
23. Restrepo M, Munoz N, Day N, et al. Birth defects among children born to a population occupationally exposed to pesticides in Colombia. Scand J Work Environ Health 1990;16:239–46.
24. Merchant D, Stallones L, Keefer S, Rickard R. An ecologic analysis of congenital anomalies and agricultural chemicals in Colorado, 1989–1991. J Agric Saf Health 1996;2:197–206.
25. Deane M, Swan S, Harris J, Epstein R, Neytra R. Adverse pregnancy outcomes in relation to water contamination, Santa Clara County, California, 1980–1981. Am J Epidemiol 1989;129:894–904.
26. Holmberg P, Hernberg K, Kurppa K, Rantala K, Riala R. Oral clefts and organic solvent exposure during pregnancy. Int Arch Occup Environ Health 1982;50:371–76.
27. Reed DB, Claunch DT. Nonfatal farm injuries incidence and disability to children. Am J Prev Med 2000;18:70–9.
28. National Research Council. Pesticides in the diets of infants and children. Washington: National Academy Press, 1993.
29. Cooper S, Darragh A, Vernon S, et al. Ascertainment of pesticide exposures of migrant and seasonal farmworker children: findings from focus groups. Am J Ind Med 2001;40:531–37.
30. Mensinga T, Speijers G, Menlenbelt J. Health implications of exposure to environmental nitrogenous compounds. Toxicol Rev 2003;22:41–51.
31. Wen ST, Chu KY. Preliminary schistosomiasis survey in the lower Volta River below Akosombo Dam, Ghana. Ann Trop Med Parasitol 1984;78:129–33.
32. Habbari K, Tifnouti A, Bitton G, Mandil A. Helminthic infections associated with the use of raw wastewater for agricultural purposes in Beni Mellal, Morocco. Rev Santé Mediterrané Orientale 1999;5:912–21.
33. Bouhoum K, Amahmid O. Health effect of wastewater reuse in agriculture. Schriftenr Ver Wasser Boden Lufthyg 2000;105:241–7.
34. Cifuentes E, Gomez M, Blumenthal U, et al. Risk factors for *Giardia intestinalis* infection in agricultural villages practicing wastewater irrigation in Mexico. Am J Trop Med Hyg 2000;62:388–92.
35. Cifuentes E, Blumenthal U, Ruiz-Palacios G, Bennett S, Quigley M. Health risk in agricultural villages practicing wastewater irrigation in Central Mexico: Perspectives for protection. Schriftenr Ver Wasser Boden Lufthyg 2000;105: 249–56.
36. Singh N, Mishra AK. Anopheline ecology and malaria transmission at a new irrigation project area (Bargi Dam) in Jabalpur (central India). J Am Mosquit Con Assoc 2000;16:279–87.
37. Kobayashi J, Somboon P, Keomanila H, Inthavongsa S, Nambanya S. Malaria prevalence and a brief entomological survey in a village surrounded by rice fields in Khammouan province, Lao PDR. Trop Med Intern Health 2000;5:17–21.
38. Antoniou M, Economou I, Wang X, et al. Fourteen-year seroepidemiological study of zoonoses in a Greek village. Am J Trop Med Hyg 2002;66:80–5.
39. Broste S, Hansen D, Strand R, Stueland D. Hearing loss among high school farm students. Am J Public Health 1989;79:619–22.
40. Waters T. Musculoskeletal disorders among children and adolescents working in agriculture. J Agric Saf Health 2002;8:253–5.
41. Rivara F. Fatal and nonfatal farm injuries to children and adolescents in the United States. Pediatrics 1985;76:567–73.

42. Rivara F. Fatal and nonfatal farm injuries to children and adolescents in the United States, 1990–3. Inj Prev 1997;3:190–4.
43. McCurdy S, Samuels S, Carroll D, Beaumont J, Morrin L. Injury risks in children of California migrant Hispanic farm worker families. Am J Ind Med 2002;42:124–33.
44. Mason C, Earle-Richardson G. New York state child agricultural injuries: how often is maturity a potential contributing factor? Am J Ind Med 2002;S2:36–42.
45. Browning S, Westneat S, Donnelly C, Reed D. Agricultural tasks and injuries among Kentucky farm children: results of the Farm Family Health and Hazard Surveillance Project. S Med J 2003;96:1203–12.
46. Pryor S, Caruth A. Children's injuries in agriculture related events: the effects of supervision on the injury experience. Iss Comp Pediatr Nurs 2002;25:189–205.
47. Hubler C, Hupcey J. Incidence and nature of farm-related injuries among Pennsylvania Amish children: implications for education. J Emerg Nurs 2002;28:284–88.
48. Stueland D, Lee B, Nordstrom D, Layde P, Wittman L. A population based case-control study of agricultural injuries in children. Inj Prev 1996;2:192–6.
49. Stallones L. Fatal unintentional injuries among Kentucky farm children: 1979–1985. J Rural Health 1989;5:246–56.
50. Stallones L, Gunderson P. Epidemiological perspectives on childhood agricultural injuries within the United States. J Agromed 1994;1:3–18.
51. Lim G, Belton K, Pickett W, Schopflocher D, Voaklander D. Fatal and non-fatal machine-related injuries suffered by children in Alberta, Canada, 1990–1997. Am J Ind Med 2004;45:177–85.
52. Darragh AR, Stallones L, Sample PL, Sweitzer K. Perceptions of farm hazards and personal safety behavior among adolescent farmworkers. J Agric Saf Health 1998;S1:159–69.
53. Hawk C, Gay J, Donham K. Rural youth disability prevention program pilot survey: results from 169 Iowa farm families. J Rural Health 1991;7:170–79.
54. Aherin RA, Todd CM. Accident risk taking behavior and injury experience of farm youth. New Orleans, Proceedings ASAE Annual Meeting, 1989.
55. Kidd P, Townley K, Cole H, McKnight R, Piercy L. The process of chore teaching: implications for farm youth injury. Fam Commun Health 1997;19:78–89.
56. Marlenga B, Pickett W, Berg RL. Evaluation of an enhanced approach to dissemination of the North American Guidelines for Children's Agricultural Tasks: a randomized controlled trial. Prev Med 2002;35:150–9.
57. Pickett W, Hartling L, Crumley E, Klassen T, Brison R. A Systematic Review of Prevention Strategies for Childhood Farm Injuries. Final report to Safe Kids Canada. http://www.safekidscanada.ca/ENGLISH/IP_PROFESSIONALS/RuralSafetyProgram/SafeKidsFullRuralReport.pdf), 2003.
58. Rasmussen RC, Schermann MA, Shutske JM, Olson DK. Use of the North American Guidelines for children's agricultural tasks among Hmong farm families. J Agric Saf Health 2003;9:265–74.

13

Chemical Exposure: An Overview

James E. Lessenger

Key words: pesticides, growth regulators, fertilizers, nutrients, buffers, petroleum products

Agricultural chemicals comprise thousands of formulations, including petroleum products, pesticides, growth regulators, buffers, nutrients and fertilizers, and veterinary medications. These chemicals may be used as solids in granular, powder, pellet, or block form; liquids in mists and sprays; or in gaseous forms as fumigants or fuels. Application of chemicals to crops may be by sprays of liquids from aircraft or ground machines; broadcast of solids from aircraft, vehicles, or stationary sources; injection of gas, liquid, or solids into water, soil, animals, or feed; or gaseous exposure in fumigation cells. Animals may be dipped in pools of dilute insecticides to remove surface insects. To save on manpower and fuel, it is common to apply five or more chemicals at once to a crop, making it difficult to determine which are the relevant agents. Mass casualty situations may result from the sudden release of large quantities of chemicals from a manufacturing, storage, or transportation facility, or from the group's perception of a release as in mass psychogenic hysteria (Table 13.1) (1–3).

Exposure does not necessarily equal poisoning. If a person is working in an area where a chemical is being used, he or she may not be exposed. Exposure to a chemical may not mean there will be enough external or internal contact to produce the physiological changes of poisoning. Poisoning may not produce a clinical level of illness, impairment, or disability. It is a mistake to assume a person has become ill from a chemical just because he or she was present in the vicinity where it was thought to have been used. It is important to consider the differential diagnoses of chemical illness when evaluating an alleged chemical injury for causation (1).

The massive amount of information and misinformation in the public media about farm chemicals complicates the evaluation of the patient. Some chemicals produce a particularly noxious odor that can cause nausea or anxiety about exposure, yet cause none of the physiological processes of poisoning. Dursban™, for example, has a particularly obnoxious odor, and small

TABLE 13.1. Farm chemicals, pesticides, and other chemical agents (1,2,16).

- Farm chemicals
  - Gasoline fuels
  - Diesel fuels
  - Jet fuels
  - Oils and lubricants
  - Fluids (hydraulic, etc)
  - Kerosene (mixed with chemicals as applied to crops to make the pesticides settle on the leaves)
- Pesticides (Chapter 16)
  - Insecticides
    - Organochlorines
    - Organophosphates
    - Carbamates
    - Pyrethrins
    - Synthetic pyrethroids
    - Nicotine
    - Rotenone
    - Microbiologicals *(Bacillus thuringiensis)*
    - Elemental substances (sulfur)
  - Herbicides
    - Trichloro/dichlorophenoxyherbicides
    - Urea derivatives
    - Carbamates
    - Triazines
    - Glyphosate
  - Rodenticides
    - Coumadin and other anticoagulants
    - Strychnine
    - Sodium fluoroacetate
  - Fungicides
  - Carbamates
    - Organophosphates
    - Others, including sulfur, captan, captofol
  - Antimicrobials (disinfectants)
    - Triazine-S-triones,
    - Chlorine-releasing agents
    - Chlorine
    - Dichloronitrobenzene
- Growth regulators (Chapter 15)
  - Plant regulators
  - Insect regulators
- Buffers (to bring chemical mixtures to neutral pH before application)
- Nutrients and fertilizers (Chapter 14)
  - Elemental compounds
  - Anhydrous ammonia
  - Gypsum
  - Others
- Veterinary medications
  - Immunizations
  - Antibiotics
  - Hormones to promote growth and production

Source: Data from Lessenger (1), O'Malley (2), Tordoir et al. (4), Reigart and Roberts (5).

amounts can cause anxiety and fear in people when no significant exposure has occurred. As urban growth encroaches upon farmland, more and more people live adjacent to farms and farm animals. Unpleasant odors familiar to those people working in agriculture may be misinterpreted by new arrivals as dangerous toxicants. A careful history and physical examination can differentiate fears and anxiety from actual poisoning (6,7).

Clinical Presentation

An emergent presentation is seen in a person who is exposed to a chemical and becomes immediately ill and thinks agricultural chemicals are to blame. Most emergent chemical-related illnesses are seen in the hospital emergency department. A nonemergent situation is seen by many physicians in their offices where the patient may be sent after an emergency department visit. Alternatively, the patient may arrive directly from the workplace, either the

same day of the exposure or sometime later. The vital signs are typically stable and there may be a question whether the person was actually exposed or poisoned. The emergency department may not have the time to do a thorough history or have the resources of past records, private investigators' reports, governmental reports, site visits, and research to aid in the diagnosis and the determination of causation, impairments, disabilities, or future medical care. The office-based physician is often asked to determine these issues (1,7,8).

Case Study 1

A 34-year-old man who works as a certified pesticide applicator became profoundly vertiginous and collapsed while applying hydrogen cyanamide, a growth regulator applied to promote uniform budding in citrus. He was wearing a full protective ensemble, including overalls, boots, gloves, mask, goggles, and helmet. The patient was questioned extensively because hydrogen cyanamide can cause an Antabuse reaction when used by a person who has recently consumed alcohol or used alcohol-containing products. He denied using alcohol in any way, including after-shave and hair tonic.

In accordance with longstanding company protocols, coworkers removed the employee from the field, removed the protective ensemble, and decontaminated him with water. An ambulance was called and emergency medical technicians (EMTs) responded. They donned full protective gear, placed barriers around the patient, started intravenous fluids, and transported him to the hospital. The employee's blood pressure in the ambulance and on the way to the hospital was 90/40 mm Hg. At the emergency department, the patient was assessed by a triage nurse in the ambulance and sent through a decontamination shower. After decontamination, the patient was given intravenous fluids. Drug and alcohol blood tests were normal. The patient was hospitalized and his hypotension improved with intravenous fluids. He was still slightly hypotensive upon discharge.

Upon presentation at the consultant's office, the patient was still hypotensive and vertiginous. He denied using any alcohol or products containing alcohol for the 2 years he had been applying hydrogen cyanamide. Research confirmed that the chemical was a growth regulator and that concomitant use of it and alcohol would produce profound hypotension. A report was made to the health department, using a state form, and appropriate workers' compensation documents filed. Private investigators and government investigations failed to reveal any alcohol use by the patient. A review of the patient's complete medical records failed to reveal any other cause of the symptomatology and physical findings. Motion pictures of the patient taken by a private investigator failed to reveal any alcohol or drug use. The consultant arranged for a "hold" tube of blood from the emergency department to be analyzed. The only abnormal substance discovered was hydrogen cyanamide at levels just above the detection limit. The patient was followed by the

consultant for 6 weeks until his blood pressure returned to the normal range and his vertigo resolved. Three months after the incident the patient was working without symptoms. A repeated blood level of the chemical had the same results as the first one, demonstrating that trace amounts in the patient's blood was not the cause of the acute symptoms and physical findings. The worker was discharged as cured.

Case Discussion

The cause of the hypotension and vertigo was never fully delineated, even with a thorough workup, private investigator's investigation, and other tests. The patient was removed from exposure, decontaminated in the field and at the emergency department, and appropriately treated. A "hold" tube of blood showed only trace amounts of the substance, an anticipated finding. No specific treatment or antidote was necessary, other than intravenous fluids. By following proper procedures, the patient was treated without contaminating coworkers or emergency personnel.

Diagnosis

History

The history may be the only positive finding. It is important to list the precise symptoms and detail where and when they started. A precise record of when the symptoms started can establish a cause-and-effect relationship if they first occurred directly after a suspected exposure. Record what the patient was doing when the symptoms started and when he or she thought exposure occurred. When the patient thinks exposure occurred and what actually occurred may be more subjective than objectively true (Table 13.2).

Record the parameters of exposure. Was the patient working in a packinghouse and, if so, was the patient packing boxes of fruit or doing another job such as sorting out rotten fruit where the possibility of exposure to chemicals is greater? Was the patient operating equipment within a closed cab, becoming ill with no obvious exposure other than a strange odor? If the person was spraying in a closed cab and filtered air environment, there may be another cause of the illness such as influenza, food poisoning, or carbon monoxide poisoning from a leak from the exhaust pipes to the cab (Table 13.3).

If the person claims to have been exposed to a chemical, it is important to ask if the chemical was a liquid, solid, or gas, and what it smelled like. The color of the chemical is also important, because many chemicals are colorless but may have a distinctive odor. Ask if the patient actually saw the chemical or just assumed it was there. Sometimes the patient may be ill from another cause such as uncontrolled diabetes but may ascribe the illness to a chemical exposure.

TABLE 13.2. Diagnosis and treatment.

- Removal from exposure:
  - Evacuate patient
  - Retreat to a protected area (closed building)
  - Don protective gear
- Decontamination:
  - Remove contaminated clothing and dispose of properly (as chemical waste)
  - Shower and shampoo the patient carefully and completely
  - Protect medical handlers from secondary contamination
- Treat acute symptoms:
  - Cardiopulmonary resuscitation
  - Antidotes
  - Antiemetics
  - Anticonvulsants
  - Cardiorespiratory support
- When (or if initially) stable:
  - Learn the accurate name or names of the substances:
    - Material Safety Data Sheet (MSDS)
    - Containers and labels
    - Application records
    - Poison control centers
  - History:
    - Was the worker in the vicinity of the chemicals being used?
    - Was there contact and exposure?
    - Was there poisoning and illness?
    - Are there impairments?
    - Is there disability?
  - Physical examination:
    - Describe findings and how they evolve over time
  - Other sources:
    - Prior medical records
    - Private investigator's reports
    - Governmental investigations
    - Eyewitness accounts
    - Media accounts
    - Employer accounts
  - Research (see Table 13.4)
  - Work-site visit (Chapter 11)
- Decision making:
  - Treatment: may not be necessary after removal from exposure and decontamination
  - Causation:
    - Establish a most likely cause-and-effect relationship
    - Look for internal consistency of the patient's history and physical examination
    - External consistency with the research and other sources
  - Impairments:
    - Based on objective findings and compared to AMA guidelines of evaluation of impairment
  - Disabilities:
    - Inability to perform social functions such as work
  - Treatment plan for further medical care:
    - Design a treatment plan for long term care, if necessary

Ask for what purpose the chemical was being used and what is the normal use; the two uses may not be the same. Finally, ask about the progression of symptoms, and what made them better or worse. Since removal from exposure, have the symptoms improved?

It is important to ask when the person last ate before the onset of symptoms and if he or she was drinking alcoholic beverages, taking over-the-counter or prescription medicines, or using perfume. Fragrances can cause acute allergic symptoms; alcohol use while using certain growth regulators such as hydrogen cyanamide can cause an Antabuse reaction; and meals eaten at the site of contaminated fields can result in the accidental ingestion of chemicals (10–12).

Symptoms may vary by the formulation used, concentration, length of exposure, and personal protective equipment. For example, a person spraying

TABLE 13.3. Differential diagnosis in pesticide exposure.

Irritant contact dermatitis	Bronchitis
Dermatitis, solvents	Pityriasis rosea
Dermatitis, other chemical	Folliculitis
Allergic contact dermatitis	Urticaria
Dermatitis, detergent	Insect bite
Dermatitis, plants and insects	Epistaxis
Scabies	Thyroid disease
Chicken pox	Drug misuse (legal and illegal)
Drug eruption	Food poisoning
Influenza	Carbon monoxide poisoning
Gastroenteritis	Mass psychogenic hysteria
Sinusitis	Fraud
Acne vulgaris	Intentional homicide
Herpes zoster	Intentional suicide
Tinea cruris	Accidental suicide
Diabetes mellitus	

Source: Data from Lessenger et al. (8) and Lessenger and Reese (15).

organophosphates may only have one or two of the classic symptoms if the exposure is minimal. On the other hand, a person with headaches, nausea, vomiting, chills, and fever may have influenza and not a chemically related disease, even if the patient had been spraying all day without protective equipment. It is important, especially when determining causation, that the patient's history be internally consistent and consistent with his workplace and work task, and with what is known about the chemicals (9,13).

The differential diagnosis should be considered in each situation, and appropriate testing performed to rule out conditions such as diabetes, thyroid disease, and drug use that may mimic the symptoms of chemical exposure in an agricultural worker (Table 13.3) (8).

Physical Examination

The physical examination may not be helpful in determining if an exposure occurred. Rashes need to be carefully described and secondary changes due to scratching, infection, or treatment documented. Halogenated hydrocarbons can produce chloracne that may be confused with acne vulgaris in adolescents. Anhydrous ammonia can cause a characteristic hyperpigmented area after a burn heals. Petroleum products may cause irritative dermatitis. Scabies is common among farm workers. Allergic contact dermatitis may have a variety of causative agents (Table 13.3) (1,13).

Inhalation of dusts, mists, and gases may cause instantaneous or delayed bronchospasms, producing a constellation of symptoms from wheezing to respiratory collapse. Nausea, vomiting, diarrhea, and abdominal pain can be the result of chemical exposure or from alternate illnesses such as diabetes, food poisoning, or influenza. Food poisoning is common in people who work

in the fields and do not have the facilities to refrigerate their lunches. Anaphylaxis can result from envenomation by biting or stinging insects (9,14).

Neurological symptoms such as burning, numbness, tingling, twitching, or seizures may be immediate or can be a delayed result of exposures. For example, low-level chronic exposure to organophosphates can cause a delayed polyneuropathy or memory loss (15).

Ocular symptoms are common in persons exposed to powders, dusts, sprays, or mists. After decontamination, the sclera may be erythemic. The corneas must be carefully examined for clouding or opacities.

Laboratory Studies

Urine, blood, or hair testing for specific offending chemicals is expensive and time-consuming, and must be collected immediately after the exposure to obtain reliable results. In many cases the patient may be cured or deceased before results are returned from reference laboratories. Nevertheless, when looking retrospectively at an alleged chemical illness to see if exposure actually occurred or if the illness can be attributed to a specific substance, a blood or urine test for the specific offending chemical can be helpful. Therefore, it is useful to draw an extra tube of blood in the laboratory or emergency department and freeze it for later testing (1,8,9).

Blood, liver, and renal test results may be obscured by a preexisting disease and may be abnormal only in severe exposures. Nevertheless, such tests should be done as soon after the alleged exposure as possible to establish a baseline and to exclude other illnesses such as anemia, diabetes, thyroid disease, and infectious diseases. Rapid drug and alcohol tests can quickly document drug intoxication concomitant with, or masquerading as, a chemical related illness. Cholinesterase testing for organophosphate poisoning is discussed in Chapter 9 (16).

Research

Poison control centers are effective at calling employers, chemical companies, government agencies, or other entities to determine the exact name of the offending compound. These centers can also give a list of signs and symptoms to look for, assist in making a diagnosis, and advise on the latest treatment protocols (Table 13.4).

United States law mandates that employees exposed to chemicals must be given the Material Safety Data Sheet (MSDS) for any chemical with which they come in contact. Some employees may come into the emergency department or consultant's office with the MSDSs in hand along with container labels and other information. Container labels can give the precise chemicals and formulations to which the patient was exposed. Textbooks such as *Ellenhorn's Medical Toxicology* can be an invaluable aid. Online services through TOXLINE and PUBMED give timely and concise information on diagnosis

TABLE 13.4. Information resources.

Ellenhorn MJ, Schonwald S, Ordog G, Wasserberger J. Ellenhorn's Medical Toxicology. Baltimore: Williams and Wilkins, 1997.
Reigart R, Roberts J. Recognition and Management of Pesticide Poisonings, 5th ed. Washington, DC: U.S. Environmental Protection Agency, 1999.
Tordoir W, Maroni M, He F. Health Surveillance of Pesticide Workers. Shannon: Elsevier, 1994.
Poison control centers
U.S. National Poison Control Hotline:
800-222-1222 (emergency)
202-362-3867 (administrative)
202-362-8561 (TDD)
National Library of Medicine.
PubMed: www.hcbi.nlm.nih.gov/PubMed/
United States Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. ATSDAR Tox Profiles, 2003.
National Pesticide Information Center:
800-858-7378
nptn@ace.orst.edu
Global Information Network on Chemicals (GINC), maintained by the National Institute of Health Sciences, Japan. www.nihs.go.jp/GINC/
Material Safety Data Sheets (obtain from employer)

and treatment. The Agency for Toxic Substances and Disease Registry produces the ATSDR TOX Profiles, another helpful guide (Table 13.4) (5,17,18).

Site Visits

Visits to the location where the exposure or event occurred can greatly assist the physician in learning what happened, where the patient or patients were, and how the exposure occurred. Sometimes it can be demonstrated that no exposure could have occurred and there was mass psychogenic hysteria or intentional fraud (see Chapter 11) (19).

Case Study 2

A 12-year-old boy was riding his bicycle to a fast-food restaurant when he slipped and fell in a shallow puddle of a foul-smelling liquid in the restaurant's parking lot. He became nauseous, vomited, and left the parking lot feeling dizzy and with blurred vision. He stumbled home, pushing his bicycle. A bystander smelled the puddle of liquid and notified the police who discovered that a farm vehicle had spilled a 50-gallon barrel of dicofol, a chlorinated hydrocarbon and DDT analogue. The barrel was spilled as a truck drove into the fast-food restaurant and the employees didn't bother to clean it up.

At home, the boy lay on his bed with his soaked clothing and slept. When his mother came home, she found him somnolent and insisted he shower.

After the shower he felt better, but his mother laundered the clothing he was wearing, along with the bedding, and returned them to the boy's room. He continued to be symptomatic, even though she laundered the clothing several times. A week later the boy was referred to the consultant's office by the health department.

In the office, the boy was wearing clothing (not those he was wearing the day of the incident) that reeked of a hydrocarbon chemical. He was led to a back room and asked to disrobe. The clothing was taken outside and bagged. While the vital signs were normal, the boy was ataxic, demonstrated nystagmus, and his speech was slurred. His breath had a hydrocarbon odor. Samples of his blood, subcutaneous fat and urine were collected and were later found by a reference laboratory to be positive for dicofol. A complete blood count, urinalysis, and blood chemistries were all normal.

The boy's mother was asked to destroy all clothing, furniture, and appliances that had come in contact with the contaminated clothes the boy was wearing the day of the incident. This resulted in the destruction of the family's entire wardrobe, the boy's bed, a couch, and the washer. A report was made to the county health department as required by state law. A week after the decontamination, the ataxia, nystagmus, and hydrocarbon breath were gone. The slurred speech resolved in 2 weeks. A month after the exposure, a psychological test demonstrated cognitive and emotional deficiencies. A second test performed 2 months later was normal. Three months after decontamination, the boy was completely normal and he remained so for another 2 years of monitoring. No medication or treatment was given other than removal from exposure and decontamination.

Case Discussion

This case demonstrates the critical importance of removal from exposure and decontamination. Both were delayed in this case and the delay caused the persistence of the symptoms and the possible exposure of other family members. Once the patient was removed from exposure and the house properly decontaminated, his symptoms subsided. The boy was monitored for 2 years before the case was completely closed, but he suffered no residual impairments or disabilities once he was over the acute phase.

Management

Presentation

It is helpful to stage chemical injuries as mild, moderate, and severe based on symptoms and signs. Mild poisonings demonstrate few symptoms and normal vital signs. Moderate poisonings demonstrate more severe symptoms, objective signs, and normal vital signs. Severe poisonings demonstrate multiple complaints, objective signs, and unstable (or abnormal) vital signs.

Mild and moderate poisonings can usually be evaluated on an outpatient basis. Once patients have been removed from exposure and decontaminated, they rarely require treatment other than an antiemetic for nausea and vomiting or topical steroids for a rash (1,8).

Severe poisonings usually require hospitalization and intensive physiological support. Decontamination may include gastrointestinal lavage for accidental or deliberate ingestion. In cases of suicide or homicide, one or more poisons may be involved (2,12).

Removal from Exposure

Whether the patient is seen in the emergency department or the office, it is imperative that the patient be removed from exposure until the symptoms and causes of the illness can be diagnosed and decontamination assured. Removal from exposure may not equate with complete removal from work. It may be possible to return the employee to modified duty while the workup and treatment are in progress. In mass causality situations, evacuation to a safe location or sequestration in a secure building with the windows closed and the air conditioning off may be necessary to prevent further inhalation of the agents (4,12).

Resuscitation

In emergent cases where the vital signs are unstable and there is respiratory arrest or cardiac arrest, aggressive resuscitation using the standard protocols is indicated. If the patient is unstable with abnormal vital signs, decontamination can be carried out simultaneously with resuscitation (1,3,4).

Decontamination

Decontamination includes removal of the offending chemical from the person, clothing, and personal protective equipment. Decontamination of the person should include a thorough irrigation of the eyes if they have been subjected to any exposure. The sooner the eyes are irrigated, the less damage that will occur and workers are taught to use eye irrigation stations near their work site in the event of eye exposure. Careful attention should be paid to scalp hair, the axillae, and pubic hair because they are usually ignored in decontamination. Improved decontamination can be carried out if screens or other mechanisms are used to ensure privacy when exposed workers disrobe. Medical personnel are at risk of exposure during decontamination and should use protective measures, including chemical-resistant gloves (2,12).

If the offending chemical is consumed, typically by eating contaminated food in the fields, it may be necessary to decontaminate the gut. Recalling that many agricultural chemicals are based on hydrocarbons, activated char-

coal may be the best method so that vomiting won't be induced, with its accompanied risk of aspiration into the lungs (12).

It is typically impossible to decontaminate contaminated clothing. If they are laundered, the laundry machines can become contaminated. They are typically placed in plastic bags as chemical waste to be disposed of in compliance with local rules, either by incineration or removal to a hazardous waste depository.

Antidotes

Antidotes such as atropine, pralidoxime, and vitamin K are rare. In China, studies have demonstrated that the use of antidotes brought people near death when they didn't have a pesticide injury. Atropine and pralidoxime are useful as antidotes in organophosphate and carbamate poisoning when they are used to treat bradycardia and hypotension, and in drying up copious secretions (Table 13.5) (4,17,20).

TABLE 13.5. Antidotes and specific treatments.

Atropine	Organophosphate or carbamate poisoning	Adults: 2–4 mg every 10–15 minutes to symptoms, i.v. Children: 0.015 to 0.5 mg/kg every 15 minutes to symptoms, i.v.
Pralidoxime (2PAM) Protopam™	Organophosphate and carbamate poisoning (cholinesterase reactivant)	Adults: 4 mg/kg over 4 to 6 hours or 8 to 10 mg/kg/hr, i.v. or 1 to 2 g over 15 to 30 minutes, i.v., repeated every 1 to 2 hours by symptoms Children: 25 mg/kg loading dose, followed by 20 mg/kg/hr until symptoms have abated
Vitamin K Phytonadione Mephyton™ AquaMephyton™	Coumadin (Rodenticide)	Adults: 10 to 25 mg/kg p.o. or 2 to 5 mg p.o. 2.5 to 25 mg s.q. or i.m. (or rarely up to 50 mg) every 6 hours to symptoms Children: 5 to 10 mg/kg p.o. or 2.5 to 25 mg s.q. or i.v. every 6 hours adjusted to severity of symptoms
Physostigmine	Muscarinic effects of anticholinesterase chemicals; use in situations of severe poisoning and excessive agitation, long-lasting seizures, and cardiac arrhythmias	Adults: 2 mg i.v. and 1 to 2 mg every 20 minutes until response Children: 0.02 mg/kg i.v.

continued

TABLE 13.5. Antidotes and specific treatments. (continued)

Diazepam	Seizures in cholinesterase and carbamate poisoning	Adults: 5 to 10 mg i.v., s.q., or rectally Children: 1 to 5 mg, i.v., s.q., or rectally
Perchlorperazine Compazine™	Antiemetic	Adults: 5 to 10 mg, p.o. every 6 to 8 hours, 5 to 10 mg i.m. every 6 to 8 hours, 2.5 to 10 mg i.v. every 6 to 8 hours to symptoms Children: Not indicated under 2 years. Over 2 years of age: 0.06 mg/lb every 6 to 8 hours
Promethazine (Phenergan)	Antiemetic	Adults: 25 mg p.o. or i.m. every 4 to 6 hours Children: 0.5 mg/lb every 4 to 6 hours i.m. or p.o.

Source: Data from Tordoir et al. (4) and Ellenhorn et al. (17).

Reports

In jurisdictions where required, reports must be made to the workers' compensation insurance carrier and appropriate government agency.

Follow-Up

Serial examinations to follow chronic sequelae of chemical exposures may be necessary. Work impairments and disability status require documentation on an ongoing basis, especially if the patient is receiving disability payments. A long-term treatment plan may be required by insurance companies.

References

1. Lessenger JE. The pesticide-exposed worker: an approach to the office evaluation. J Am Board Fam Pract 1993;6:33–41.
2. O'Malley M. Clinical evaluation of pesticide exposure and poisonings. Lancet 1997;349:1161–6.
3. Jones TF, Craig AS, Hoy D, et al. Mass psychogenic illness attributed to toxic exposure at a high school. N Engl J Med 2000;342:96–100.
4. Tordoir W, Maroni M, He F. Health Surveillance of Pesticide Workers. Shannon: Elsevier, 1994.
5. Reigart R, Roberts J. Recognition and Management of Pesticide Poisonings, 5th ed. Washington, DC: U.S. Environmental Protection Agency, 1999.
6. Schiffman SS, Walker JM, Dalton P, et al. Potential health effects of odor from animal operations, wastewater treatment and recycling of byproducts. J Agromed 2000;7:7–81.
7. Simpson WM, Brock CD. Chemophobia, family medicine, and the doctor-patient relationship. J Agromed 2003;9:7–16.

8. Lessenger JE, Estock MD, Younglove T. Analysis of 190 cases of suspected pesticide illness. J Am Board Fam Pract 1995;8:278–82.
9. Agency for Toxic Substances and Disease Registry. Obtaining an exposure history. Am Fam Physician 1993;48:483–91.
10. Lessenger JE. Occupational acute anaphylactic reaction to assault by perfume spray in the face. J Am Board Fam Pract 2001;14(2):137–40.
11. Lessenger JE. Case study: hypotension, nausea and vertigo linked to hydrogen cyanamide exposure. J Agromed 1998;5(3):5–11.
12. Kales SN, Christiani DC. Acute chemical emergencies. N Engl J Med 2004;350:800–8.
13. Danse IR. Common Sense Toxics in the Workplace. New York: Van Nostrand Reinhold, 1991.
14. Waller K, Prendergast TJ, Slagle A, Jackson RJ. Seizures after eating a snack food contaminated with the pesticide Endrin. West J Med 1992;157:648–51.
15. Lessenger JL, Reese BE. The pathophysiology of acethlcholinesterase inhibiting pesticides. J Agromed 2000;7:5–19.
16. Lessenger JE, Reese BE. The rational use of cholinesterase testing in pesticide poisoning. J Am Board Fam Pract 1999;12:307–14.
17. Ellenhorn MJ, Schonwald S, Ordog G, Wasserberger J. Ellenhorn's Medical Toxicology, 2nd ed. Baltimore: Williams and Wilkins, 1997.
18. Agency for Toxic Substances and Disease Registry. ASTAR Tox Profiles. Atlanta: Department of Health and Human Services, 2003.
19. Lessenger, JE. Case report: fraudulent pesticide injury: value of the work site visit. J Agromed 1996;3:27–32.
20. He F, Wang S, Liu L, Chen S, Zhang Z, Sun J. Clinical manifestations and diagnosis of acute pyrethroid poisoning. Arch Toxicol 1989;63:54–8.

14

Fertilizers and Nutrients

Hitoshi Nakaishi and James E. Lessenger

Key words: ammonia, nitrogen, phosphorus, potassium, micronutrients

A fertilizer is any substance used to make soil more fertile. Plants need large amounts of three nutrients, commonly referred to as macronutrients:

1. Nitrogen
2. Phosphorus
3. Potassium

Fertilizer manufacturers extract these three nutrients from natural sources and convert them into soluble forms that plants can easily use.

Nitrogen-Containing Fertilizers

Ammonia

Ammonia (NH_3) is used as an applied fertilizer or as a building block for other fertilizer products. At room temperature it is a colorless, flammable gas with a pungent, suffocating odor. It becomes a clear, colorless liquid under increased pressure and is usually shipped as a compressed liquid in steel cylinders. Anhydrous ammonia is the form used primarily in refrigeration and agriculture. Ammonia is also stored as a refrigerated liquid under pressure and is injected into the soil or irrigation water as a gas after being exposed to air.

Ammonia dissolves in water to form ammonium hydroxide, a basic corrosive solution. Concentrations of ammonium hydroxide vary from 5% to 10% for household use and 25% or more for industrial use (1).

The American Conference of Governmental Industrial Hygienists (ACGIH) occupational exposure limits for ammonia are 25 ppm for 8-hour time-weighted average (TWA) and 35 ppm for short-term exposure (less than 15 minutes). Advice on the correct medical treatment for exposed persons must be available at all work areas (1).

The most common way for ammonia to enter the body is through the respiratory system (inhalation). Clinical results of ammonia inhalation can

include coughing, hoarseness, wheezing, narrowing of throat, pulmonary edema, upper airway obstruction, chest pain, runny nose, tearing of the eyes, impaired vision, headache, and dizziness (2–4).

Ammonia irritates the skin and can cause chemical burns ranging from mild to severe, depending on the concentration of the ammonia solution or vapor and the length of time of the exposure. Concentrated vapor or solution may cause pain, redness of the skin, and blisters. Liquefied ammonia splashed or sprayed on skin can cause frostbite, tissue necrosis, or severe burns. These burns are caused by a freeze-dry effect that can freeze and desiccate large areas of skin and produce deep ulcerations if not properly and quickly decontaminated (5,6).

Ammonia, even at low concentrations, can irritate the eyes and cause burning, edema, photophobia, sloughing of the surface cells of the eye, and, in severe cases, blindness. Immediate burning in the mouth and throat occurs when ammonium hydroxide is swallowed, typically in a suicide attempt. Ingestion of concentrated solution can cause severe pain in the mouth, chest, and abdomen, swallowing difficulty, drooling, and vomiting. Burns and perforation of the esophagus or stomach can occur (6,7).

As the concentration of ammonia vapor increases, the symptoms of exposure become more severe. Acute exposures to ammonia can cause immediate burning of the eyes, nose, throat, and respiratory system and can result in death. Itchy eyes, coughing, and a burning nose are warning signs of potentially hazardous exposure levels. Continued short-term exposure may lead to tolerance of the ammonia scent, and workers may no longer be aware of ammonia's presence and potentially increasing and dangerous concentrations. The very young, the elderly, and people with pulmonary problems are at an increased risk from the effects of ammonia exposure (Table 14.1) (4–8).

Short-term exposures to ammonia do not often result in long-term or chronic health effects, except for eye injuries. Long-term effects are usually found with people who have repeated exposures to ammonia. These repeated ammonia exposures can have chronic effects on the lungs, nose, and eyes. Case reports have noted chronic inflammation of bronchi, airway hyperactivity, and chronic irritation of the eye membranes. Some authors reported

TABLE 14.1. Symptomatology at various exposure levels.

Ammonia concentration (ppm)	Effect on health
100	Concentration can be tolerated for several hours
400	Throat irritation
700 (visible cloud)	Eye injury, lung irritation, skin irritation
1700	Laryngospasm, coughing, glottal edema, labored breathing
2500	A half-hour exposure can be fatal
5000 or greater	Death results from cardiorespiratory arrest

Source: Data from Lessenger (8).

interstitial lung disease due to repetitive occupational exposure to ammonia. Consequences of chronic exposure may also include pneumonia, kidney damage, cataracts, glaucoma, ulceration and perforation of the cornea, and blindness (7,9).

Before working with ammonia, workers should be trained in its proper handling and storage and should know how to use proper personal protective equipment (7,9).

Materials Management

Ammonia should be stored in a cool, dry, well-ventilated area and in tightly sealed containers protected from exposure to weather, extreme temperature changes, and physical damage. It should be separated from oxidizers, combustible materials, heat, sparks, and open flame. As a liquefied gas, ammonia is flammable. Sources of ignition usually include smoking or open flames. Ammonia is considered a strong oxidizer, and steps should be taken to separate ammonia and ammonia products from incompatible materials such as copper, brass, bronze, galvanized steel, tin, or zinc (10).

Personal Protective Equipment

Workers can avoid skin contact with ammonia by wearing protective gloves and chemical-resistant clothing when handling ammonia. The U.S. National Institute for Occupational Safety and Health (NIOSH) recommends that workers wear gloves made of butyl, Teflon, or Viton for up to 8 hours of exposure, and nitrile gloves for up to 4 hours of exposure. Workers should also wear safety glasses when handling cylinders. During change-out of tanks or when exposure to gas is a risk, workers should wear vapor-proof goggles and a face shield. Respiratory protection should be approved by NIOSH specifically for ammonia and used in accordance with the Occupational Safety and Health Administration (OSHA) Respiratory Protection Standard (9,10). Under routine exposures where the ambient concentration of ammonia exceeds 25 ppm, the workers should use an air-purifying, full-face respirator equipped with chemical cartridges appropriate for ammonia. For exposures of unknown concentrations of ammonia, such as uncontrolled releases, only a pressure-demand, self-contained breathing apparatus (SCBA) is appropriate. Respirator use must be limited to individuals who have been adequately trained, have undergone a qualifying medical examination, and have been fitted for the respirator face piece. Refer to the Process Safety Management of Highly Hazardous Chemicals Standard. Ammonia presents a potential for a catastrophic event at or above the threshold quantity of 10,000 ppm according to the List of Highly Hazardous Chemicals, Toxics and Reactives (Mandatory) (in 29 CFR 1926.64 Appendix A) (11,12).

Anhydrous ammonia is used in vast quantities in worldwide agriculture. As a consequence, exposures to it can be used as a prototype for exposures to other fertilizers and nutrients.

First-Aid Management

If an ammonia spill or leak occurs, it is very important to remove the exposed person(s) to fresh air. Notify fire and company safety personnel. If the worker is contaminated with ammonia, follow these steps for decontamination prior to administering first aid:

1. If the worker is not breathing, begin artificial respiration.
2. If the worker is breathing, place him or her in a seated position or lying down with the head and upper body in an upright position. Encourage slow, deep, regular breaths. Administer oxygen as soon as possible.
3. Keep the person warm and quiet. Seek medical attention. Persons with serious symptoms may need to be hospitalized (9).

Decontamination

Clothing or skin soaked with ammonia solutions may be caustic and expose rescuers, as well as workers, to vapors. To decontaminate, all soaked clothing should be removed from the worker and immediately double-bagged. Exposed skin and hair should be irrigated with water for 15 minutes, and seek medical attention immediately if frostbite has occurred. Do not rub the skin. Care must be exercised in removing the clothing as the cloth may be frozen to the skin and if the cloth is rapidly removed, whole slabs of skin may come with it. Exposed or irritated eyes should be flushed with water or saline solution for 15 minutes. Contact lenses should be removed. For ingested ammonia, give the worker at least two glasses of water or milk immediately and remove to an emergency department or similar facility (8,9).

Hospital Care

Decontamination needs to be ensured as soon as the injured worker reaches the hospital to limit the extent of the injuries and avoid contamination of hospital workers. Table 14.2 provides a triage guide to separate injured workers into treatment categories. Severe eye injuries require ophthalmological consultation; severe lung injuries require aggressive management with oxygen, antibiotics, bronchodilators, and steroids. Skin burns may require aggressive decontamination and open management to allow for the degassing of the ammonia from liquefaction of the wounds. Full-thickness burns may eventually require grafts.

Spill Management

Ammonia spills can become increasingly dangerous if they are not contained promptly. Table 14.3 summarizes the actions to be taken if a spill has occurred.

TABLE 14.2. Ammonia emergency triage guide.

Severity	Findings and disposition	Findings
Mild	Symptoms	Mild catarrhal symptoms
		Stinging in eyes and mouth
		Pain on swallowing
		Tightness of the throat
	Vital signs	Stable and normal
	Signs	Good color
		Swelling of eyelids
		Reddening of lips, mouth tongue
		Odor of ammonia
		Minimal throat edema
		Normal chest sounds
	Disposition	Can usually be sent home with minimal treatment
Moderate	Symptoms	Burning of eyes, mouth throat
		Tightness of chest
		Hoarseness
		Difficulty swallowing
	Vital signs	Abnormal or normal
	Signs	Cough, productive of tenacious, blood-stained sputum
		Conjunctiva and eyelids swollen
		Tearing mucous membrane with edema and patches of denuded tissue
		Rales and rhonchi on chest examination
	Disposition	Admission, treatment and further tests
Severe	Symptoms	Decreased level of consciousness and extreme pain
	Vital signs	Unstable and abnormal
	Signs	Shock
		Pulmonary edema
		Severe respiratory distress
		Corneal and skin burns
	Disposition	Admission, intensive care; cardiopulmonary support

Source: Data from Brautbar et al. (7) and Lessenger (8).

TABLE 14.3. Response to a anhydrous ammonia spill.

Notify trained response personnel immediately. Untrained persons or those without proper personal protective equipment must not enter areas with high concentrations of ammonia or visible vapor clouds.

Evacuate people for at least 50 feet in all directions and have them stay upwind from the ammonia release. If evacuation is impossible, people should be sheltered in a building with the doors and windows shut and air conditioners turned off.

Stop or control the source of exposure. If the exposure is from a leaking cylinder, take the cylinder outdoors or to an open area until it has completely drained and the contents have evaporated.

Ventilate potentially explosive atmospheres by opening windows and doors.

Keep combustibles such as wood, paper, and oil away from the leak.

Remove all sources of heat and ignition.

Refer to the manufacturer's Material Safety Data Sheet (MSDS) for more information.

Source: Data from McCunney (9).

Case Study

A 22-year-old man was running a hose from an anhydrous ammonia tank to a water standpipe to allow the ammonia to bubble into the irrigation water to fertilize crops. As the worker turned on the ammonia, the hose ruptured, spraying the worker on his leg with a stream of ammonia and releasing a cloud of ammonia vapor. The worker collapsed to the ground. A coworker who witnessed the release approached the tank from upwind, and shut the spray off at the valve on the top of the tank. The coworker drove the worker to the emergency room where the exposed worker was found to have a large part of his left trousers leg frozen to his thigh. His eyes were erythemic, but his lungs were clear to auscultation. Immediately, his eyes were irrigated with copious amounts of normal saline and the frozen area of his thigh gently warmed with tap water until the cloth fell off on its own and without tugging. The freeze-burns were copiously irrigated and left open to the air to off-gas (Figure 14.1).

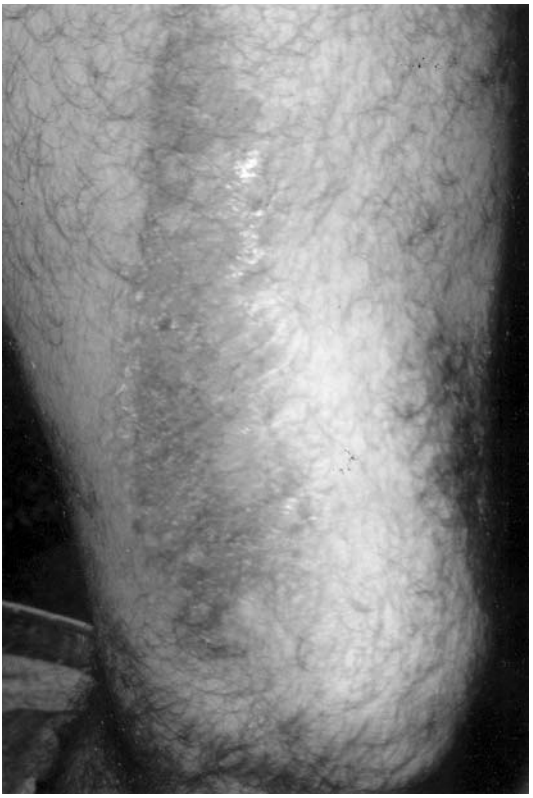


FIGURE 14.1. Chemical freeze-burn on a thigh caused by anhydrous ammonia. (Photo by James E. Lessenger.)

A week later, the eye complaints were resolved. It took a full 2 months for the freeze-burns to resolve, but the patient was left with areas of permanent hyperpigmentation where the burns had been.

Case Discussion

This worker's fellow employees missed the opportunity to flush his eyes out with water and irrigate the injured area in the field. As a consequence, his injuries were worse than they could have been. Ammonia, as an alkali, forms viscous skin liquefaction when it comes in contact with skin, as opposed to acids, which cauterize the wound. The viscous liquefaction contains ammonia that continues to propagate the wound until it degasses or becomes dilute. As a consequence, the wound needs to be copiously irrigated and ointments and creams avoided (6–8).

Urea

Urea [$(NH_2)_2$ CO] is a solid nitrogen product typically applied to crops in granular form. It can also be combined with ammonium nitrate and dissolved in water to make liquid nitrogen fertilizer. Urea can be absorbed into the body by inhalation of its aerosol and by ingestion. Urea's evaporation point at 20° C is negligible. A nuisance-causing concentration of airborne particles can be reached quickly if urea is powdered (11,12).

Urea irritates the eyes, skin, and respiratory tract. Urea inhalation produces cough, shortness of breath, and sore throat. Exposure to skin or eye evokes redness. Ingestion may produce convulsions, headache, nausea, and vomiting. Repeated or prolonged contact with skin may cause dermatitis. To prevent such effects, rinse and wash skin with water and soap and rinse the eyes with plenty of water. In case of ingestion, allow the patient to drink plenty of water to dilute the urea (12,13).

Ammonium Nitrate

Another solid nitrogen product typically applied in granular form, ammonium nitrate (NH_4NO_3) does not have any reported occupational health problems. The dust arising from ammonium nitrate is of low toxicity and is generally regarded as a nuisance dust; 10 mg/m^3 (for an 8-hour exposure) is accepted as the permitted level provided the particle size is above 5 fm. Ammonium nitrate may decompose in a fire, and storage areas should be suitably designed for the presence of combustible material with easy access to stacks of bags, with spacing between stacks. Oxides of nitrogen are emitted during decomposition of ammonium nitrate (14).

Ammonium Sulfate

Ammonium sulfate [$(NH_4)_2SO_4$] is a solid product that is largely a by-product of coke ovens where sulfuric acid is used to remove ammonia evolved from the coal. Its oral human median toxic dose (TD_{50}) is 1500 mg/kg, the domestic animal median lethal dose (LD_{50}) is 3500 mg/kg, and rat lethal dose (LD_{50}) is 3000 mg/kg. No known adverse chronic effects are associated with ammonium sulfate (15,16).

The material consists of brownish gray to white crystals or granules. Ammonium sulfate is moderately irritating to the eyes and skin, especially with prolonged contact to dust. Inhalation may cause sore throat, coughing, or shortness of breath. It is moderately toxic by ingestion and may cause sore throat, abdominal pain, diarrhea, nausea, and vomiting. Animal studies suggest that ulceration or hemorrhage of the gastrointestinal tract can occur. Systemic ammonia poisoning is possible if sufficient absorption occurs (16).

Ammonium sulfate does not burn but decomposes at 282°C to release ammonia gases and sulfur oxides. Individuals with asthma may be at increased risk from exposure to ammonium sulfate (16–18).

First-Aid Measures

These measures are the same as for anhydrous ammonia.

Spill Management

Firefighters should wear a National Institute for Occupational Safety and Health (NIOSH) approved self-contained breathing apparatus with a full face piece and protective clothing to prevent contact with skin and eyes. Use a water spray to cool fire-exposed containers. Do not spray water directly on the material. Accidental mixing with oxidizers like potassium chlorate, potassium nitrate, or potassium nitrite may result in an explosion hazard during fires. Sulfur oxides and ammonia gases may be formed in fires involving ammonium sulfate (10–12).

Storage and Use

Workers should wear personal protective equipment and avoid contact with skin, eyes, and clothing. Workers must avoid breathing dusts, wash thoroughly after handling, and use with adequate ventilation. Contaminated clothing should be laundered before reuse.

Ammonium sulfate should be stored in a cool, dry area, away from strong oxidizers. For exposure control and personal protection, natural or mechanical ventilation sufficient to maintain levels below the recommended exposure levels should be provided. In adequately ventilated areas, respiratory protection is not required. For exposure above the threshold limit value (TLV), a NIOSH-approved dust respirator should be used.

For eye protection, indirectly vented safety goggles are recommended against nuisance dust containing ammonium sulfate. Workers handling such dust should not wear contact lenses. For skin protection, workers handling ammonium sulfate should wear long-sleeved shirt and pants or coveralls and work gloves to minimize skin contact. An eyewash station and safety shower should be provided that are convenient to the work area.

Ammonium sulfate should not be stored or used near oxidizers, peroxides, potassium chlorate, potassium nitrate, sodium nitrate, metal chlorates, and strong bases. It is corrosive to carbon steel, copper, and copper alloys and should not be heated above 100°C to avoid decomposition (10–12).

Phosphorus-Containing Fertilizers

Monammonium phosphate (MAP) and diammonium phosphate (DAP) are called ammoniated phosphates because phosphoric acid is treated with ammonia to form these basic phosphate products that also contain nitrogen. They are widely produced in the granular form for blending with other types of fertilizers and are also produced in nongranular forms for use in liquid fertilizers. MAP and DAP can be toxic to the lungs in high concentrations. There are several emission standards for hazardous air pollutants from phosphoric acid and phosphate fertilizer production (18,19).

Potassium-Containing Fertilizers

After potassium is mined as potash, potassium chloride (KCl) is separated from the mixture, resulting in a granular fertilizer.

As an inhalation risk, evaporation at 20°C is negligible. A nuisance-causing concentration of airborne particles can be reached quickly when dispersed, especially in powdered form. Inhalation of KCl causes cough and sore throat, and exposure to the substance brings about eye redness or pain. Therefore, workers handling KCl should wear safety goggles. Exposed eyes should be rinsed with plenty of water for several minutes and contact lenses should be removed. Medical consultation should be sought as soon as possible.

Potassium chloride can be absorbed into the body by accidental or deliberate ingestion. When potassium chloride is ingested, diarrhea, nausea and vomiting, and sometimes weakness or convulsions may be evoked. KCl poisoning results in cardiac dysrhythmias when ingested at high amounts. To avoid such incidents, workers should be prohibited from eating, drinking, or smoking during application of fertilizer. In cases when ingestion is suspected, the mouth should be rinsed. In conscious persons, induce vomiting (20).

Micronutrient Fertilizers

Micronutrients are typically not combined with insecticide or fungicide sprays unless the manufacturer's directions indicate that this may be done. They can be applied to soil, irrigation water, or directly to the foliage of the plants.

Calcium

Airflow obstruction is reported among workers handling limestone. Results of human exposure to elemental calcium or carbonates is limited to contact dermatitis, irritation of the eyes, and lung irritation if the dusts are inhaled. There are no specific treatments or antidotes (21).

Magnesium

Magnesium (Mg) is a minimally toxic substance in agriculture. If swallowed, large amounts of concentrated solution can be fatal, due to cardiac dysrhythmias. Magnesium can also cause contact dermatitis and eye irritation. Magnesium competes with calcium in the body, so calcium can be used as an antidote in magnesium poisoning. The adult dose of calcium gluconate is 10 mL of 10% solution over 15 minutes (22).

Manganese

Workers chronically exposed to manganese-laden dust in agricultural settings develop neuropsychological changes that resemble Parkinson's disease. Acute renal failure following ingestion of manganese-containing fertilizer is reported. After decontamination, treatment is supportive (23,24).

Zinc

Zinc oxide is the most common cause of metal fume fever, a condition characterized by shortness-of-breath, fatigue, cough, dyspnea, leukocytosis, thirst, salivation, and an elevated temperature caused by the inhalation of metal fumes. The most common source of metal fume fever and zinc exposure in agriculture is through welding zinc-coated metal products. Other causes of metal fume fever are fumes of copper, magnesium, aluminum, antimony, iron, manganese, and nickel. Metal fume fever from agriculture micronutrients has not been described in the literature. The condition is usually self-limiting and treatment is supportive (25).

Copper

Copper sulfate is a gastric irritant that produces erosion of the lining of the gastrointestinal tract. Chronic copper toxicity is rare and primarily affects the liver. Copper poisoning in agriculture is rare and is usually associated with metal fume fever or accidental ingestion. Treatment is supportive and, in the case of ingestion, requires cathartics and activated charcoal (26).

Boron

In humans, chronic, low-level boron exposure has been shown to cause growth retardation, cutaneous disorders, and suppression of the male reproductive system function. Treatment is limited to removal from exposure and treatment of cutaneous disorders by decontamination and topical steroids (27,28).

References

1. American Conference of Governmental Industrial Hygienists (ACGIH). Documentation of the Threshold Limit Values and Biological Exposure Indices, 6th ed. Cincinnati: ACGIH, 1996.
2. Leduc D, Gris P, Lheureux P, Gevenois PA, De Vuyst P, Yernault JC. Acute and long term respiratory damage following inhalation of ammonia. Thorax 1992;47:571–6.
3. Flury KE, Dines DE, Rodarte JR, Rodgers R. Airway obstruction due to inhalation of ammonia. Mayo Clin Proc 1983;58:389–93.
4. Close LG, Catlin FI, Cohn AM. Acute and chronic effects of ammonia burns on the respiratory tract. Arch Otolaryngol 1980;106:151–8.
5. Latenger BA, Lucktong TA. Anhydrous ammonia burns: case presentation and literature review. J Burn Care Rehab 2000;21:40–2.
6. Lessenger J. Medical management of anhydrous ammonia emergencies. Plant Operations Progress 1985;4:20–5.
7. Brautbar N, Wu MP, Richter ED. Chronic ammonia inhalation and interstitial pulmonary fibrosis: a case report and review of the literature. Arch Environ Health 2003;58:592–6.
8. Lessenger JE. Anhydrous Ammonia injuries. J Agromed 1996;3:13–26.
9. McCunney RJ. Emergency response to environmental toxic incidents: the role of the occupational physician. Occup Med (London) 1996;46:397–401.
10. Occupational Safety and Hazard Administration. Respiratory Protection Standard, 29 CFR (Code of Federal Regulations) 1910.134.
11. Occupational Safety and Hazard Administration. Process Safety Management of Highly Hazardous Chemicals Standard 29 CFR 1910.119.
12. Occupational Safety and Hazard Administration. List of Highly Hazardous Chemicals, Toxics and Reactives (Mandatory), 29 CFR 1926.64 Appendix A.
13. Zlatev Z, Todorova K, Anastasova N, Chuturkova R, Yaneva A, Sabera Y. Assessment of the working-environment harmful factors and health risk of workers in a nitrogen fertilizer plant. Int Arch Occup Environ Health 1998;71:S97–100.

14. Donoghue AM. Inhalation of ammonium nitrate fuel oil explosive (ANFO). Occup Environ Med 1998;55:144.
15. Merget R, Buenemann A, Kulzer R, et al. A cross sectional study of chemical industry workers with occupational exposure to persulphates. Occup Environ Med 1996;53:422–6.
16. Utell MJ, Morrow PE, Speers DM, Darling J, Hyde RW. Airway responses to sulfate and sulfic acid aerosols in asthmatics. An exposure-response relationship. Am Rev Respir Dis 1983;128:485490.
17. Wrbitzky R, Drexler H, Letzel S. Early reaction type allergies and diseases of the respiratory passages in employees from persulphate production. Int Arch Occup Environ Health 1995;67:413–7.
18. Bhat MR, Ramaswamy C. Effect of ammonia, urea and diammonium phosphate (DAP) on lung functions in fertilizer plant workers. Indian J Physiol Pharmacol 1993;37:221–4.
19. U.S. Environmental Protection Agency. National Emission Standards for Hazardous Air Pollutants from Phosphoric Acid Manufacturing Plants and Phosphate Fertilizers Production Plants 40 CFR Part 63.
20. Saxena K. Clinical features and management of poisoning due to potassium chloride. Med Toxicol Adverse Drug Exp 1989;4;429–43.
21. Bohadana AB, Massin N, Wild P, Berthiot G. Airflow obstruction in chalk powder and sugar workers. Int Arch Occup Environ Health. 1996;68:243–8.
22. Rizzo AM, Fisher M, Lock JP. Hypermagnesemia pseudocoma. Arch Intern Med 1993;153:1130–6.
23. Olanow CW. Manganese-induced parkinsonism and Parkinson's disease. Ann N Y Acad Sci 2004;1012:209–23.
24. Huang WH, Lin JL. Acute renal failure following ingestion of manganese-containing fertilizer. J Toxicol Clin Toxicol 2004;42:305–7.
25. Blount BW. Two types of metal fume fever: mild vs serious. Milit Med 1990;1155:372–7.
26. Barceloux DG. Copper. J Toxicol Clin Toxicol 1999;37:217–30.
27. Minoia C, Gregotti C, Di Nucci A, Candura SM, Tonini M, Manzo L. Toxicology and health impact of environmental exposure to boron. A review. G Ital Med Lav 1987;9:119–24.
28. Von Burg R. Boron, boric acid, borates and boron oxide. J Appl Toxicol 1992;12:149–52.

15

Plant Growth Regulators

Louise Ferguson and James E. Lessenger

Key words: plant hormones, auxins, gibberellins, cytokinins, ethylene, abscisic acid, phenolics alkaloids

Plant growth regulators (PGRs) were first discovered in plants at the beginning of the 20th century. An endogenous PGR is a plant hormone, in academic terms "an organic compound synthesized in one part of a plant and translocated to another part of a plant where, in very low concentrations, it causes a physiological response" in the plant. As knowledge and commercial use of PGRs grew, compounds formerly extracted could be synthesized. Thus PGRs are now both natural (extracted) and synthetic (synthesized) in origin. Even if a synthesized PGR is identical in structure to a hormone extracted from a plant, it is not considered a plant hormone (1).

Use of Plant Growth Regulators in Agriculture

In agricultural application a PGR is defined as "a substance used for controlling or modifying plant growth processes without appreciable phytotoxic effect at the dosage applied." In order for a PGR to be registered by the U.S. Environmental Protection Agency, its use, as recommended on the label, must be safe for the plant, its applicator, and the environment as far as can be feasibly determined. Thus, neither plant nor human injury is to be expected from most properly applied PGRs (2).

The PGRs are divided into five general groups of compounds based on their chemical structures and effects on plants. The groups are auxins, gibberellins, cytokinins, ethylene, and a group called inhibitors, which includes abscisic acid, phenolics, and alkaloids. Some new PGRs do not fit neatly into these classifications but are described as having effects that resemble those for known PGRs. For example, *cytokinin-like* is a term used to describe new products extracted from seaweed products. A new PGR may be developed to counter the effects of a known plant hormone by interfering with natural plant hormone production. A general description of each growth regulator's effect on plant growth follows.

Auxins

Auxins stimulate cell division and elongation, stimulating a plant stem to grow taller, or in a specific direction.

Gibberellins

Gibberellins stimulate extension growth of plants and delay aging. This generally produces a plant that grows and produces faster, or fruit peels that remain green longer than an untreated plant.

Cytokinins

Cytokinins affect cytokinesis, or cell division, cell enlargement, dormancy, flowering and fruiting, and senescence. In agricultural application this translates into propagating new plants in the nursery, breaking seed dormancy, or delaying senescence.

Ethylene

Ethylene affects growth, ripening, and senescence in plants. In agricultural applications it is used primarily to promote ripening.

Abscisic Acid

Abscisic acid generally inhibits growth and germination and promotes dormancy.

Phenolics

Phenolics affect the metabolic system of plants. In agricultural application, phenolics are used primarily to delay abscission of fruits.

Toxic Effects of Plant Growth Regulators

Details of the effects of some representative PGRs on various species, including humans, are given in Table 15.1. If properly used, PGRs have an excellent safety record. However, if the wrong concentration is used, if safety equipment is not properly used, or if the application times are not correct, poisoning can occur in plants, animals, and humans.

A good example is hydrogen cyanamide. This PGR is considered very effective and economical in assuring uniform bud break in crops including peaches, kiwis, and grapes. Uniform maturation of buds results in the uniform ripening of the fruit so that all the fruit on one tree can be harvested at

TABLE 15.1. Plant growth regulators.

Compound Chemical name Common name Trade name	Target crop	Action on plant	Sentinel human effect
Chemical name: (α-cyclopropyl-α-(4-methoxyphenyl)-5-pyrimidine methanol) *Common name(s):* *ancymidol* *(registered with EPA)* Trade name(s) and manufacturer(s): (A-Rest®) Dow Elanco & Co.	A-Rest® controls the height of container-grown lilies, poinsettias, chrysanthemums, dahlias, tulips, and foliage and bedding plants; effectively reduces internode elongation, resulting in more compact plants	A-Rest® is a plant growth regulator that reduces internode elongation	• Acute toxicity (ancymidol) Mouse: LD_{50} 5000 mg/kg Rat, adult: LD_{50} 4500 mg/kg Rat, newborn: LD_{50} 350 mg/kg Dog: LD_{50} > 500 mg/kg (emesis) Monkey: LD_{50} > 500 mg/kg (emesis) Chicken: LD_{50} > 500 mg/kg For A-REST®, the oral LD_{50} in rates is > 5 mL/kg • Subacute toxicity: all rats survived without significant toxicity when fed 8000 ppm of ancymidol for 3 months. Dogs given daily oral 200 mg/kg doses of ancymidol for 3 months survived without significant toxicity Dermal toxicity and inhalation dangers: when ancymidol and A-REST® at a concentration of 5 mg/L of air were applied to the back of rabbits, subjects were unaffected
Chemical name: n-(phenylmethyl)-9-(tetrahydro-2h-pyran-2-yl)-9h-purine-6-amine *Common name(s):* *SD8339 (registered with EPA)*	Increases the number of lateral branches developed on chrysanthemums, carnations, and roses	Synthetic cytokinin, which stimulates growth of dormant lateral buds in several plant species	• General toxicity to wildlife and fish: TLM – 96 hr – 52 mg/L (blue gill) TLM – 24 hr – 3 mg/L (trout) • Acute toxicity—LD_{50} 926 mg/kg (mice), 1640 mg/kg (rats) • Subacute toxicity—NEL > 10,000 ppm (mallard) NEL > 4,640 ppm (bobwhite quail)

Trade name(s) and manufacturer(s): ACCEL® Plant Growth Regulator, Abbott Laboratories			• Chronic toxicity—no teratogenic effect at 320 mg/kg in rabbits • Dermal toxicity and inhalation dangers—no identified hazards at use concentrations
Chemical name: (2-chloro-*n*-[2,6-dinitro-4-(trifluoromethyl)-phenyl]-*n*-ethyl-6-fluorbenzenemethanamine *Common name(s):* *CGA-41065M, PRIME+* Trade name(s) and manufacturer(s): PRIME + 1.2E	Chemical control of axillary bud (sucker) growth after topping the floral portion of tobacco	There is no information on the mechanism of action of CGA-41065 in controlling the growth and development of tobacco suckers Interferes with cell division by binding to tubulin, preventing tubulin from forming microtubules which are required for proper spindle development and mitotic division	• Acute toxicity to mammals CGA-40065 Technical / Prime + 1.2E Acute oral LD_{50} (rat): >5000 mg/kg / 4400 mg/kg Acute dermal LD_{50} (rabbit): >2000 mg/kg / 2010 mg/kg Eye irritation (rabbit): Moderately Irrigating / Corrosive on contact Primary skin irrigation: Mildly irritating / Moderately irritating
Chemical name: Gibberellic acid *Common name(s):* *Gibberellic acid, GA_3 (registered with EPA)* Trade name(s) and manufacturer(s): Berelex (ICI), observed Gib-Tabs (Microbial Resources), Gib-Sol (Microbial Resources), Pro-Gibb (Abbott), Pro-Gibb Plus (Abbott)	Improving fruit set of blueberries with insufficient pollination; used for better color, firmer fruit, larger fruit, and to prolong the harvest period of cherries; used to reduce cherry flowering and fruiting to minimize the competitive effect of early fruiting on tree development; for cluster loosening and elongation and berry size increase of grapes	GA_3 is a growth promoter; it accelerates vegetative growth of shoot producing larger plants; mostly due to cell elongation but sometimes cell multiplication may be involved; induces flowering by breaking dormancy	• Acute toxicity—oral administration of massive single doses of 1 g kg^{-1} produced no toxic symptoms in rats; mice – 15 g kg^{-1} no toxic symptoms • Subacute toxicity—dogs and rats have no ill effects from daily doses of 1 g kg^{-1} 6 days per week for 90 days; one group of rats has been fed for 14 months, no toxic symptoms observed • Chronic toxicity—no ill effect on rats fed 5 to 8 weeks with 5% GA_3 in diet; no changes found in organs tissue; guinea pigs – no toxic signs fed with kale for 3 months, treated with 250 ppm.

continued

TABLE 15.1. Plant growth regulators. (continued)

Compound Chemical name Common name Trade name	Target crop	Action on plant	Sentinel human effect
Chemical name: 1.1-dimethyl-piperidinium chloride *Common name(s).* *Mepiquat-chloride (registered with EPA)* Trade name(s) and manufacturer(s): PIX-BAS 08300E by BASF Wyandotte Corp.	Systemic plant growth regulator for limiting undesired vegetative growth of the cotton plant; reduces growth, increases boll set; affects maturity, yield, boll rot	Decreases plant height, increases boll set and yield; inhibits all elongation and node formation and increases leaf mesophyll structure; possibly inhibits biosynthesis of gibberellin acid	• Acute oral toxicity—oral LD_{50} (rats) = 1420 mg/kg; no eye irritation • Dermal toxicity and inhalation dangers—acute dermal LD_{50} (rats) is greater than 5000 mg/kg; inhalation toxicity (rats) no reaction after 4-hour exposure
Chemical name: n-[2,4-dimethyl-5-[[(trifluoromethyl)-sulfonyl] amino]phenyl]acetamide *Common name(s):* *Mefluidide (WSSA, ANSI) (registered with EPA)* Trade name(s) and manufacturer(s): EMBARK® 2-s PBI/Gordon Col.	Regulates the growth of various species of turf grasses and broadleaf vegetation by suppressing seed-head formation	Inhibition of growth and development of the meristematic regions of responsive plants	• Acute toxicity Mice oral LD_{50} 1920 mg/kg Rats oral LD_{50} > 4000 mg/kg Rabbits dermal LD_{50} > 4000 mg/kg • Subacute toxicity Dogs 90-day feeding "no effect" at 1000 ppm in diet Rats 90-day feeding "no effect" at 6000 ppm in diet • Chronic toxicity—in lifetime feeding studies with rats and mice no adverse effects related to ingestion of mefluidide at a dose level of 600 ppm in the diet were observed. Reproduction and pup survival were not affected by mefluidide up to 6000 ppm in the diet during a 18-month 3-generation study with rats

			• Dermal toxicity and inhalation dangers—rabbits primary skin irritation study: no irritation to abraded and nonabraded skin; rats 4-hour acute aerosol inhalation LD_{50}: > 8.5 mg/L air
Chemical name: 1-naphthaleneacetic acid *Common name(s):* *NAA (registered with EPA)* Trade name(s) and manufacturer(s): NAA-800; Fruitone®; In Rootone® Rhone-Poulenc Ag Company Products Co., Inc.	Thin apples, olive and pear blossoms; control apple and pear preharvest drop; stimulate root formation	Auxin activity	• Acute toxicity (rats)—LD_{50} approximately 1000 mg/kg body weight • Chronic toxicity—8-day dietary LC_{50} (bobwhite quail): acute LC_{50} estimated to be greater than 10,000 ppm; 8-day dietary LC_{50} (mallard duck): acute LC_{50} estimated to be greater than 10,000 ppm • Dermal toxicity and inhalation dangers—acute dermal toxicity (rabbits)—LD_{50} greater than 5.0 mg/kg body weight; not considered to have potential as a primary skin irritant; primary eye irritation (rabbits)—considered an eye irritant; acute inhalation toxicity (rats)—not considered toxic by the route of administration
Chemical name: ga_4-(1α, 2β,4aα,4bβ,10β)-2,4a-dihydroxy-1-methyl-8-methylene gibbane-1,10-dicarboxylic acid,1,4a-lactone ga_7-(1α, 2β,4aα,4bβ,10β)-2,4a-dihydroxy-1-methyl-8-methylene gibb-3-ene-1,10-dicarboxylic acid,1,4a-lactone	Spray gynoecious cucumbers to develop male flowers	Close similarity in growth regulating activity of GA_3 but differs in its capability of influencing growth in some species in ways not achievable with gibberellic acid	• Acute toxicity—the acute oral LD_{50} of gibberellin A_4, A_7 is >500 mg/kg (for mice) • Dermal toxicity and inhalation dangers—avoid use in poorly ventilated areas

continued

TABLE 15.1. Plant growth regulators. (continued)

Compound Chemical name Common name Trade name	Target crop	Action on plant	Sentinel human effect
Common name(s): *Mixture of $GA_4 + GA_7$* *(registered with EPA)* Trade name(s) and manufacturer(s): Pro-Gibb 47, Abbott Labs Regulex, ICI Plant Protection			
Chemical name(s): ba-6-benzylamino purine Ga_4-(1α, 2β,4aα,4bβ,10β)-2, 4a-dihydroxy-1-methyl-8-methylene gibbane-1, 10-dicarboxylic acid,1, 4a-lactone ga_7-(1α, 2β,4aα,4bβ,10β)-2, 4a-dihydroxy-1-methyl-8-methylene gibb-3-ene-1, 10-dicarboxylic acid,1, 4a-lactone *Common name(s):* *Mixture of BA + GA_4 + GA_7* *(registered with EPA)*	Increases red delicious apple size, weight	Gibberellin activity	• Acute toxicity: the acute oral LD_{50} of N-(phenyl methyl)-1H-purine on mice is 1690 mg/kg, while for gibberellin A_4,A_7 it is greater than 500 mg/kg • Dermal toxicity and inhalation dangers: promalin is nonirritating in dermal toxicity testing but does cause injury to the eye

Trade name(s) and manufacturer(s): Promalin, Abbott Labs			
Chemical name: (2-chloroethylphosphoric acid) *Common name(s):* *Ethephon (ANSI)* *(registered with EPA)* Trade name(s) and manufacturer(s): CERONE®, ETHREL®, Plant Regulator, ETHREL® Pineapple Growth Regular, PREP, CHIPCOR®, FLOREL™ Plant Growth Regulator – Rhone-Poulenc Ag Company	*Apples:* promoting fruit maturity and loosening fruit; promoting uniform ripening and coloring of red varieties without loosening fruit; increasing flower bud development on young trees *Cantaloupes:* promoting fruit abscission *Cherries:* uniform ripening and loosening fruit, increasing dormant fruit bud hardiness, and delaying spring bloom of sweet cherries in the Pacific Northwest. *Cotton:* accelerating uniform boll opening *Cucumbers and squash:* modifying sex expression for seed production *Daffodils:* use a drench for shortening stems of forced bulbs. *Geraniums:* to increase branching *Greenhouse roses:* use for basal bud stimulation *Peppers:* early, uniform ripening and coloring fruit	Releases ethylene in plant tissues	• Acute toxicity: rats—LD_{50} 4229 mg/kg body weight • Subacute toxicity: 8-day dietary LC_{50} (mallard ducks) 196 LC_{50} greater than 10,000 ppm; static 96-hour toxicity (blue-gill sunfish)—TL_{50} estimated to be about 311 ppm Static 96-hour toxicity (rainbow trout)—TL_{50} estimated to be about 357 ppm • Chronic toxicity: considered noncarcinogenic, nonmutagenic, nonteratogenic • Dermal toxicity and inhalation dangers: acute dermal irritation (rabbits)—5730 mg/kg—a single instillation of 0.1 ml of Ethrel into the eye showed corneal damage in the nonirrigated group at day 14 whereas the irrigated group had recovered; acute inhalation toxicity (rats)—inhalation of 2 mg/L air caused signs of irritation during 1 hour exposure; all animals appeared normal during 14 days following exposure

continued

TABLE 15.1. Plant growth regulators. (continued)

Compound Chemical name Common name Trade name	Target crop	Action on plant	Sentinel human effect
	Tobacco: hastening "yellowing" of mature tobacco and reducing curing time *Tomatoes:* accelerating and concentrating fruit ripening *Walnuts:* loosening walnuts and improving full removal		
Chemical name: Butanedioic acid mono (2,2-dimethylhydrazide) (formerly succinic acid-2,2-dimethylhydrazide) *Common name(s):* *Daminozide (ANSO, ISO, BSI); Former literature references include SADH, B995, B9, and aminozide. Note: Food uses will be canceled. Ornamental uses remain in effect.* Trade name(s): and manufacturer(s): ALAR-85, KYLAR-85, B-NINE-SP by Uniroyal Chemical	Used on fruit-bearing trees, peanuts, ornamentals, grapes, and tomatoes; daminozide has a wide range of effects, from retarding vegetative growth, to controlling harvest quality factors, increase red color in apples, to concentrating maturity	Plant growth regulant of unknown mechanism	• Acute toxicity: acute oral LD_{50} (rat): 8,400 mg/kg • Subacute toxicity: in a 90-day feeding study with rats, technical-grade daminozide had no adverse effect when fed at 43,200 ppm in a daily diet • Chronic toxicity: a 2-year feeding test with rats and dogs indicated that technical-grade daminozide had no adverse effect at 3000 ppm in the daily diet (highest rate tested); a three-generation reproduction and lactation study with rats fed 300 ppm technical-grade daminozide in the diet showed no significant effect on either fertility or reproductive capacity • Dermal toxicity and inhalation dangers: Acute dermal LD_{50} (rabbit): > 5000 mg/kg Acute inhalation LC_{50} (rat): > 147 mg/L • Symptoms of poisoning: no known symptoms

Chemical name: 2-chloroethyltrimethyl ammonium chloride *Common name(s):* *Chlormequat chloride(BSI); other names are CCC, chlorocholine chloride, El 38,555 (Registered with EPA)* Trade name(s) and manufacturer(s): CYCOCEL® Plant Growth Regulant, American Cyanamid Company; HORMOCEL, All India Medical Corporation	*Pears and apples:* promotion of fruit bud formation, and increasing yields; also allows young trees to bear sooner *Azaleas:* to produce early budded, compact symmetrical plants for use in commercial forcing of early blooming azaleas		• Acute toxicity: LD_{50} oral: male albino rats 0.48–0.94 g/kg • Subacute toxicity: repeated feeding to rats for 29 days at 500, 1000, and 2000 mg/kg; all animals had normal behavior and food intake and weight gain of the test rodents remained within normal limits • Chronic toxicity: 12 months of feeding of rats at 500 and 1000 ppm gave no symptoms of poisoning, differences in mean body weight, appearance or behavior, no differences in various hematological and clinical chemical determinations, and no untimely deaths were observed; in 12-month feeding studies with dogs on a diet containing 300 ppm (calculated on dry weight), regular examination of animals showed no gross or microscopic pathology referable to the compound; determinations of acetyl-cholinesterase in erythrocytes and plasma made after 4, 8, and 12 months on test indicated that the compound had no effect on red blood cells or plasma
Chemical name: (±)-r*,r*)-β-[(4-chlorophenyl) methyl]-α-(1,1-dimethylethyl)-1*h*-1,2,4-triazole-1-ethanol *Common name(s):* *Paclobutrazol (registered with EPA)* Trade name(s) and manufacturer(s): Clipper® Tree Growth Regulator	Tree growth retardant	Inhibitor of gibberellin biosynthesis	• General toxicity to wildlife and fish: contains methanol and cannot be made nonpoisonous • Symptoms of poisoning: same as methanol

Source: Data from Cutler and Schneider (2).

the same time. For many years hydrogen cyanamide was used as a medication for the treatment of alcoholism in humans (albeit in much smaller concentrations than is used on plants). The chemical causes an Antabuse reaction in people who consume alcohol, including nausea, vertigo, hypotension, and, in extreme cases, circulatory collapse and death. Therefore, people who mix and apply the chemical must wear full protective ensembles, used closed air supply cabs for the tractors, and never consume any alcohol in liquid form or as a perfume or after-shave. Care must be exercised to isolate the field until the reentry period has passed. Treatment is supportive (see Chapter 13) (3,4).

References

1. Salisbury FB, Ross CW. Plant Physiology, 2nd ed. Belmont, CA: Wadsworth, 1978.
2. Cutler HG, Schneider BA. Plant Growth Regulator Handbook. LaGrange, GA: Plant Growth Regulator Society of America, 1990.
3. Lessenger JE. Case study: hypotension, nausea and vertigo linked to hydrogen cyanamide exposure. J Agromed 1998;5:5–11.
4. Formoli TA. Estimation of exposure in persons in California to pesticide products that contain hydrogen cyanamide. Sacramento: California Environmental Protection Agency, 1993.

16

Pesticides

William M. Simpson, Jr.

Key words: norbicides, herbicides, insecticides, fungicides, rodenticides, adjuvants

World pesticide use exceeded 5.6 billion pounds of active ingredient (AI) in 1999, the latest year for which figures are available. Herbicides (chemicals used to control plants, usually weeds) accounted for the largest proportion (38%). Insecticides and fungicides were 25% and 10% of the total used, respectively (1).

The United States used 1.2 billion pounds of AI or more than 20% of the world's pesticide consumption. Herbicides were the largest category of use (46%), but insecticides were only 9% and fungicides 7% of the total pesticide market. While fungicide use in the United States and world markets is similar, insecticides are much more heavily used globally primarily due to the need for more widespread mosquito control (1).

Other pesticides account for 27% and 38% of the world and United States pesticide use, respectively. Categories included in other pesticides category are nematicides, fumigants, rodenticides, molluscicides, aquatic and fish/bird pesticides, plus other chemicals used as pesticides (e.g., sulfur and oils) (1).

Specialty biocides (used for recreational and industrial water treatment and as disinfectants and sanitizers), chlorine and hypochlorites (used as disinfectants for potable, waste, and recreational water), and wood preservatives are also considered pesticides. If the amount of AI used for these purposes is included in pesticide use data, total AI used in the world and the United States is four times higher (e.g., 5 billion pounds of AI in the United States).

Gross AI figures do not accurately reflect what has happened in world and U.S. agriculture over the past 20 years. Total pesticide use has dropped by about 20% over that time period—herbicides by 10% and insecticides by 50% (this does not reflect the likely increase in use of insecticides for West Nile virus prevention that has occurred in the last 5 years), and fungicides by 30%. In addition, the specific types of AI have also changed. The trend, generally, has been to decrease use of more toxic pesticides of all types and replace them with lower risk products (lower risk to humans, birds, fish, and beneficial insects) (1).

Approach to Pesticide Poisoning

Before discussing individual chemicals, a few principles of pesticide poisoning management should be addressed. The most important issue is proper diagnosis. Without it, all other interventions are potentially ineffective and possibly harmful.

Whenever possible, get the label of the suspected poison. It will contain principles of management and contact information for the manufacturer. The local poison control center and the National Pesticide Telecommunications Network (1-800-858-7378 Monday to Friday 9:30 a.m. to 7:30 p.m.) are also available for further advice. If coworkers have not been able to identify the suspect chemical, Cooperative Extension Service agents may also serve as a resource for commonly used chemicals at particular times of the year on specific crops.

Remember that careful decontamination of the patient is necessary to prevent possible further injury to the patient and possible injury to emergency department staff. Physical decontamination by removing clothing that has been in contact with the chemical, washing the skin with soap and water, and copiously irrigating the eyes is important. Recent evidence-based position statements from the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists suggest that gastric lavage, activated charcoal, cathartics, and ipecac should not be used routinely in poisoned patients. They can be considered within 60 minutes of presentation if a potentially life-threatening amount of poison has been ingested. Even in this circumstance, contraindications exist for the use of each: lavage is contraindicated in hydrocarbon ingestion; cathartic in volume depletion, hypotension, electrolyte imbalance, or ingestion of a corrosive substance; activated charcoal in an unprotected airway, a nonintact gastrointestinal (GI) tract or hydrocarbon ingestion; and ipecac in a nonalert patient or with ingestion of a hydrocarbon or corrosive substance (2).

Herbicides

The most widely used pesticides in the world, herbicides are designed to kill plants and attack plant metabolic pathways that do not exist in humans and other animals. Therefore, in general, they have relatively low animal toxicity. There are hundreds of herbicides and herbicide mixtures on the market in the United States and throughout the world. Seven of the top 10 pesticide active ingredients (by amount used) are herbicides. Chlorophenoxy herbicides are plant growth regulators. They are commonly used for broadleaf weed control on cereal crops and pastures. Common chlorophenoxy herbicides include 2,4-D; Dicamba; and Silvex. Many products available to consumers include a mixture of salts in a petroleum base. Most toxicity from contact with skin or eyes or ingestion involves mucous membrane irritation. Very high dose

exposure may result in neurological symptoms including muscle twitching, seizures, and coma. Renal and hepatic dysfunction may occur with large ingestions. Long-term health effects of low to moderate exposure include alleged, but not confirmed, carcinogenicity, teratogenicity, and reproductive abnormalities. Although no specific antidote is known, alkaline diuresis has been reported to be of value in severe overdose. Otherwise, aggressive supportive care including protection of the airway, correction of hypotension, and treatment of arrhythmias, hyperthermia, and seizures may be required (3).

Atrazine and glyphosate, triazine, and phosphonate herbicides are also widely used for weed control. Glyphosate was developed specifically as a much safer alternative to paraquat (discussed in a subsequent paragraph). Mucous membrane irritation is the most common adverse reaction to exposure to these chemicals and their many relatives. Gastrointestinal tract erosions were the primary adverse events in large-volume ingestions (all accidental or intentional), but renal, hepatic, central nervous system, and pulmonary involvement was sometimes noted. Since no antidote is known, supportive care is also indicated for these groups of agents (4,5).

Carbamate herbicides, unlike carbamate insecticides, do not produce inhibition of cholinesterase enzymes or the "all faucets on" cholinergic syndrome. Toxicity is uncommon. Common generic names for carbamate herbicides include asulam, terbucarb, butylate, pebulate, triallate, and thiobencarb. Mucous membrane irritation is the most common adverse effect. After removal of the chemical by soap and water, flushing the eyes, and increased fluid intake, treatment is supportive.

Urea-substituted herbicides are photosynthesis inhibitors, mainly used for weed control in noncrop areas. Chemicals in this class have names ending in "-uron" or "-oron"—e.g., chlorimuron, diuron, siduron, tebuthioron, and tetrafluoron. Urea-substituted herbicides have low systemic toxicity based on animal feeding studies; they may, however, produce methemoglobinemia with heavy ingestion. Methemoglobin and sulfhemoglobin levels should be measured in patients with dyspnea or cyanosis and a history of urea-substituted herbicide ingestion. Otherwise treatment of these ingestions is decontamination and supportive care.

The most dangerous group of herbicides is the bipyridyls. Paraquat is the most important of the bipyridyl group. Others in the group include diquat, chlormequat, and morfamquat. Bypyridyls exert their herbicidal activity by interfering with reduction of nicotinamide adenine dinucleotide phosphate (NADP) to reduced nicotinamide adenine dinucleotide phosphate (NADPH) during photosynthesis, producing superoxide, singlet oxygen, and hydroxyl and peroxide radicals. This eventually destroys lipid cell membranes, including those in the lungs, leading to late and irreversible pulmonary fibrosis. Major local effects of paraquat are due to its caustic properties. Corneal ulceration has been reported after paraquat concentrate was splashed in the eyes. Gastrointestinal tract ulceration including esophageal ulceration with

perforation has occurred. After ingestion of >30 mg/kg of paraquat concentrate, pulmonary, cardiac, renal, and hepatic failure can occur within hours. Ingestion of 4 mL/kg or more may cause renal failure, resulting in impaired paraquat excretion and higher serum concentrations. Pulmonary involvement is the major target of ingested paraquat with an adult respiratory distress syndrome (ARDS)-like syndrome developing 1 to 2 days after ingestion, progressing to pulmonary fibrosis in a few days.

Treatment of paraquat ingestion is aimed at several points along the toxicity pathway—removing toxin from the GI tract, increasing excretion from the blood, and preventing pulmonary damage with anti-inflammatory agents. Cautious aspiration with a nasogastric tube is appropriate if the patient presents within the first hour after ingestion. Because of the possibility of severe toxicity, some authorities still recommend activated charcoal (1 to 2 g/kg) if the patient is seen within 1 to 2 hours, repeated 4 hours later. Hemodialysis is effective for removing paraquat from the blood. Pulmonary damage is increased by oxygen supplementation, so low-oxygen breathing mixtures are recommended. Immunosuppression has been attempted with corticosteroids and cyclophosphamide or other similar agents, with limited success. Deferoxamine and *N*-acetylcysteine have been used as antioxidants. Prospective studies supporting immunosuppressive and antioxidant therapies are lacking. Diquat is felt to have much less pulmonary toxicity, but pulmonary fibrosis may also occur, especially if oxygen supplementation is used. Chlormequat toxicity resembles organophosphate toxicity but should not be treated as such (see the discussion of organophosphate pesticides in the next section). Treatment is by GI decontamination and supportive care. Morfamquat is rarely used. No human or animal toxicity has been reported with morfamquat, but poisoning with the chemical should probably be treated initially as a paraquat poisoning (6).

Insecticides

Organophosphates are still the most widely used insecticides in the United States and the world, but botanical insecticides and insect growth regulators are becoming much more widely used, due to their lower toxicity. Also included in this category are the organochlorines (such as DDT), the carbamates, and insect repellants (DEET and p-dichlorobenzene).

Organophosphates (OPs) are the most common cause of insecticide poisoning and cause a few deaths each year in the United States. OPs are used for suicide in both the United States and particularly in the Third World, where more than 100,000 people per year are estimated (by the World Health Organization) to take their own lives using this group of chemicals.

Organophosphates are so widely used because of their effectiveness against a wide variety of insects and their lack of persistence in the environment (compared to organochlorines). The toxicity of OPs varies greatly—a drop of

the OP nerve agents VX, soman, or sarin may be lethal, while malathion has an oral median lethal dose (LD_{50}) of approximately 1 g/kg. Most of the OPs are rapidly absorbed by all routes. They may be classified as direct (the nerve gases) or indirect (most commercially used crop, animal, and home products) cholinesterase inhibitors. Metabolism, primarily by the CYP450 system, is required to activate the indirect inhibitors. Direct inhibitors may have almost immediate effects, or up to 2 to 3 hours delay after dermal absorption. Indirect inhibitors may not produce symptoms until 6 to 24 hours after exposure.

The toxicologic effects of OPs are almost entirely due to inhibition of acetylcholinesterase in the nervous system, which causes acetylcholine to accumulate in the synapses and myoneural junctions. Muscarinic, central nervous system, and nicotinic effects are produced as outlined in Table 16.1, usually in that order. The most common clinical presentation is a patient with an odor similar to garlic, with miosis, increased airways secretion, lacrimation, bradycardia, and GI complaints (7). This constellation of findings should be managed as OP poisoning until proven otherwise (8).

Serum and red blood cell (RBC) cholinesterase levels should be obtained early, but therapy should not be delayed pending laboratory confirmation. Treatment should include attention to the airway and adequate oxygenation with atropine administered until secretions dry. The initial dose of atropine should be 1 to 2 mg for adults and 0.05 mg/kg for children, administered intravenously if possible, and repeated every 15 to 30 minutes until signs of atropinization develop (flushing, drying of secretions, and dilation of pupils, if they were miotic at presentation). Atropine may be required for 24 hours and should be tapered, rather that abruptly stopped. Pralidoxine (2-PAM) is a specific OP antidote. It should be administered as soon as possible in all

TABLE 16.1. Clinical effects of organophosphate poisoning.

Site	Physiologic Effect
Muscarinic effects	
Sweat glands	Sweating
Pupils	Miosis
Ciliary body	Blurred vision
Lacrimal glands	Lacrimation
Salivary glands	Salivation
Bronchi	Constriction with wheezing
Gastrointestinal	Cramping, vomiting, diarrhea, tenesmus
Cardiovascular	Bradycardia, hypotension
Bladder	Incontinence
CNS Effects	
	Anxiety, restlessness, ataxia, convulsions, coma
*Nicotinic Effect*s	
	Decreased reflexes, respiratory/circulatory depression
Striated muscle	Fasciculations, cramps, weakness, paralysis, respiratory depression, hypoxia, respiratory arrest
Sympathetic ganglia	Tachycardia, hypertension

clinically significant poisonings. The initial dose is 1 to 2 mg for adults and 25 to 50 mg/kg for children given intravenously over 15 to 30 minutes. A continuous infusion of 10 to 20 mg/kg, up to 500 mg/h, is then used in severe OP poisoning. More detailed information on OP poisoning management is found in standard texts on poisoning and drug overdose. Severe OP poisoning has been associated with chronic neurological sequelae including cognitive impairment, depression, and peripheral neuropathies. An intermediate syndrome, termed organophosphate-induced delayed-onset neuropathy (OPDIN) associates hyperreflexia and hypertonicity with long-term, low-dose exposure to OPs. Both syndromes are rarely recognized (7,9).

Carbamates are also cholinesterase inhibitors, producing the syndrome of cholinergic crisis as described for OPs. The syndrome is of shorter duration and more benign than with OPs because carbamates dissociate from the cholinesterase much more readily than OPs, producing a reversible inhibition. Carbamates also poorly penetrate the central nervous system (CNS), rarely producing seizures, ataxia, and central depression of the respiratory and circulatory centers. Red blood cell and serum cholinesterase levels return to normal within hours of exposure. Treatment of carbamate poisoning is also with atropine (in doses identical to those used for OPs but for only 6 to 12 hours because of the shorter duration of enzyme inhibition) and oxygen supplementation. Pralidoxime is not indicated in pure carbamate poisoning, but if the poison is not known for certain and cholinergic symptoms exist, it can be used, pending identification of the poison.

Because of their persistence in the environment, organochlorine insecticides are in limited use in the United States. They are, however, used around the world in mosquito control. Lindane is still used in the United States as a general garden insecticide, for control of ticks, scabies, and lice and for extermination of powderpost beetles. It is absorbed by inhalation and ingestion and less well by dermal contact, unless the skin is abraded or treated repeatedly.

Lindane interferes with normal nerve impulse transmission by disruption of sodium and potassium channels in the axon membrane, leading to multiple action potentials for each stimulus. Clinically this may result in confusion, apprehension, tremors, muscle twitching, paresthesias, dizziness, seizures, or coma—usually in the face of a history of repeated treatment for scabies or lice. Wheezing, rales, or cyanosis may be found if hydrocarbon (a frequent vehicle) aspiration has occurred. Diagnosis is based on a history of exposure or intentional ingestion with physical manifestations of CNS hyperexcitability. Treatment is decontamination with supportive and symptomatic care. Seizures may require lorazepam or diazepam. Arrhythmias should be treated with lidocaine.

Commonly used botanical insecticides include pyrethrum, nicotine, rotenone, and *Bacillus thuringiensis*. Other botanicals are used in small quantities but are rarely associated with adverse health effects. Pyrethrum is the oleoresin extract of dried chrysanthemum flowers. It contains about 50%

active insecticidal ingredients known as pyrethrins. Synthetic derivatives of these compounds, called pyrethroids, are much more widely used today. Most insecticides containing pyrethroids also contain piperonyl butoxide, a synergist that increases their effectiveness by retarding enzymatic degradation of the active ingredient.

Pyrethrum-based insecticides are considered to have low toxicity, but they can produce nausea, vomiting, diarrhea, tremors, muscle weakness, and paresthesias. Very high levels of exposure can produce temporary paralysis and respiratory failure. Treatment is supportive. Allergic reactions to the pyrethroids are more common, with about 50% of patients sensitive to ragweed, and cross-reacting to pyrethrum. Pyrethrum and the pyrethroids are well absorbed from the GI tract and minimally absorbed from dermal exposure. They are rapidly metabolized by the liver, leading to their relative lack of systemic toxicity in humans. Persons exposed to prolonged contact with high concentrations of pyrethroids report paresthesias in unprotected skin. Vitamin E oil has been reported to relieve these paresthesias, by an unknown mechanism. Otherwise treatment of toxicity is symptomatic and supportive. Allergic symptoms are treated as with other allergens, by avoidance and antihistamines for mild symptoms, and corticosteroids and epinephrine for severe bronchospasm (10).

Nicotine, usually derived from tobacco, was used as an insecticide in the past. Now rarely used, most nicotine poisoning is as a result of ingestion of tobacco products or incorrect use of nicotine patches, gum, or nasal sprays. Decontamination is the treatment of choice. Care is supportive, since there is no specific antidote for nicotine. Severe hypersecretion or bradycardia may be treated with atropine.

Rotenone, prepared from the roots of derris, *Lonchocarpus*, and *Tephrosia* plants, is used as a household and horticultural insecticide. Piperonyl butoxide is also used as a synergist with this compound. Toxic to fish, bird, and insect nervous systems, it has produced little human toxicity in decades of use. However, fresh derris root from Malaya has been used for suicides. Numbness of mucous membranes has been reported in exposed workers, along with dermatitis and respiratory tract irritation. Treatment of these symptoms is with decontamination and supportive care.

Several subspecies of *Bacillus thuringiensis* (BT) are pathogenic to some insects. The product is used both as a spray to be applied to certain food crops and, incorporated into the genetic material of certain plants as a "built-in" insecticide. Infections of humans with these organisms is extremely rare. One volunteer ingesting a BT variety not used as a pesticide developed fever and GI symptoms. A single corneal ulcer has been associated with a splash of BT suspension in the eye. The GI symptoms resolved spontaneously; the ulcer resolved with antibiotic treatment (11).

Insect repellants are intended for human use and are therefore designed to be nontoxic in routine use. Two insect repellants have produced poisoning syndromes: DEET (*N,N*-diethyltoluamide) and *p*-dichlorobenzene. DEET is

minimally absorbed through the skin and is rapidly eliminated, primarily in the urine. Excessive use of high concentrations of this compound has been associated with a idiopathic toxic encephalopathy, particularly in girls and female infants. Symptoms may include lethargy, anxiety, opisthotonos, athetosis, ataxia, seizures, and coma. Ingestion of 50 mL of high concentration DEET (50% to 90%) has produced coma, seizures, and hypotension within an hour of ingestion and death in at least two cases. Irritant contact dermatitis and conjunctivitis have also been reported, as has an anaphylactic reaction in one case. There are no characteristic physical findings. Treatment is symptomatic and supportive.

Originally used as a moth repellant and insecticide, *p*-dichlorobenzene is now more commonly used as a deodorizer. Ingestion is fairly common when children eat a part of a deodorant cake in a toilet bowl or diaper pail. It is a mucous membrane irritant and can produce allergic symptoms. Massive ingestions may produce tremors and hepatic or renal injury. There are no characteristic features on physical examination or laboratory studies. Diagnosis is by history of ingestion, and treatment is supportive.

Fungicides

Widely used in industry, agriculture, home, and garden, fungicides are used for many purposes—protection of seed grain during storage, transport, and germination; protection of crops, seedlings, and grasses in the field, in storage, and during shipment; suppression of mold; control of slime in paper processing, and protection of carpets and fabrics. Fungicides, used properly, rarely cause severe poisonings. Most have inherently low mammalian toxicity and are absorbed poorly (at least partly because they are formulated as suspensions of wettable powders or granules). Most are applied using methods that intensively expose only a few individuals. Irritant injuries to skin and mucous membranes are relatively common in heavily exposed individuals, however (12).

Of the substituted benzene herbicides, only hexachlorobenzene has produced systemic toxicity. This occurred when hexachlorobenzene-treated seed wheat was used instead for human consumption. In 4 years, approximately 3000 persons developed porphyria due to impaired hemoglobin synthesis. Most affected individuals recovered, but some infants nursed by affected mothers died.

Thiocarbamates, unlike the *N*-methyl carbamates, have little insecticide activity. Instead they are used to protect seeds, turf, ornamentals, vegetables, and fruit from fungi. Bisdithiocarbamates, represented by thiram, are structurally similar to disulfuram. With heavy exposure an Antabuse-like reaction can be produced if alcohol is ingested subsequently. This reaction is characterized by flushing, sweating, headache, tachycardia, and hypotension.

Other thiocarbamates—ziram, ferbam, and metam-sodium—should theoretically predispose to the Antabuse reaction, but no occurrences have been reported. Metam-sodium decomposition in water yields methyl isothiocyanate, a gas that is extremely irritating to mucous membranes. Inhalation of the gas may cause pulmonary edema. Metam-sodium is considered a fumigant and should be used in outdoor settings only. Persons caring for a victim with metam-sodium ingestion should avoid inhalation of evolved gas. Treatment of exposure is with skin and GI decontamination, oxygen supplementation, fluid support, and avoidance of alcohol.

Ethylene bisdithiocarbamates (EBDC compounds) are another group of fungicides that may irritate skin, respiratory tract, and eyes. Maneb, zineb, nabam, and mancozeb represent this class. Treatment of the irritant effects of these chemicals is by decontamination. Thiophthalimides, represented by captan, captafol, and folpet, are agents used to protect seed, field crops, and stored produce. All of these fungicides are moderately irritating to the skin, eyes, and respiratory tract. They may produce skin sensitization. No systemic poisonings have been reported with these chemicals.

Copper compounds, both inorganic and organic, are irritating to skin, respiratory tract, and eyes. Soluble copper salts, such as copper sulfate and acetate, are corrosive to mucous membranes and the cornea. Systemic toxicity is low, probably due to limited solubility and absorption. Treatment of poisoning is with GI and skin decontamination. Ophthalmologic consultation should be obtained if eye irritation persists after flushing the eyes with saline. Intentional ingestions of large volumes of these compounds may result in hemolysis with circulatory collapse and shock, with renal and hepatic failure. In these severe cases, fluid replacement, alkalinization of the urine, chelating agents, and hemodialysis may be required.

Organomercury compounds have been used primarily as seed protectants. Toxicity has occurred primarily when methyl mercury–treated grain intended for planting was consumed in food. Poisonings have also occurred from eating meat from animals fed mercury-treated seed. Organic mercury is efficiently absorbed from the gut and is concentrated in the nervous system and red cells. Early symptoms of mercury poisoning are metallic taste, distal paresthesias, tremor, headache, and fatigue. Further symptoms target the CNS with incoordination, slurred speech, spasticity, rigidity, and decline in mental status. Treatment is by skin and GI decontamination and chelation.

Cadmium has been used to treat fungal diseases of turf and bark of orchard trees. Cadmium salts and oxides are very irritating to mucous membranes of the respiratory and GI tracts. Inhaled cadmium dust or fumes can produce a mild, self-limited respiratory illness with fever, cough, and malaise, similar to metal fume fever. More severe symptoms with labored breathing, chest pain, and hemorrhagic pulmonary edema are associated with heavier exposure and resemble chemical pneumonitis. Cadmium ingestion may produce severe nausea, vomiting, diarrhea, abdominal pain, and tenesmus. Chronic obstructive pulmonary disease (COPD), renal and hepatic injury,

and pathological fractures have been associated with chronic cadmium exposure. Treatment is skin and GI decontamination, respiratory support, and chelation therapy (for severe, acute poisoning, though the possibility of inducing renal failure with a large load of cadmium exists).

A long list of miscellaneous organic fungicides is in use in many crop, ornamental, and turf applications. Reports of adverse effects on humans are rare or absent entirely. As with all pesticides, following label directions for use is the key to prevention of adverse events, even with these low-risk chemicals.

Rodenticides

Rodenticides are designed to kill nuisance rodents such as rats, mice, moles, voles, ground squirrels, gophers, and prairie dogs. These animals may damage crops in the field or in storage and can transmit disease to humans and other animals through their droppings or bites. A wide variety of organic and inorganic chemicals have been used to control rodents. Plant-derived materials such as strychnine and red squill or inorganic compounds such as thallium or arsenic trioxide were among chemicals used early for rodent control. Newer agents tend to be synthetic organic compounds. All pose particular risks for accidental poisonings. Since these agents are designed to kill mammals, their toxicity is often similar for the target rodents and for humans. Also, since rodents often share environments with humans and other mammals, the risk of accidental exposure to the rodenticide is high because of their placement in those environments. As rodents have become resistant to some chemicals, more toxic chemicals have been developed, exposing those applying them and those living in areas where they are used to increased risk of toxicity. There are over 150 trade name rodenticides in the United States alone, many with very similar names. While important for all poisonings, in rodenticide poisoning, having the label to guide therapy is critical.

Long-acting anticoagulants are responsible for nearly 80% of human rodenticide exposures reported in the United States. Introduced in the 1970s, they have essentially replaced warfarin-based products. They have the same mechanism of action as warfarin but are more potent and have longer half-lives. They are effective in a single feeding (or a limited number of feedings) and in animals that have developed resistance to the older anticoagulants.

Treatment of superwarfarin ingestion depends on the dose. A child who ingests a few pellets or grains of the material can be observed at home for the development of bleeding. A person with a bleeding disorder or who takes an anticoagulant is at much greater risk of excess bleeding, even with a small exposure. Patients with large ingestions (>0.1 mg/kg) should have gastric decontamination if they are seen within an hour or two of the ingestion. If there has been a longer delay, activated charcoal is indicated. Prothrombin

time (PT) and partial thromboplastin time (PTT) should be measured at 24 and 48 hours after a significant ingestion. If any value is elevated, phytonadione (vitamin K_1) should be started (1 to 5 mg for children and 15 to 20 mg for adults) by subcutaneous injection and repeated as necessary. Critically ill adults can be given 50 to 200 mg via slow intravenous infusion (0.5 mg/min). The PT and PTT should be checked every 4 hours until stable and then every 24 hours. Once the PT and PTT are stable, the phytonadione may be switched to the oral form (15 to 25 mg daily for adults, 5 to 10 mg for children), tapering the dose as the PT levels decline to normal (over a period sometimes as long as 6 months).

Warfarin-based products are still available, but single exposures, unless large amounts (>0.5 mg/kg) are ingested, can be observed without therapy. Recent large exposures should be treated with activated charcoal. The PT and PTT should be measured at 12 and 24 hours. If the PT is two times normal or more, phytonadione should be given (1 to 5 mg for children, 10 mg for adults orally or intramuscularly and repeated as necessary. The PT should be measured every 4 hours until stable, then every 24 hours until normalized (13).

Bromethalin, a relatively new rodenticide introduced in 1985, is a neurotoxin that produces its effect by uncoupling mitochondrial oxidative phosphorylation. This results in increased intracranial pressure, decreased nerve impulse conduction, paralysis, and eventual death. No human exposures have been reported. Its effectiveness as a rodenticide is based on the rodent's consuming a relatively larger dose per kilogram than other larger animals. There is no antidote, so treatment of poisoning would be symptomatic and supportive.

Cholecalciferol (vitamin D_3) takes advantage of the fact that rodents are sensitive to small percentage changes in calcium levels in their blood. Cholecalciferol increases serum calcium by mobilizing calcium from bone, resulting in calcium deposition in tissues and nerve and muscle dysfunction and cardiac dysrhythmias. Ingestion of several bait pellets or treated seeds should not be toxic, and no treatment is necessary. Larger ingestions should be treated with gastric lavage if recognized early and activated charcoal in several doses if after 1 to 2 hours of ingestion. Serum calcium should be checked at 24 and 48 hours and treatment initiated if hypercalcemia develops. Forced diuresis with furosemide and a low-calcium diet should be initiated along with prednisone (5 to 15 mg every 6 hours). Calcitonin and/or mithramycin may be necessary for patients unresponsive to above measures.

Red squill is a botanic rodenticide derived from the red sea onion (*Urginea maritima*). It contains two cardiac glycosides that produce effects similar to digitalis. Treatment of ingestion is the same as for digitalis toxicity, including the use of Digibind.

Strychnine is another botanical, found in seeds of *Strychnos nux-vomica,* a tree native to India. Used in Germany in the 16th century as a poison for rats and other animals, it is still available in many rodenticides. It is a neurotoxin, producing twitching of facial (*risus sardonicus*) and neck muscles, reflex

excitability and generalized seizures. Treatment should include activated charcoal and anticonvulsants (diazepam, phenobarbital, or phenytoin if unresponsive to diazepam). Stimulation of the patient should be minimized; respiratory support including intubation and mechanical ventilation may be required.

Thallium rodenticides are not used in the United States, but are available around the world. Treatment of poisoning is difficult. Gastric decontamination should be attempted with lavage and activated charcoal. Fluid support with potassium chloride theoretically displaces thallium and increases its excretion.

Zinc and aluminum phosphides are used to protect stored grains from rodents and other pests. On contact with moisture, phosphides release phosphine gas, which is the primary cause of toxicity. Oral exposures to phosphides occur as a result of intentional ingestion for suicidal purposes. Phosphine inhibits oxidative phosphorylation, leading to cell death, manifested by severe GI irritation, hypotension, and cardiac and respiratory dysfunction. Management is by activated charcoal and gastric lavage. Intragastric sodium bicarbonate and/or potassium permanganate have been suggested to decrease phosphine gas release. Oxygen should be supplemented (100% via rebreather). Treatment is otherwise symptomatic and supportive (14).

The fifth edition of *Recognition and Management of Pesticide Poisoning,* edited by Drs. Routt Reigart and James Roberts of the Medical University of South Carolina, contains a table that lists manifestations caused by specific pesticides, which may be useful in evaluating possible pesticide exposures and toxicities. The entire textbook is available on the Environmental Protection Agency Web site at http://www.epa.gov/pesticides/safety/healthcare/handbook.htm (see "Index of Signs and Symptoms" or pages 213 to 224) by request from the Environmental Protection Agency, Office of Prevention, Pesticides, and Toxic Substances at 703-305-7666.

Miscellaneous Solvents and Adjuvants

The liquids in which pesticides are dissolved and the solids on which they are adsorbed are chosen by the manufacturers to make handling and application easy and to achieve maximal stability and effectiveness of the active ingredient. The most commonly used solvents are petroleum distillates. The petroleum distillate may produce toxicities in itself in large-volume ingestions. Most adjuvants (emulsifiers, penetrants, and safeners) are potentially skin and eye irritants but with very low or no systemic toxicity.

References

1. About Pesticides. U.S. EPA 1998-1999 Pesticide Market Estimates. Washington, DC: US Government Printing Office, 2003.
2. American Academy of Clinical Toxicology, European Association of Poisons Centers and Clinical Toxicologists. Position statements. J Toxicol Clin Toxicol 1997;35:711–52.
3. Shaner DL. Herbicide safety relative to common targets in plants and mammals. Pest Man Sci 2004;60:17–24.
4. Williams GM, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Reg Toxicol Pharmacol 2000;31(2 pt 1):117–65.
5. Talbot RA, Shiaw M, Huang J, et al. Acute poisoning with a glyphosate-surfactant herbicide: a review of 93 cases. Hum Exp Toxicol 1991;10:1–8.
6. Winchester JF. Paraquat and the bipyridyl herbicides. In: Haddad LM, Shannon MW, Winchester JR, eds. Clinical Management of Poisoning and Drug Overdose. Philadelphia: Saunders, 1998.
7. Eyer P. The role of oximes in the management of organophosphorus pesticide poisoning. Toxicol Rev 2003;22(3):165–90.
8. Aygum D. Diagnosis in an acute organophosphate poisoning: report of three interesting cases and review of the literature. Eur J Emerg Med 2004;11:55–8.
9. Carlton FB, Simpson WM, Haddad LM. The organophospates and other insecticides. In: Haddad LM, Shannon MW, Winchester JF, eds. Clinical Management of Poisoning and Drug Overdose. Philadelphia: Saunders, 1998.
10. Ray DE, Forshaw PJ. Pyrethroid insecticides: poisoning syndromes, synergies, and therapy. J Toxicol 2000;38(2):95–101.
11. Sudakin DL. Biopesticides. Toxicol Rev 2003;22(2):83–90.
12. O'Malley MA. Skin reactions to pesticides. J Occup Med 1997;12:327–45.
13. Burkhart KK. Anticoagulant rodenticides. In: Ford MD, Delaney KA, Ling LJ, Erickson T, eds. Clinical Toxicology. Philadelphia: Saunders, 2001:848–53.
14. Cienki JJ. Non-anticoagulant rodenticides. In: Ford MD, Delaney KA, Ling LJ, Erickson T, eds. Clinical Toxicology. Philadelphia: Saunders, 2001.

17

Neurological Injuries in Agriculture

Nikita B. Katz, Olga Katz, and Steven Mandel

Key words: emergent care, management, neuropathies, low back pain

Neurological conditions and diseases have a unique position in agriculture. From acute trauma to insidious neuropathies, from assessment of fitness to operate machinery to issues in rehabilitation, it is the neurological examination, specialized studies, diagnosis, and management that in many cases determines the future quality of life, disability, and survival of the patient.

This chapter concentrates on selected issues that are directly relevant to a practicing physician from the standpoint of pathogenesis, evaluation, and diagnosis. A more general review will be given of treatment modalities as they often are fine-tuned based on the unique condition of the patient both before and after the development of a neurological condition, as well as on availability of services and unpredictable rates of response that may be observed even with mainstay medications.

Approach to Central Nervous System Injury

Initial Considerations

Important considerations in an acute setting of central nervous system (CNS) trauma are:

1. Consciousness
2. Intracranial pressure
3. Cerebral perfusion
4. Cranial structures volume changes (the Kellie-Monroe principle) (1,2)

A dramatic change in any of these usually signifies an impending or already developing trend and directly affects the patient's survival and prognosis.

Consciousness is defined as the ability to be aware of oneself and one's surroundings and is loosely attributed to the activity of the reticular formation, an extensive and fragile neuronal network (2).

Intracranial pressure (ICP) is the normally positive pressure of the cerebrospinal fluid (CSF) present in the cranial cavity. It ranges from 5 mm Hg in an infant to 15 mm Hg in an adult (2).

Cerebral perfusion pressure (CPP) equals mean blood pressure minus ICP and physiologically should be higher than 70 mm Hg in adults and 60 mm Hg in children. Another measure is the cerebral perfusion rate: it is well known from emergency practice that if cerebral perfusion falls below 12 mL of blood per mg of neural tissue per minute, irreversible brain damage occurs (3).

Since the cranial space is closed, the Kellie-Monro principle asserts that changes in one of the intracranial components (e.g., CSF or blood) will result in compensatory alteration in the others (e.g., brain volume.) In practice, increases of ICP cause herniation of the brain matter through natural openings such as the tentorium hiatus (uncal herniation, commonly associated with the ipsilateral compression of cranial nerve III and dilatation of the ipsilateral pupil) or the foramen magnum (hindbrain herniation). Both can result in brainstem compression and death (conning) (4).

Both direct impact and contrecoup injuries, in which the moving brain careens onto the skull opposite the point of impact, can result in focal bleeding beneath the calvarium. Such bleeding can result in an intracerebral focal contusion or hemorrhage as well as an extracerebral hemorrhage. Axonal injury increasingly has been recognized as a structural sequela of brain injury. Interestingly, a prominent locus of axonal damage has been the fornices, which are important for memory and cognition. More severe and diffuse axonal injury has been found to correlate with vegetative states and the acute onset of coma following injury (2,4).

Emergent Care

Realistically, a neurologist is likely to be involved in management of an acute CNS trauma patient as a part of a larger team that should necessarily include an emergency physician. As a result, the most important points of approach are not those at the scene of the accident but rather upon hospitalization. Basic knowledge of the principles of management of any obvious or potential CNS injury is valuable. On the scene, the circumstances of the accident or injury should be assessed quickly, and any potential risk of CNS injury identified alongside the rest of the injuries in order to help guide appropriate care. It is often stated that the patient should be moved as little as possible, especially for patients who suffered machinery-related injuries. Most importantly, the patient's neck (and the rest of the spine) should not be hyperextended, hyperflexed, or rotated. Use of spinal boards and neck immobilizers is very important; they should be made readily available to medical personnel and, in the agricultural setting, other educated and capable individuals (1,4).

Physical Examination

The Glasgow Coma Scale (GCS) score should be obtained, and the test repeated as needed. Although not part of the original concept, separate constituent parts of the total GCS score (e.g., eye opening, verbal response) are more informative when communicated to another health professional than merely the total score, which is useful in generalized triage and classification of the severity of the injury as minor (GCS score >14), moderate (GCS score <13 and >9), or severe (GCS score < 8) (4).

In performing a neurological examination, begin by specifically looking for signs of skull base fracture (raccoon eyes, hemotympanum, CSF rhinorrhea or otorrhea, the Battle sign), usually after 8 to 12 hours. If fractures are suspected or confirmed, especially those of the facial bones, perform careful auscultation of the carotids for possible carotid dissection.

Other highlights of a neurological examination in such cases are listed in Table 17.1.

Although the popular Mini-Mental State Examination disproportionately emphasizes left hemisphere functioning, studies have documented its usefulness even in the long-term. For example, one study indicated that 23% of patients with mild head injuries score less than 24 out of 30 points 1 year after injury. Motor regulation can be assessed rapidly using the Luria "fist, chop, slap" sequencing task (5).

An antisaccade task, in which the patient looks away from the offered visual stimulus, recently has been shown to be impaired in patients with symptomatic whiplash injury compared to controls, although the sensitivity of this test in detecting brain injury has been questioned.

Letter fluency, in which the patient names as many words as possible beginning with a specific letter in 1 minute, and category fluency, in which the

Table 17.1. Neurological signs in acute trauma.

Sign	Note
Visual acuity	If the level of consciousness allows assessment
Pupillary light reflexes	Both direct and consensual must be tested
Fundus examination (direct or indirect)	Look for signs of retinal detachment, hemorrhages, or papilledema
Spinal tenderness	May be assessed by wincing and avoidance in unconscious patients; such assessment is controversial and results are hard to interpret
Limb movements	In a cooperating conscious patient
Reflexes	In all patients
Plantar response	Babinski sign should be addressed specifically
Motor weaknesses	In a cooperating, conscious patient
Gross sensory deficits	In a cooperating, conscious patient

Source: Data from Working Party of the Royal College of Surgeons of England (2) and Procaccio et al. (4).

patient names as many items as possible in a certain category in 1 minute, provide further information about self-generative frontal processes.

An untimed Trails B test, in which the patient alternates between number and letter sequences, allows further qualitative testing of frontal functioning (2).

Testing

Patients must be reassessed frequently as their neurological condition often changes rapidly and even precipitously. Assessment every 2 hours is warranted in all patients with moderate head injury (GCS score less than 13 but higher than 8). These patients should also undergo computed tomography (CT) scan of the head and should be admitted to the hospital. If no improvement is noticed within hours after admission for observation, the CT scan should be repeated.

The most useful role of electroencephalography (EEG) in head injuries may be to assist in the diagnosis of nonconvulsive status epilepticus, which may account for a substantial number of coma presentations (up to 8% in one study). Extreme accuracy (99.5%) in prediction of the negative outcome in brain injury is associated with the bilateral absence of somatosensory evoked potentials (6).

Magnetic resonance imaging (MRI) typically is reserved for patients who have mental status abnormalities unexplained by CT scan findings. Magnetic resonance imaging has been demonstrated to be more sensitive than CT scanning, particularly at identifying nonhemorrhagic diffuse axonal injury lesions. In some cases, MRI has shown degeneration of the corpus callosum following severe head injuries with axonal damage. Increased total lesion volume on fluid-attenuated inversion-recovery (FLAIR) MRI images has been demonstrated to correlate with poor clinical outcomes, while diffusion-weighted imaging may disclose abnormal lesions in patients with head injury even when their conventional MRI scans are unremarkable. Remember that white matter hyperintensities in patients with head trauma may recede when initial MRI scans are compared with those obtained in the months following the injury (1,4).

Management

In severe head injury, CT scan and neurosurgical referral are important, and, if signs of brain herniation (Kellie-Monroe signs) are present or developing, simple but often effective means of decreasing the intracranial pressure should be ascertained and implemented:

1. The head should be elevated (30° to 45°). Keep the neck straight and avoid constriction of venous return.
2. Maintain normovolemia and normal blood pressure (BP) (mean BP > 90 mm Hg).

3. Ventilate to normocapnia and avoid hypocapnia (P_{CO_2} >3.5 kPa).
4. Use light sedation and analgesia (e.g., codeine phosphate at 30 to 60 mg IM q4h).
5. Insert an ICP bolt to monitor the pressure status.
6. Consider administration of mannitol (1 g/kg IV immediately) (7).

Because of the likelihood of spinal injury, any patient with traumatic injury should be treated as having potential spinal injury until radiographic and clinical evidence indicates otherwise. Imaging of the spine should include at least plain x-ray films of the cervical spine (anteroposterior and lateral, a peg view, and with the C7-T1 junction visible). When a spinal injury is strongly suggested, either because of the mode of injury or because of indicative findings on the x-ray film, a CT scan of the spine should be performed next (8).

All physicians must remember that CT scanning is not an absolute diagnostic test. It is worth noting that spinal cord injury without noticeable radiographic abnormality occurs in up to 5% of spinal injuries (8).

Common types of injury that can be seen on CT include atlanto-occipital dislocation (usually fatal), atlas fractures (often treated conservatively), axis fractures (in most cases challenging), and C3-T1 injuries in which earliest alignment and decompression of the spinal cord is desirable (8).

Spinal cord trauma patients must be immediately assessed for proper localization and determination of the extent of the lesion. Physicians are reminded that in the acute phase, the classic syndrome of complete spinal cord transection presents with the following:

1. Possible respiratory insufficiency
2. Lower and upper extremity areflexia combined with anesthesia below the affected level
3. Neurogenic shock with hypothermia and hypotension without compensatory tachycardia (not observed commonly in low thoracic and lumbar spinal cord lesions)
4. Loss of rectal and bladder sphincter tone
5. Urinary and bowel retention leading to abdominal distention, ileus, and delayed gastric emptying (9)

Ipsilateral ptosis, miosis, and anhydrosis (Horner's syndrome) may also present because of interruption of the descending sympathetic pathways (9).

In the anterior cord syndrome, the patient presents with paralysis, loss of pain and temperature sensation below the level of the lesion, and relative sparing of touch, vibration, and proprioception.

Trauma commonly leads to central cord syndrome, often associated with significant arm weakness, less pronounced leg weakness, and variable sensory deficits. Pain and temperature sensations are affected most commonly, a modality known as "dissociated sensory loss" that may present in a cape-like fashion (8,9).

The other common traumatic presentations include Brown-Séquard syndrome (a hemicordectomy with ipsilateral paralysis, loss of vibration and position sense below the level of the lesion with hyperreflexia, while contralaterally, loss of pain and temperature sensation occurs two to three segments below the level of the lesion) and the cauda equina and conus medullaris syndromes (8–10).

Patients with lesions affecting only the cauda equina can present with a polyradiculopathy with pain, radicular sensory changes, asymmetric lower motor neuron–type leg weakness, and sphincter disturbances. This can be difficult to distinguish from involvement of the lumbosacral plexus or multiple nerves. Lesions affecting only the conus medullaris cause early disturbance of bowel/bladder function (11).

Treatment Modalities

The National Acute Spinal Cord Injury Studies (NASCIS) I and II published in the 1990s demonstrated significant benefit in administering high doses of methylprednisolone early after a spinal cord injury (within 8 hours). The dose is 30 mg/kg IV over 15 minutes, followed by 5.4 mg/kg/h via continuous intravenous infusion over 24 hours (12,13).

In cases of failure of the listed approaches and procedures, resuscitative/stabilizing measures of increasingly heroic nature are attempted:

1. Heavy sedation to achieve paralysis
2. Increased rate of mannitol infusion, 1 g/kg, followed by 0.25 g/kg every 6 hours; serum osmolality maintained around 320 mOsm, consider alternating with furosemide at 1 mg/kg
3. Hyperventilation of the patient to achieve a P_{CO_2} of 3 to 3.5 kPa and induce a high-dose barbiturate coma; the latter may serve as an excitotoxicity-limiting measure (14).

In the acute setting, use of phenytoin and nifedipine has been suggested. Phenytoin reduces the incidence of early posttraumatic seizures, and nifedipine is a potential neuroprotective agent. As a calcium channel blocker, nifedipine is expected to minimize the toxic effect of calcium ion flux in excitotoxicity cascade. The possibility of an allergic response to phenytoin and apparent lack of dramatic improvement with nifedipine are likely to limit the use of these drugs in the field (15).

The long-term management of patients who suffered head trauma in the agricultural or other industrial setting is oriented toward a hard-to-achieve twofold goal: restoration of normal tonicity and restoration of cognitive function. Both of these consequences of brain trauma are disabling, and patients need a thorough and systematic evaluation of their employment prognosis. In our experience, in hypertonicity, spasticity, or dystonia with attendant muscle spasms both baclofen and tizanidine are preferred medications because of their more favorable side-effect profiles. Intrathecal baclofen is an excellent

option for many patients and is usually tolerated well. A more direct approach that requires multiple injections and excellent knowledge of anatomy (as well as the ability to identify anatomical variations on the fly) is injection of botulinum toxins types A and B. Other medications may include benzodiazepines (e.g., diazepam) and dantrolene. In all cases the physician must evaluate for tremor, dystonia, parkinsonism, myoclonus, and hemiballism, as all of these are common (more that 10% of head trama cases) and tend to persist long-term in head injury patients (16–18).

Cognitive enhancement is a much more vaguely defined goal and, as a result, most of the research performed in the area is either small-sample or poorly controlled. Anecdotal data suggests that methylphenidate, levodopa, amantadine, memantine, and donepezil may be useful. Amantadine is also an excellent fatigue-controlling agent and has few side effects. The use of the atypical members of the stimulant family, modafinil and adrafinil, is even less studied, although these medications show some promise. European colleagues often use piracetam and related compounds. These medications are not readily available in the United States, except for levetiracetam, which has not been studied in the cognitive restoration setting but may be of use in controlling seizures in some patients. Some consultants report the use of a semi-synthetic analogue of vasopressin (desmopressin) for the purposes of restoration of cognitive acuity. None of these approaches is in widespread use in the United States and should be considered experimental at best (16–18).

The physician must always remember that an initial grading of "mild" does not necessarily mean a mild outcome of any given brain injury. Recent studies have demonstrated that following mild head injury, only 54% to 79% of patients are able to return to full preinjury employment. Another study of 148 patients with mild head injury discovered that after 1 year, 26% had moderate disability and 3% had severe disability. Significant neuropsychological dysfunction, primarily of attentional and memory domains, may persist after mild head injury alone. Irritability, posttraumatic headache (often complicated by the analgesic rebound headache), and fatigue are often the defining complaints in all cases of brain injury, regardless of the initial grading. Another concern is the issue of posttraumatic epilepsy that is diagnosed in about 4% of patients who sustained head injuries. As in other cases, 24-hour EEG monitoring is likely to detect or rule out seizure activity (19–23).

The main goal in the long-term care of spinal cord trauma patients is to prevent medical complications, a complex goal that requires administration of empiric antibiotics as indicated, maintenance of adequate perfusion (mean arterial pressure must remain above 70 mm Hg at all times), prophylaxis of deep vein thrombosis and pulmonary embolism, as well as bladder and bowel care to prevent distention, discomfort, impaction, and infection.

Pain and anxiety control is often required but may be difficult. Narcotics must be used judiciously or avoided because of adverse bowel and bladder

effects. Drugs causing depression of the CNS (e.g., benzodiazepines) should be used with caution due to the possibility of respiratory failure (24,25).

Gastrointestinal prophylaxis against ulcers is mandatory. Patients with spinal cord injury have a high incidence of stress ulcers, which can also be exacerbated by the concomitant use of steroids in the acute phase. The use of antiinflammatory drugs should be very cautious since even highly promoted cyclooxygenase-2 (COX-2) inhibitors possess the intrinsic risk of promotion of GI ulceration (24).

Psychological and emotional support throughout the patient's disease course is necessary and is best provided informally and continuously by the caregivers; however, formal intervention by specialists may be required (24,25).

Neurological Disease and Operation of Machinery

Employment in the agricultural sphere entails operation of tools and machinery, including apparatus that demand specific and highly developed sequences of decisions and actions by the operator. Impairments of any aspect of neurological functioning may contribute to impairment of such abilities and to permanent disability in more severe cases. In addition to personal risk and morbidity, patients are often found in situations where their actions are likely to affect the risk of injury and even death of others. This consideration places a social demand on the physician who is assessing fitness of the patient to drive and operate agricultural machinery (26).

Unfortunately, the ability to safely drive or operate machinery cannot be determined in a medical office. Issues such as judgment and unnecessary risk-taking behavior may be impossible to address in an examination room. Unrealistic expectations on the part of the patient, the employer, and various government agencies also persist, even though it should be fairly obvious that physicians are not specifically trained in this highly technical area in the same way that certified driving instructors or equipment manufacturer representatives are (27,28).

The general consensus is that patients severely affected by dementia, including posttraumatic epilepsy, multiple sclerosis, or movement disorders, should be thoroughly evaluated for their fitness to drive or operate machinery. No consensus or guidelines exist that would serve as a reliable "calibration" tool applicable to at least a substantial majority of patients (29,30).

Evaluation for Machinery Use

We propose a simplified algorithm (inspired by the GCS and multiple personal driving experiences, as well as assessment of thousands of patients) for such evaluation with the stipulation that it should be viewed as a suggestion rather than a prescription (Table 17.2).

Table 17.2. Proposed driving or machinery operating disability scoring matrix.

Task or manifestation	A: Normal or better	B: Somewhat impaired ("leaning positive")	C: Definitely impaired ("leaning negative")	D: Incompatible with safe driving/ operating of machinery
Visual field and acuity	0	1	2	3
Impulsivity and risk-taking	0	1	2	3
Speed of response	0	1	3	6
Motor function	0	2	6	8
Seizure or pseudoseizure disorder diagnosis	0	2	4	6
Seizure-free for more than 18 months	0	–2	–1	0
Pseudoseizures presenting with abrupt loss of control	0	2	4	6
Sleep disorder suspected	0	1	2	3
Sleep apnea or other drowsiness-inducing diagnosis	0	2	4	6
Present alcohol or recreational abuse	0	2	4	8
Dementia present (based on MMSE scores or similar assessment)	0	2	4	8

MMSE, Mini–Mental Status Examination.

The physician should assess the patient and decide on the impressions: is the patient unimpaired (column A); is the patient impaired but seeming to compensate effectively (column B); are the patient's attempts to compensate inadequate (column C); or is the patient's presentation that of decompensation (column D)? Summation of the corresponding number scores produces the disability index (ideally, in a healthy patient this index is 0, while a severely impaired patient may present with the maximum score of 51). The severity indices (number in the table's cells) are based on published studies, for example, Teran-Santos et al. (31), who reported that patients with an apnea-hypopnea index of 10 or higher had an odds ratio of 6.3 (95% confidence interval [CI] = 2.4 –16.2) of having a traffic accident within a year (32).

A similar approach led to the assignment of indices for seizure disorders. Ever since Waller's research, epilepsy patients with poor compliance in taking their anticonvulsant medication, and patients who are young and abuse alcohol are justifiably believed to pose the highest risk of driving or machinery accidents. At the same time, the literature suggests that patients with seizures without loss of consciousness pose no increased risk, while those with an established pattern of exclusively nocturnal events, as well as those with consistent and prolonged auras, have much less risk than the Waller's "deviant" group. It is worth noting that the consensus statement approved in

1994 by the American Epilepsy Society and the American Academy of Neurology recommended a minimum seizure-free interval of only 3 months, although legal requirements vary widely among states (33).

In Parkinson's disease even moderate severity is often severely disabling due to the inability to initiate and stop motion, an absolute necessity in operation of all machinery. Distance judgment may also be impaired early in the disease and should be assessed separately. Patients with stroke, multiple sclerosis, and other diseases with highly heterogeneous presentation should be assessed on individual basis, although their scores may still be calculated and used in justification of the recommendation (34).

In some cases, indirect evidence obtained from coworkers, employers, and cohabitants may contribute to the establishment of general recommendations in regard to driving and machinery operating ability (Table 17.3).

Muscle Weakness: Evaluation to Management

Electrodiagnostic studies are used to elucidate abnormal neuromuscular transmission and to exclude other diseases of the motor unit that may mimic or contribute to the clinical findings. Electromyographic studies may also be useful in measuring the severity of involvement and demonstrating changes as the disease develops. Although the detailed account of available electrodiagnostic techniques would take several volumes, certain generalities are worth remembering, as they may affect both the diagnostic and treatment modalities appropriate for patients who, due to the nature of their employment (e.g., seasonal workers) may not benefit from the longer observation times often required in slow developing conditions.

The most commonly used electrodiagnostic test of neuromuscular transmission involves repetitive stimulation of a motor nerve while recording compound muscle action potentials (CMAP) from a muscle innervated by that

TABLE 17.3. Assessing the patient's fitness to drive or operate machinery.

Question	Red flag answer
Is patient's alertness adequate?	"Inadequate" or "slow"
Is patient's vision adequate?	"Fails to see (sides, blind spots, etc.)"
Is patient's reaction adequate?	"Slow to react" or "Reacts too fast and incorrectly (e.g., begins to move when the left turn arrow lights up at a complex intersection even though there is red light for his/her lane)"
Is the patient's movement adequate?	"Fails to work levers, gears etc." "Drives in one gear"
Is the patient's cognition adequate?	"Fails to get to destination" "Forgets known routes, avoids unfamiliar routes etc."
Is the patient's vigilance and fine motor control adequate?	"Can't drive and talk at the same time" "Swerves when changing radio settings"

Source: Data from Meyers et al. (27), Zesiewicz et al. (29), and Rau (30).

nerve. The result is abnormal if progressively fewer muscle fibers respond to nerve stimulation during a train of stimuli, producing a "decrementing" pattern in the CMAP (35).

Weakness from abnormal neuromuscular transmission improves after intravenous administration of 10 mg (in fractional doses) edrophonium chloride (Tensilon). For a Tensilon test to be considered positive, a dramatic, unequivocal improvement in muscle function should be observed directly by the examiner. Increasing weakness after administration of these doses of Tensilon (a paradoxical response) is also an indication that neuromuscular transmission is impaired. This test carries significant risks of adverse effects (respiratory and circulatory) and should not be viewed as "first line" (36).

Electromyography

Abnormal neuromuscular transmission may be seen in electromyography (EMG) recordings as variability in the shape or amplitude of motor unit action potentials (MUAPs). Unstable MUAPs also are observed in denervating disease, especially motor neuron disease, and thus are not specific for myasthenia gravis (MG). When seen without other evidence of neuronal disease, unstable MUAP should prompt an assessment for MG or other diseases of neuromuscular transmission (36).

Single-Fiber EMG

Single-fiber EMG (SFEMG) is the most sensitive electrodiagnostic test of neuromuscular transmission. It demonstrates increased jitter in a limb or face muscle in almost all patients with MG. Because of its marked sensitivity, SFEMG also demonstrates abnormal jitter in other diseases of nerve and muscle; thus, the results must be interpreted in conjunction with the results of more conventional electrodiagnostic studies (37).

Other Diagnostic Tests

Although no evidence exists in the literature regarding incidence of specific types and presentations of neuropathy in the agricultural setting, some preliminary conclusions can be drawn from a commonsense approach. Specific types of motion may lead to increased risk of entrapment and trauma of peripheral nerves, and metabolic disease (e.g., diabetes) or nutritional deficiency (e.g., due to malnutrition or alcohol abuse) will either predispose the patient to development of neuropathy or exacerbate the course of disease. These considerations necessitate the following minimal battery of laboratory tests for patients with suspected neuropathic process:

1. Complete blood count
2. Fasting blood glucose

3. Hemoglobin A_{1C}
4. Antinuclear antibody
5. Erythrocyte sedimentation rate
6. Renal function tests
7. Paraproteinemia workup
8. Angiotensin-converting enzyme level
9. Lyme serology
10. Thyroid function tests
11. Rapid plasma reagent (RPR) and HIV serology

In addition, we recommend complete hepatitis serology and workup. In our experience and according to the literature, hepatitis C may present with symptoms resembling neuropathy. This disease is commonly missed even in a setting with a well-organized system of delivery of medical services and is vastly underdiagnosed in the rural population. Results of these tests will elucidate the possible etiology and pathogenesis of the specific disease and complement the electrodiagnostic methods.

Mononeuropathies

In the agricultural setting, mononeuropathies can occur secondary to direct trauma, compression, stretch injury, ischemia, infection, or inflammatory disease. Especially common are the nerve entrapments with compression of the nerve either by normally present anatomical structures or by an external source. The most common nerve entrapments are at the median nerve of the wrist (carpal tunnel syndrome) and ulnar nerve of the elbow (cubital tunnel syndrome). Other mononeuropathies such as femoral (including lateral femoral cutaneous) and peroneal mononeuropathy are less commonly observed, while lumbosacral disk syndromes are exceedingly common but are best addressed in conjunction with aggressive pain management and surgical evaluation, a modality that requires team approach (38–41).

Compression and entrapment neuropathies are predominantly demyelinating and result in slowing of the nerve conduction through the affected fibers. A complete block is observed in acute compression and is uncommon in the chronic presentation. Secondary axonal changes are expected in patients with unresolved compression or entrapment that leads to ischemia and nerve transection and are often irreversible as they may lead to both wallerian degeneration distally and changes in self-regulation of the neuronal networks at the spinal level, while simple demyelinating lesions typically have a better capacity to recover.

Nerve conduction studies (NCS) and EMG are extremely useful in defining the lesion location, the type of damage, and thus the prognosis. It is often necessary to test more than one nerve in any given extremity to avoid the misdiagnosis of a mononeuropathy in a patient with polyneuropathic disease (42).

Radial Neuropathy

In the rural setting, radial neuropathies may result from injury, subluxation of the radius, compression, or ischemia. The most common complaint is wrist drop, but other symptoms are noted, especially numbness of the forearm and hand (if the lesion is above the elbow), and pain that resembles tennis elbow. Paresthesias of the back of the hand are almost always an indication of lesion localization at the wrist level.

Due to the complexity of anatomy and somewhat generic presentation of radial mononeuropathy, both NCS and EMG are considered to be the gold standard in diagnosis of this condition and in determining severity of the lesion and prognosis, including disability in the patient (38).

Management

Since management of lesions of the radial nerve involves the decision between a conservative approach and surgical decompression (especially at the forearm level), the earliest and most precise diagnosis is associated with potential restoration of function and return to work. A repeat NCS or EMG study should be performed after several months of conservative management to ascertain the possible regrowth of the nerve fibers and, thus, the need for reanastomosis via surgery.

Ulnar Mononeuropathy

Because the ulnar nerve is a mixed nerve, supplying muscles in the forearm and hand and providing sensation over the fourth and fifth digits of the hand, palm, and posterior aspect of the forearm, very specific symptoms are associated with its pathology. Physicians are reminded that the most common site of entrapment is in the wrist (carpal tunnel syndrome) with the elbow being the second most common. Both the axons and the myelin sheaths may be affected, often in a selective manner, which in axonal pathology may involve fascicles to individual muscles, leading to motor unit loss and amplitude/area reduction. Involvement of myelin sheaths (usually as isolated demyelination) presents as slowing of conduction (abnormal temporal dispersion) (39).

Interestingly, men are more susceptible to wrist entrapment than women, a finding that may be of value in the rural setting where trauma of the elbow is a common occurrence, while carpal tunnel–associated trauma (i.e., typing) is less common. Patients commonly present with changes in sensation and individual muscle strength; some present with a clawed posture of the hand(s) (38).

Two signs need to be ascertained: the Froment sign (indicates weakness of the adductor pollicis muscle) and Tinel-2 sign (useful in assessment of carpal tunnel syndrome–associated neuropathic changes). The Froment sign is manifested by activation of the flexor pollicis longus while the patient attempts to

pinch the thumb and forefinger or grasping a sheet of paper (the patient may notice this and describe a failure of the thumb to move "on its own" to reach the forefinger). The Tinel-2 sign is elicited by tapping over the carpal tunnel; in a positive sign, this results in a tingling sensation in the distribution of the median nerve (38).

In all patients NCSs with or without EMG are viewed as the ultimate diagnostic and monitoring studies. The NCS measures basic sensory and motor nerve parameters such as latency, amplitude, and conduction velocity. With stimulation above and below the elbow and recording from the main belly of an involved muscle (commonly, abductor digitorum quinti [ADQ] or first dorsal interosseous [FDI]), the neurologist will both localize the site of involvement and decide on its severity. We recommend the use of the "inching" technique (more formally known as the short segment stimulation technique) for increased resolution and differential diagnosis between infracondylar (commonly, in the cubital tunnel) or supracondylar (commonly as the ulnar palsy tarda) conduction blocks (38,39).

Physicians are also reminded of the common (about 25% of the population) anatomical variation, known as the Martin-Gruber anastomosis in which fibers from the median nerve, typically the motor branches, cross over and join with the ulnar nerve in the forearm. This abnormal pattern of innervation may lead to confusing findings (e.g., the larger median CMAP amplitude at the elbow has an initial downward deflection, which is not seen at the wrist). Electrophysiological findings may also ascertain the ongoing loss of muscle fibers via detection of abnormal spontaneous activity (such as fibrillation potentials and fasciculations) (43).

Management

Patients with ulnar nerve damage should be treated aggressively and with a certain degree of creativity and personalization of care. Depending on the general medical health status, medications that address vascular and metabolic components of the neuropathic process are warranted. Pain may respond to nonsteroidal antiinflammatory drugs, opioids, tricyclic antidepressants, stimulants (e.g., methylphenidate), and many anticonvulsants (e.g., gabapentin). Many patients may need surgical care; thus all patients should be referred for an appropriate consultation. Electrodiagnostic studies should be repeated as needed, especially in cases of severe pathology (with motor amplitude of 10% of normal or a greatly reduced recruitment of motor units, which, in our opinion, is a sign of poor prognosis for recovery) (43).

Femoral Mononeuropathy

Femoral mononeuropathy in the agricultural setting may be caused primarily by compression of the nerve as it passes through the psoas muscle and through the iliopsoas groove. This compression may be caused by excessive

flexion, abduction, and external rotation of the hip, which occur relatively commonly in workers whose daily routine requires manipulation of heavy objects. Blunt trauma to the nerve is also common, as is resulting hemorrhage that exacerbates the degree of neuropathy (41).

Patients may present with "knee buckling," another manifestation of muscle weakness that develops relatively rapidly. Paresthesias are rare but possible, especially if there is involvement of the lateral femoral cutaneous branch (meralgia paresthetica); in many cases numbness of the medial thigh and the calf is also present. Decreased patellar reflex and quadriceps wasting are expected in these patients, as there may be slow and often partial involvement of the iliopsoas (41).

Evaluation for femoral nerve dysfunction includes NCSs and needle EMG. If an NCS is performed, it should include sensory studies of the saphenous nerve and motor studies of the femoral nerve, while EMG should show neuropathic changes in the quadriceps and possibly iliopsoas. The EMG should be performed in cases of suspected involvement of the lateral femoral cutaneous nerve, as it is the easiest modality that allows ruling out upper lumbar radiculopathy (41).

Peroneal mononeuropathy is common and may be caused by prolonged sitting in a slightly tilted position, as, for example, in a tractor driver's seat or airplane seat, especially in patients who cross their legs or fold the left leg underneath while pushing the pedals with their right foot. Squatting, especially in persons of thin stature, is a known risk factor, while obesity is emerging as the most commonly overlooked source of peroneal nerve compression (40).

In cases of peroneal mononeuropathy, patients present with foot drop that often spares plantar flexion and foot inversion, night cramps ("charley horse," especially early in the course of the disease), and sensory manifestations such as neuropathic numbness and neuropathic tingling. The gait may be either high-stepping or foot-slapping or both. Asking patients to walk on their heels may aid in diagnosis as weakness of foot dorsiflexion will become more obvious. Differentials include generalized neuropathy, chronic inflammatory demyelinating neuropathy, and L5 radiculopathy. All of these can present with a foot drop but usually spare the foot inverters (40).

Both NCS and EMG are recommended in these patients. The NCS may indicate peroneal nerve abnormalities, especially in the presence of axonal damage, which manifests as a smaller compound muscle action potential. The NCS also allows differentiation among mononeuropathy, vasculitic mononeuritis multiplex, and generalized polyneuropathy of other (e.g., diabetic) etiology.

The EMG is especially valuable in localizing the compression/lesion area(s) and in differentiation between L5 radiculopathy and peroneal mononeuropathy. The EMG may also suggest involvement of the thigh muscles, which may necessitate an MRI study of the thigh to rule out mass lesions (40).

Management

Treatment is dependent on the etiology and location of the lesion. Most patients with lower extremity mononeuropathies should be treated conservatively with physical therapy, avoidance of motions and postures that caused or contributed to their condition (e.g., excessive hip abduction and external rotation in femoral involvement, leg crossing or folding in a "semi-lotus" position in peroneal disorder), and specific braces. Surgery for decompression may be indicated but may not lead to a complete reversal of symptoms. Pain may be effectively controlled with analgesics and, more recently, anticonvulsants, which are rapidly becoming a standard part of the armamentarium. In cases of neuropathy due to diabetes or vasculitis, immunomodulating therapy may be attempted (39,40).

Occupational therapy and physical therapy are always desired, as are patient education and support programs. Unfortunately, the availability of such programs and treatment modalities may be very limited.

Lower Back Pain

Lower back pain (LBP) is ubiquitous and potentially debilitating and disabling, especially in the context of manual labor–oriented occupations and occupations that involve strain or vibration applied to the spine. Patients with LBP require investigation and evaluation by a knowledgeable physician and, in some cases, by a team of specialists, including a physician and a physical therapist, and with surgical, occupational, and pain-control consults as needed.

Diagnosis

There are numerous well-documented approaches to LBP diagnosis and management. All patients presenting with LBP should be thoroughly examined. Although most are candidates for electrodiagnostic and imaging studies, the "hands-on" examination may reveal information that would otherwise be missed. All patients require palpation of the spine and muscles, with determination of whether tender or trigger (tender plus spastic response) points are present in lumbar musculature (often neglected is the quadratus lumborum muscle, a major source of tender points in conditions such as fibromyalgia and in somatic presentations). A dolorimetric examination in which a simple device (dolorimeter) is used to deliver measured amounts of pressure (up to 10 kg/cm^2) is valuable in evaluation of tender points and may provide evidence of pain pathology (e.g., hyperalgesia or hyperpathia). Tenderness on palpation of the lower extremity may be due to referred pain, and tenderness at the level of an involved intervertebral disk is also common (44).

Another often-neglected examination technique is the establishment of the range of motion of the affected spine. Range of flexion, extension, lateral bending, and rotation should be documented. We recommend the Schober test as a simple and quick method of measurement of range of flexion of the spine. In this test, one point is marked midway between the two posterior sacroiliac spines, and the second and third points are marked 5 cm (2 inches) below and 10 cm (4 inches) above the initial mark. The distance between the three points is measured (surprisingly, it is rarely exactly 15 cm!). The distance is remeasured upon the patient's flexing of the spine and may be remeasured several times, for example, after the patient lies down and relaxes the muscles for several minutes. The change between erect and flexed measurements of less than 4 cm (1.6 inches) is indicative of restricted range of flexion (44).

Although time-consuming, dermatomal sensory examination may be needed in cases of lumbar radiculopathy that are not clear-cut and may contribute to an improved choice of locations for needle EMG and other diagnostic studies. Hyperesthesia is common, but, since this is a subjective presentation, its value in diagnosis is controversial (44).

Examination must include bilateral testing of reflexes, with any sign of asymmetry carefully noted. Provocative maneuvers, such as straight leg raising, may provide evidence of increased dural tension, indicating underlying nerve root pathology. They are also somewhat patient-dependent, but common consensus is that the straight leg raising test is only considered positive if pain occurs when the leg is elevated 30 to 70 degrees and when pain travels down below the knee, as nerve root tension is negligible if the leg is elevated less than 30 degrees, while painful presentation above 70 degrees is most likely related to muscular pain in the hamstrings or gluteal muscles (44).

Computed tomography scan of the lumbar spine provides superior anatomical imaging of the osseous structures of the spine and good resolution for disk herniation. However, its sensitivity for detecting disk herniations when used with myelography is inferior to that of MRI, especially the T2-weighted images, which may show areas of intervertebral disk degeneration (showing as darker areas due to loss of hydration). Results of CT and MRI should not be overinterpreted, as many healthy subjects show sometimes dramatic changes in disk anatomy, especially as they age. In a sobering study, Jensen and colleagues (45) found that out of 98 asymptomatic people, 64% of subjects without any back pain had a bulge, protrusion, or extrusion of the intervertebral disk at one level, and 38% had an disk abnormality at more than one level.

Electrodiagnostic studies, including NCS, needle EMG, and somatosensory evoked potentials (SSEPs), should be considered for all patients with LBP: to clarify the diagnosis in patients with limb pain; to exclude or confirm presence of peripheral neuropathy and motor neuron disease; and, most important, to quantify the extent and acuity of radiculopathies, something

that no other diagnostic modality can provide. We usually recommend performing electrodiagnostic studies after 3 to 4 weeks have elapsed from the moment of acute injury; axonal changes may be unnoticeable on studies performed before that time. Diagnostic assessment of the late responses, such as the H-reflex is also a necessity to address the issue of whether proximal nerve or nerve root (or both) are involved, especially at the S1 level. Needle EMG affords a particularly high diagnostic yield, especially if the patient had the onset of symptoms less than 6 to 9 months prior. The SSEP study is indicated in all cases when involvement of the somatosensory pathways is suspected or obviously present during the sensory examination (46).

Management

Upon diagnosis, all patients are referred to a physical therapist for a personalized treatment and rehabilitation program. Commonly used modalities are the McKenzie exercise approach, spine stabilization exercises, and strengthening of the abdominal and gluteal muscle groups. Vertebral axial decompression (traction) may be considered; however, currently there is no consensus regarding its efficacy and long-term effects (47).

Surgical consultation may be needed, and the patient is often presented with choices of simple diskectomy, diskectomy plus fusion, and, less commonly, chemonucleolysis, as well as the more modern developments such as percutaneous diskectomy and microdiskectomy. It is not uncommon to see that patients remain in pain despite successful surgery. In these patients a comprehensive battery of imaging and electrodiagnostic studies may be needed, including a diagnostic selective neural blockade, which may help determine the involvement of specific nerve root(s), particularly when EMG alone is hard to interpret (47).

A growing and extremely promising modality is that of therapeutic injections. It is, in our opinion, a valid and often surgery-sparing option that may be of limited availability in the rural setting due to scarcity of trained specialists; it should be strongly considered in all cases when the patient does not have medical contraindications and is willing to travel to the location of a specialized treatment center or specialist's practice (48).

A variety of medications including analgesics (opioid and nonopioid), anticonvulsants, steroidal and nonsteroidal antiinflammatory agents, locally injected agents (e.g., anesthetics, steroids), topical agents (e.g., lidocaine patches, fentanyl patches), stimulants, antidepressants and antiparkinsonian agents have been all tried and have showed various degrees of efficacy. Table 17.4 lists some of the most commonly prescribed medications for LPB. As always, a thorough and creative approach to pain management is mandatory. The authors assert that the mere fact of inclusion of a drug in this table does not imply any endorsement or that the drug is officially approved in the United States for the purpose of treatment of LBP-associated neurological conditions.

TABLE 17.4. Selected medications commonly prescribed for pain management.

Medication	Adult dose	Contraindications	Interactions	Precautions
Nonsteroidal antiinflammatory drugs (NSAIDs)				
Celecoxib (Celebrex)	200 mg/d PO qd; alternatively, 100 mg PO b.i.d.	Documented hypersensitivity to ibuprofen or other NSAIDs; aspirin/ NSAID-induced asthma	NSAIDs may increase retention of sodium and fluid and may raise blood pressure with ACE inhibitors and diuretics; may especially increase the risk of bleeding (e.g., GI) among individuals already taking alcohol, aspirin, corticosteroids, heparin, and warfarin; to minimize risks of adverse effects, patients should avoid taking multiple NSAIDs concurrently	Caution with any history of GI bleeding, hypertension, or CHF; caution in elderly patients; most NSAIDs are considered class-D (unsafe) during the third trimester of pregnancy; avoid use during the third trimester of pregnancy due to potential risk of effecting closure of the ductus arteriosus
Ibuprofen (Motrin)	200–400 mg PO q4–6h while symptoms persist; not to exceed 3.2 g/d	Documented hypersensitivity; peptic ulcer disease; recent GI bleeding or perforation; renal insufficiency; high risk of bleeding, NSAIDs-induced asthma	Coadministration with aspirin increases risk of inducing serious NSAID-related adverse effects; may decrease effect of hydralazine, captopril, and beta-blockers; may decrease diuretic effects of furosemide and thiazides; may increase PT when taking anticoagulants; phenytoin levels may be increased when administered concurrently	Category D in third trimester of pregnancy; caution in congestive heart failure, hypertension, and decreased renal and hepatic function; caution in anticoagulation abnormalities or during anticoagulant therapy

Steroids				
Prednisone	Dosage varies and needs to be personalized; commonly, 5–60 mg/d PO in 1–2 divided doses initially, followed by tapering off the medication over 8–10 d	Documented hypersensitivity; viral, fungal, or tubercular skin infections	Coadministration with digoxin may increase digitalis toxicity secondary to hypokalemia; estrogens may increase levels of methylprednisolone; phenobarbital, phenytoin, and rifampin may decrease levels of methylprednisolone (adjust dose); monitor patients for hypokalemia when taking medication concurrently with diuretics	Pregnancy category C; hyperglycemia, edema, osteonecrosis, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, growth suppression, myopathy, and infections are possible
Ketoprofen (Orudis, Oruvail, Actron)	25–50 mg PO q6–8h prn; not to exceed 300 mg/d	Documented hypersensitivity	Similar to ibuprofen (see above)	Category D in third trimester of pregnancy; caution in CHF, hypertension, and decreased renal and hepatic function; caution in coagulation abnormalities or during anticoagulant therapy
Opioids and related compounds				
Oxycodone (OxyContin)	10 mg PO b.i.d. initially	Patients with a significant history of respiratory depression whose respiratory functions are not being closely monitored; severe bronchial asthma; patients with hypocarbia; paralytic ileus	Phenothiazines may antagonize analgesic effects; MAOIs, general anesthesia, CNS depressants, and tricyclic antidepressants may increase toxicity	Pregnancy category B (D if used for prolonged periods or in high doses); caution in COPD, emphysema, and renal insufficiency

continued

TABLE 17.4. Selected medications commonly prescribed for pain management. (continued)

Medication	Adult dose	Contraindications	Interactions	Precautions
Tramadol (Ultram)	50–100 mg q4–6h; not to exceed 400 mg/d	Documented hypersensitivity; opioid-dependent patients; concurrent use of MAOIs or use within 14 days; use of SSRIs, TCAs, or opioids; acute alcohol intoxication	Decreases carbamazepine effects significantly; cimetidine increases toxicity; risk of serotonin syndrome with coadministration of antidepressants	Can cause dizziness, nausea, constipation, sweating, and/or pruritus; additive sedation with alcohol and TCAs; adjust dose in liver disease, myxedema, hypothyroidism, or hypoadrenalism; caution in those with seizures
Cyclobenzaprine (Flexeril)	10 mg PO t.i.d. initially; not to exceed 60 mg/d	Acute recovery phase of MI; history of arrhythmia; heart block; conduction disturbances; hyperthyroidism	Possible interaction with MAOIs, alcohol, barbiturates, and CNS depressants	Caution in angle-closure glaucoma and urinary hesitance
Metaxalone (Skelaxin)	800 mg (2 tab) PO t.i.d./q.i.d.	Documented hypersensitivity; known tendency to drug-induced hemolytic or other anemias; significantly impaired renal or hepatic function	None reported	Unsafe in pregnancy (category D); caution in hepatic impairment
Tricyclic antidepressants				
Amitriptyline (Elavil)	30–100 mg PO hs	Documented hypersensitivity; do not	Metabolized by the P450 2D6 system; therefore,	Pregnancy category D (unsafe in pregnancy); caution in cardiac

		administer to patients who have taken MAOIs in the past 14 d; use with caution in patients with seizures, cardiac arrhythmias, glaucoma, and urinary retention history	drugs that inhibit this enzyme system (i.e., cimetidine, quinidine) may increase the tricyclic levels; may interact with thyroid medications, alcohol, CNS depressants, barbiturates, and disulfiram	conduction disturbances and those with a history of hypothyroidism, renal impairment, or hepatic impairment; due to pronounced effects in the cardiovascular system, best to avoid in elderly persons
Anticonvulsants (Note that most of these drugs are not approved by the U.S. FDA for the purposes of pain control and that there is no consensus on appropriate dosing strategies. All listed medications and anticonvulsants in general should be withdrawn slowly to reduce potential for increased seizure frequency.)				
Carbamazepine (Tegretol)	200 mg PO b.i.d. and up; generally not to exceed 1600 mg/d	Documented hypersensitivity; history of bone marrow depression	Do not use concomitantly with MAOIs; cimetidine may increase plasma levels and toxicity; avoid concomitant administration with Danazol, if possible	Unsafe in pregnancy (category D); not a simple analgesic—do not use for relief of minor aches or pains; use with caution in patients with increased intraocular pressure; obtain and monitor blood counts; may produce drowsiness, dizziness, or blurred vision
Valproic acid and its derivatives (Depakote, Depakene, Depacon, Divalproex)	5–15 mg/kg/d in 1–3 divided doses, may increase by 5–10 mg/kg/wk; do not exceed 60 mg/kg/d	Documented hypersensitivity; hepatic disease/dysfunction	Cimetidine may cause decrease in clearance and increase in half-life; erythromycin may increase serum concentrations; rifampin may increase oral clearance by 40%; may increase diazepam toxicity; may affect warfarin levels and may decrease zidovudine clearance	Unsafe in pregnancy (category D); thrombocytopenia possible, obtain and monitor blood counts; hepatotoxic; may cause pancreatitis; use caution while driving or operating agricultural machinery

continued

TABLE 17.4. Selected medications commonly prescribed for pain management. (continued)

Medication	Adult dose	Contraindications	Interactions	Precautions
Gabapentin (Neurontin)	Start at 100 mg b.i.d. or t.i.d.; increase by 100–300 mg slowly; not to exceed 3600 mg total daily dose; alternatively, start at 300 mg before bed and shift to divided doses only after patient's levels of drowsiness are ascertained	Documented hypersensitivity	Antacids may reduce bioavailability by about 20% and should be administered at least 2 h before gabapentin; cimetidine may reduce clearance but may not be of clinical significance; conversely, may increase norethindrone levels by 13%	Safety for use during pregnancy has not been established (category C); use caution in patients with severe renal disease
Lamotrigine (Lamictal)	No consensus; may follow the standard approach in seizure disorders: weeks 1–2: 50 mg/d weeks 3–4: 100 mg/d in 2 divided doses; maintenance: 300–500 mg/d (in 2 divided doses)	Documented hypersensitivity	Acetaminophen increases renal clearance, decreasing effects; phenobarbital and phenytoin increase metabolism, causing decrease in levels; valproic acid increases half-life	Safety for use during pregnancy has not been established (category C); use caution in patients with impaired renal or hepatic function; associated with a rash in 5% of patients
Topiramate (Topamax)	Introduce very slowly to minimize the risk of cognitive adverse effects; commonly, begin at 25– 50 mg/d PO; titrate by 25–50 mg/d at 1-wk intervals to target dose of 200 mg b.i.d.; not to exceed 1600 mg/day	Documented hypersensitivity	Reduces digoxin and norethindrone levels; carbonic anhydrase inhibitors may increase risk of renal stone formation and should be avoided; may have additive effect with CNS depressants in CNS depression and other cognitive or	Safety for use during pregnancy has not been established (category C); may cause cognitive slowing; increases risk of developing kidney stone by 2–4 times that of untreated population (i.e., from 1.5% to 3.0–6.0%); this risk may be reduced by increasing fluid intake; use cautiously in

			neuropsychiatric adverse effects	patients with renal or hepatic impairment
Tiagabine (Gabitril)	4 mg PO qd in 2 or 4 divided doses; increase by 4–8 mg/wk until clinical response is achieved; do not exceed daily dose of 56 mg/d administered	Documented hypersensitivity	Cleared more rapidly in patients who have been treated with carbamazepine, phenytoin, primidone, or phenobarbital than in patients who have not received these drugs	Safety for use during pregnancy has not been established (category C); moderately severe to incapacitating generalized weakness has been reported in as many as 1% of patients

ACE, angiotensin-converting enzyme; CHF, congestive heart failure; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; FDA, Food and Drug Administration; MAOI, monoamine oxidase inhibitor; MI, myocardial infarction; PT. prothrombin time; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Source: Data from Physicians Desk Reference (49).

References

1. Ball K, Owsley C. Identifying correlates of accident involvement for the older driver. Hum Factors 1991;33:583–95.
2. Working Party of the Royal College of Surgeons of England. Report of the working party on the management of patients with head injuries. London: Royal College of Surgeons of England, 1999.
3. Bhatoe HS. Primary brainstem injury: benign course and improved survival. Acta Neurochir (Wien) 1999;141:515–9.
4. Procaccio F, Stocchetti N, Citerio G, et al. Guidelines for the treatment of adults with severe head trauma (part I). Initial assessment; evaluation and pre-hospital treatment; current criteria for hospital admission; systemic and cerebral monitoring. J Neurosurg Sci 2000;44:1–10.
5. Barcia-Salorio D. [A historical introduction to the neurophysiological model.] Rev Neurol 2004;39:668–81.
6. Vespa PM, Nuwer MR, Nenov V, et al. Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring. J Neurosurg 1999;91:750–60.
7. Steiner LA, Balestreri M, Johnson AJ, et al. Sustained moderate reductions in arterial CO(2) after brain trauma. Time course of cerebral blood flow velocity and intracranial pressure. Intensive Care Med 2004;12 [Epub ahead of print].
8. McDonald JW, Sadowsky C. Spinal-cord injury. Lancet 2002;359:417–25.
9. Lee BY, Ostrander LE. The Spinal Cord Injured Patient: Comprehensive Management, 2nd ed. Philadelphia: WB Saunders, 2001.
10. Kothbauer K, Seiler RW. [Tethered spinal cord syndrome in adults]. Nervenarzt 1997;68:285–91.
11. Rydevik B. Neurophysiology of cauda equina compression. Acta Orthop Scand 1993;64:52–5.
12. Coscia M, Leipzig T, Cooper D. Acute cauda equina syndrome. Diagnostic advantage of MRI. Spine 1994;19:475–8.
13. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Role of steroids. J Neurotrauma 2000;17:531–5.
14. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Use of barbiturates in the control of intracranial hypertension. J Neurotrauma 2000;17:527–30.
15. Zubkov AY, Lewis AI, Raila FA, et al. Risk factors for the development of posttraumatic cerebral vasospasm. Surg Neurol 2000;53:126–30.
16. Drake AI, Gray N, Yoder S, et al. Factors predicting return to work following mild traumatic brain injury: a discriminant analysis. J Head Trauma Rehabil 2000;15:1103–12.
17. Young RR. Spasticity: a review. Neurology 1994;44:S12–20.
18. Ivins GK. Meralgia paresthetica, the elusive diagnosis: Clinical experience with 14 adult patients. Ann Surg 2000;232:281–6.
19. Mittenberg W, Strauman S. Diagnosis of mild head injury and the postconcussion syndrome. J Head Trauma Rehabil 2000;15:783–91.
20. Keenan HT, Brundage SI, Thompson DC, et al. Does the face protect the brain? A case-control study of traumatic brain injury and facial fractures. Arch Surg 1999;134:14–7.

21. Hanlon RE, Demery JA, Martinovich Z, et al. Effects of acute injury characteristics on neurophysical status and vocational outcome following mild traumatic brain injury. Brain Inj 1999;13:873–87.
22. Bhatt M, Desai J, Mankodi A, et al. Posttraumatic akinetic-rigid syndrome resembling Parkinson's disease: a report on three patients. Mov Disord 2000;15:313–7.
23. Jordan BD, Relkin NR, Ravdin LD, et al. Apolipoprotein E epsilon 4 associated with chronic traumatic brain injury in boxing. JAMA 1997;278:136–40.
24. Ditunno JF Jr, Formal CS. Chronic spinal cord injury. N Engl J Med 1994;330:550–6.
25. Edgerton VR, Harkena SJ, Dobkin BH. Retraining the human spinal cord. In: Lin VW, ed. Spinal Cord Medicine: Principles and Practice. New York: Demos, 2003.
26. Findley LJ, Suratt PM, Dinges DF. Time-on-task decrements in "steer clear" performance of patients with sleep apnea and narcolepsy. Sleep 1999;22:804–9.
27. Meyers JE, Volbrecht M, Kaster-Bundgaard J. Driving is more than pedal pushing. Appl Neuropsychol 1999;6:154–64.
28. Barbe F, Pericas J, Munoz A, Findley L, Anto JM, Agusti AG. Automobile accidents in patients with sleep apnea syndrome. An epidemiological and mechanistic study. Am J Respir Crit Care Med 1998;158:18–22.
29. Zesiewicz TA, Cimino CR, Gardner NM. Driving safety in Parkinson's disease. Neurology 2000;54(suppl 3):A472.
30. Rau PS. NHTSA's drowsy driver research program fact sheet. Washington, DC: National Highway Traffic Safety Administration, 1996.
31. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. N Engl J Med 1999;340(11):847–51.
32. Schulte T, Strasburger H, Muller-Oehring EM. Automobile driving performance of brain-injured patients with visual field defects. Neurology 1999;52:1908–10.
33. Fisher RS, Parsonage M, Beaussart M. Epilepsy and driving: an international perspective. Joint Commission on Drivers' Licensing of the International Bureau for Epilepsy and the International League Against Epilepsy. Epilepsia 1994;35:675–84.
34. Van der Lugt PJ. Traffic accidents caused by epilepsy. Epilepsia 1975;16:747–51.
35. Campbell WW. Focal neuropathies. In: Campbell WW, ed. Essentials of Electrodiagnostic Medicine. Baltimore: Williams & Wilkins, 1999.
36. Sanders DB. Clinical neurophysiology of disorders of the neuromuscular junction. J Clin Neurophysiol 1993;10:167–80.
37. Stålberg E, Trontelj JV. Single Fiber Electromyography: Studies in Healthy and Diseased Muscle. New York: Raven Press, 1994.
38. Eaton CJ, Lister GD. Radial nerve compression. Hand Clin 1992;8:345–57.
39. Massey EW. Sensory mononeuropathies. Semin Neurol 1998;18:177–83.
40. Turner OA, Taslitz N, Ward S. Common peroneal nerve entrapment. In: Handbook of Peripheral Nerve Entrapments. New York: Humana, 1990.
41. Turner OA, Taslitz N, Ward S. Femoral nerve entrapments. In: Handbook of Peripheral Nerve Entrapments. New York: Humana, 1990.
42. Gutmann L. AAEM minimonograph 2: important anomalous innervations of the extremities. Muscle Nerve 1993;16:339–47.
43. Stewart JD. The variable clinical manifestations of ulnar neuropathies at the elbow. J Neurol Neurosurg Psychiatry 1987;50:252–8.

44. Devereaux MW. Neck and low back pain. Med Clinic North Am 2003;87:643–62.
45. Jensen MC, et al. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331:69–73.
46. Gilbert FJ, Grant AM, Gillan MG, et al. Does early imaging influence management and improve outcome in patients with low back pain? A pragmatic randomized controlled trial. Health Technol Assess 2004;8:1–131.
47. Snook SH. Work-related low back pain: secondary intervention. J Electromyogr Kinesiol 2004;14:129–33.
48. Samanta A, Samanta J. Is epidural injection of steroids effective for low back pain? BMJ 2004;328:1509–10.
49. Physicians desk reference, 2004, 58th ed. Montvale, NJ: Thomson Healthcare, 2004.

18

Dermatological Conditions

James E. Lessenger

Key words: predisposing factors, patch testing, wood's light, urticarian, dermatitis

Skin problems in worldwide agricultural workers are very common. Among California grape and tomato harvesters, pustular eruptions such as acne and folliculitis were present in 30% of studied workers. Irritant or allergic contact dermatitis was present in 2%. In Iowa, 9.6% of male farmers and 14.4% of wives of farmers reported dermatitis during the previous 12-month period. In Washington State, researchers studied 7445 claims for occupational skin disorders filed over a 5-year period. Medical bills totaled $1.22 million, and lost time payments were $1.23 million. The highest rates of occupational skin disorder claims were seen in agriculture with 2.8 claims per 10,000 full-time equivalent employee years. Most of these skin disorders were due to chemical and vegetation exposures (1–4).

Among northern Ecuadorian potato farm workers, high rates of dermatitis and pigmentation disorders were attributable to the use of pesticides and fungicides. Among California farm workers, skin disease rates were found in tomato workers (6.2%), citrus (10.8%), and vineyard workers (21.0%). Factors found to contribute to dermatitis in farm workers included the specific type of crop cultivated, specific job activity, use of personal protective measures, field and home sanitation, environmental conditions of heat and humidity, personal hygiene, allergic history (including atopy), and ethnicity. Several pesticides were shown to cause irritant and allergic contact dermatitis. Causes were found to include pesticides, naturally occurring plant substances, heat, sunlight and humidity, atopy, and infectious fungal and bacterial agents (5,6).

In Maryland, a study of watermen, people who harvest crabs, oysters and fish, demonstrated elevated rates of basal cell carcinoma, squamous cell carcinoma, and actinic keratoses (7).

Prevention Strategies

Preplacement Physical Examination

Preplacement examinations are useful in two ways: (1) making an inventory of the skin problems the worker has before beginning a task, and (2)

identifying conditions that may preclude working at a specific job task. It may be impossible to exclude a given employee from a task due to legal or political restrictions. Therefore, the preplacement physical examination can identify the problems a prospective employee has and recommend specific control measures designed to keep from making it worse. An example of a condition that may preclude working at a specific job task is chronic eczema in a person applying to work with garlic and other crops that produce allergic responses (8,9).

Training

Educating the worker in proper handling methods for agricultural products and operation of equipment is essential in preventing occupational illness and injury. The proper operation of equipment can prevent exposures to toxic substances of all kinds. For example, teaching a pesticide applicator the proper way to mix chemicals can prevent spills and lessen the possibility of exposure (10,11).

Safety Equipment

Equipment designed to provide safety barriers can significantly reduce occupational illness and injury. Examples include air-conditioned, sealed cabins in pesticide application machines, automatic spice-packing machines that require no human contact, and sun shades for field workers to protect against the sun (11).

Personal Protective Equipment and Clothing

Hats, long-sleeved shirts, long trousers, and gloves protect against plants, chemicals, and insects that can cause rashes and other skin lesions. Protective clothing can also protect against sun damage. Protective ensembles, often made of advanced fibers and with vapor barriers, are used to protect against chemical exposures. The trade-off is that these ensembles expose the worker to heat injuries. Constant air-cooling devices can sometimes mitigate the risk of heat injury, but many times the employees must work at night. Unfortunately, away from the supervisors and designers of the equipment, workers simply remove the equipment rather than risk heat exhaustion or a decrease in production (11,12).

Hygiene

The following hygiene guidelines have been suggested:

1. Provision of effective, nonirritating, nonallergenic skin cleansers
2. Use of emollients, hand lotions, and creams after hand washing

3. Frequent clothing changes, when possible
4. Daily showering
5. Rapid removal of oil and chemical soaked clothing
6. Use of company laundering facilities or separate laundering facilities in the house
7. Prohibition of eating, drinking, or smoking in the work area
8. Use of sun block (8,9,11,13)

Hand cleansing with organic solvents such as mineral oils or paint thinners, or the hand cleaners that contain them, should be discouraged. The repeated use of organic solvents can desiccate the skin of the hands and cause a chronic irritant dermatitis. When using soap and water to clean the hands, care must be taken to remove as much grease and oil as possible from the creases and pores. Small pieces of metal or organic material left in the creases can cause a foreign-body reaction and lead to chronic irritant dermatitis (11,13).

Elimination of Hazards

Solvents that cause dermatitis may be eliminated with a switch to a less irritating substance. The use of pesticides that lead to chloracne may be reduced with modern equipment using laser sensors that turn off spray nozzles when passing between trees or turning corners. A packing or production process in the open air can be moved into a shed to provide sun protection (11).

Approach to the Diagnosis

The History

Predisposing Factors

Not every worker exposed to an agricultural environment will develop an occupational skin disease. Factors that place the worker in greater or lesser jeopardy are age, the work environment, a history of atopy and other allergic conditions, the presence of concomitant skin disease such as psoriasis, plant or field cleanliness, worker cleanliness, and the gender of the worker. Younger workers may be inexperienced or not follow safety regulations. There is also the phenomenon of "hardening" seen in older workers who have been working in the particular agriculture environment for a long time. On the other hand, younger workers may heal faster (Table 18.1) (9,14).

Temperature and relative humidity are also important factors in the development of skin disorders. Cool, dry environments favor xerosis and xerotic eczema. Warm, humid environment favors the development of miliaria and folliculitis. Sun exposure leads to skin tumors, increasing in severity and number with the extent of exposure and with certain skin types. Poor hygiene

TABLE 18.1. Predisposing factors of skin disease in agriculture.

Age	Relative humidity
Younger workers	Wind
Positive	Sun exposure
Heal faster	Presence of concomitant skin disease
More resilient	Psoriasis
Negative	Atopy
Fail to follow safety regulations	Irritant contact dermatitis potentiating allergic contact dermatitis
Inexperienced in job tasks	Work-site cleanliness
Older workers	Worker cleanliness
Positive	Availability of wash stations
Hardening phenomenon	Gender of the worker
Follow safety regulations	Men are more prone to acneiform eruptions
Experienced in job task	Women tend to be more fastidious in cleanliness
Negative	Use of safety equipment and procedures
Less resilient and heal slower	
Environment	
Temperature	

Source: Data from Peate (9) and Wollenberg et al. (14).

and lack of bathing facilities may extend the time the offending substance is on the skin and exacerbate the illness (8–11,15).

Having a skin disorder can predispose a worker to other skin disorders. Workers with atopic dermatitis are more prone to allergic contact dermatitis. Psoriasis (through the Koebner phenomenon) worsens on exposure to heat, irritating chemicals, or extreme cold. Workers with preexisting irritant contact dermatitis or xerosis are more likely to develop secondary allergic sensitization (9).

Gender also makes a difference. Hairiness, sebum and sweat production, and the pH of the skin make male workers more prone to acneiform eruptions. Women seem to be more fastidious in removing dirt from skin and clothing and are thus more protected (8,9).

History of the Illness

It is important to accurately record the worker's personal data and history of the illness as summarized in Table 18.2 (8,9,16–19).

Physical Examination

Objective findings should be described in detail, beginning with where on the body the problem started. Objective information is listed in Table 18.3. Diagrams of the distribution of the lesions can be extremely helpful, especially when used in conjunction with photos. Photos may be important to document the lesions for insurance claims and to demonstrate improvement over time (Table 18.3) (16–18).

TABLE 18.2. Dermatological history.

- Worker identifying data
  - Age
  - Gender
  - Skin color
  - Job title
  - Actual job task
  - Insurance information
- Exposure information
  - Date and time of onset of skin lesion
  - Previous similar lesion from same job
  - Job task at time of onset
  - Where on the body it started
  - Whether the lesion is painful, burning, or pruritic
  - Previous treatment, over-the-counter or prescription, and did it make the lesion better or worse
  - Presence of other employees at the work site with similar skin lesions
- Work description
  - History of what the employee came in contact with on the job
  - What protective equipment was used?
  - Other jobs the employee might have
  - Use of deodorants, cosmetics, perfumes, or other hygiene products
  - A complete employment and exposure history may be necessary
- Past history
  - Prior skin exposures and lesions
  - Systemic illness
  - Allergies
  - Prior compensation claims
- Social history
  - Recreation
  - Hobbies
  - Personal habits, e.g., smoking, alcohol use, drug use
  - Jobs around the house or the employee's own ranch or farm

Source: Data from Zugerman (8), Peate (9), Lazarus et al. (16), and Lebwohl et al. (18).

TABLE 18.3. The physical examination.

- Color
- Distributions
  - Externally induced or contact
  - Photodistribution
  - Zosteriform or dermatomal
  - Other terms
    - Generalized
    - Localized
    - Symmetric
    - Flexural or extensor
    - Palmoplantar
  - Factitious
- Morphology
  - Macule
  - Patch
  - Papule
  - Nodules and tumors
  - Plaque
  - Bulla
  - Vesicle
  - Pustule
  - Ulcer
  - Erosion
  - Fissure
  - Crusting
  - Oozing
  - Wheal
  - Telangiectasia
  - Induration
  - Atrophy
  - Burrows
  - Scales
  - Lichenification
  - Comedos
- Configurations
  - Round lesions
    - Nummular eczema
    - Targetoid
    - Discoid
    - Annular
  - Serpiginous
  - Herpetiform
  - Linear
  - Reticular
  - Verrucous
  - Guttate
  - Alopecia
  - Factitious
    - Periorificial
    - Periungal
- Secondary changes
  - Excoriations
  - Hyperpigmentation
  - Hypopigmentation

Source: Data from Lazarus et al. (16), Callen et al. (17), and Lebwohl et al. (18).

Diagnostic Testing

Patch Testing

The patch test is a valuable clinical tool to establish the diagnosis of allergic, not irritant, contact dermatitis. Approximately 80% to 90% of all cases of contact dermatitis are irritant, not allergic. Because irritant contact dermatitis is influenced by the chemical nature, quantity of substance (concentration, frequency, duration), and the nature of the contact with the skin (inflammation, skin temperature), positive patch tests to irritant may be produced in most individuals. Irritant patch test reactions only indicate that a particular substance, under conditions of occlusion against a skin surface for 24 hours, is capable of causing skin inflammation. For example, oil may be used in a patch test and may produce inflammation within 24 hours, but in actual working conditions the oil contact may be dilute and transitory. Conversely, a weakly irritant substance such as alcohol may produce no inflammation under testing conditions but in an agricultural setting may cause skin drying and eventual inflammation. Therefore, the diagnosis of irritant dermatitis is based on exclusion, a reasonable index of suspicion, knowledge of the physical properties of the chemical, and an understanding of the agricultural workplace (20).

Patch testing is usually performed for one or more of the following reasons:

1. Precise identification of an allergen
2. Facilitation of management
3. Guidance in rehabilitation and return to work (20,21)

Routine patch test screen kits are aimed at the identification of the most common cutaneous allergens. These kits have been standardized so that only allergic individuals react to patch testing. The TRUE Test™ panels, which are the only patch testing devices approved by the U.S. Food and Drug Administration, consist of 24 patches, one of which is a negative control. The remaining 23 patches contain 42 unique allergens and four complex mixtures (21,22).

Nonstandardized substances taken directly from the workplace present a special problem and should not be tested unless the physician has had a great deal of experience in testing (8,9,20).

Patch testing is especially useful in documenting contact dermatitis from cosmetics, fragrances, and botanicals. Because workers in agriculture can be employed in the growing, harvesting, and processing of natural fragrances and botanicals, a patch test has the potential of confirming or ruling out the potential source of a worker's rash as industrial or nonindustrial in origin (23).

Theoretically, the positive allergic test will develop only in exposed individuals and not in unexposed controls. When testing with nonstandardized

workplace substances, as many as 20 or more controls may need to be used before a positive reaction indicates allergy and not a false-positive irritant reaction. A positive reaction is interpreted as an area of inflammation (erythema and induration) on the skin where the controls have none (20).

The material to be tested can be in either solid or liquid form. When liquids are tested, they should be placed in a relatively inert vehicle such as petroleum, water, or mineral oil. The concentration should be sufficient to elicit allergy but not to cause irritation. Some industrial chemicals are not appropriate for testing because they are too irritating; others must be diluted to concentrations of 1:100 or 1:1,000 for testing. The material is placed in chambers and taped to the patient's upper back or upper-outer arm. They remain in place for 48 hours and are read at 48, 72, or 96 hours after application (20–23).

The International Contact Dermatitis Groups has suggested the following terminology for reporting patch-test results: NT, not tested; ?+, doubtful reaction; +, weak reaction (nonvesicular); ++, strong reaction (edematous or vesicular); and +++, extreme reaction. "IR" represents an irritant reaction and "ph" placed before any of the above indicates a photoreaction (20).

False-positive patch tests can occur when:

1. The test concentration is too high.
2. There is a failure to run controls.
3. Testing is done on inflamed skin.
4. There is generalized, widespread eczema.
5. There are multiple strongly positive reactions, the allergen is contaminated, and an irritant vehicle was used.
6. There is the incorrect assumption that the allergen is actually present in the work environment (8,9,21).

False-negative reactions occur when:

1. Test concentrations are too low.
2. There are deviations from the standard testing technique.
3. There is failure to test all potential environmental exposures.
4. The wrong vehicle is used.
5. The substance is a photosensitizer.
6. There is an incorrect assumption that the allergen is not in the work environment (8,9,20,21).

Inappropriate testing may sensitize a worker to a substance to which he was not previously allergic. There may also be localized complications of the site, including pigment changes, keloid formation, scarring, infections, and a flare of generalized eczema. The strip patch test is useful in testing for substances with poor percutaneous penetration. Penetration of the substances is enhanced by repeated applications of adhesive tape prior to their application to the skin (20–22).

Biopsies

The surgical removal of skin can be diagnostic as with punch biopsies or incisional biopsies or curative as with an excisional biopsy. Written consent must be obtained, and sterile conditions maintained. Proper wound management is essential. The specimen needs to be evaluated by a pathologist or competent dermatologist. Biopsies are especially helpful in situations where neoplasms are suspected (24).

Special stains, including immunological studies, can aid in diagnosis. These special stains are useful in diagnosing rare skin cancers and deciding between irritant and allergic contact dermatitis in questionable clinical presentations (24).

Cultures

Cultures are important in confirming or disproving viral, bacterial, or mycotic skin infections. They are only as good as the techniques used to collect, transport, and evaluate them. Sensitivity reports are helpful in ensuring the correct antibiotic has been used.

Scrapings

Scrapings are useful in two ways: (1) diagnosing scabies and (2) confirming mycotic infections. Farm workers often confuse scabies with pesticide rashes. By scraping the scabietic areas and demonstrating the parts of S*arcoptes scabiei* on a slide with KOH, the worker can see that the rash is really an infestation and not due to a chemical (1,8,9).

When cutaneous mycotic infections are inspected, a useful technique is to scrape some of the top layer of the skin and place it on a microscope slide. The specimen is then treated with KOH and examined under the microscope for hyphae and conidia (8,9).

Ultraviolet (UV) Light (Wood's Light)

The actual use of the Wood's light requires minimal skill. The lamp should be allowed to warm for 1 minute and be used in a dark room. It is important the user be dark adapted to see the contrasts clearly. Wood's light is unreliable in darker skin types, and it is possible to obtain fluorescence from topical medications, lint, and soap residue. It is useful in diagnosing pigmentary disorders, cutaneous infections, and the porphyrias. A Wood's light is useful in diagnosing the following cutaneous infections:

1. *Pseudomonas* where the bacteria fluoresce green
2. Erythrasma caused by *Corynebacterium minutissimum,* which shows coral-red fluorescence
3. *Propionibacterium acne,* which shows an orange-red fluorescence and is useful in distinguishing the chloracne of organochloride exposure from adolescent acne

4. Dermatophytes
5. Tinea versicolor caused by *Malassezia furfur,* which shows a yellowish-white or copper-orange fluorescence and is common in agricultural workers who work in damp areas or water (25)

Site Visits

The dermatological site visit can have a preventative as well as a diagnostic value. Site visits allow the physician to do the following:

1. Make an etiological diagnosis by observing working conditions, personal hygiene, and work exposures
2. Make practical recommendations for job modification to manage skin disease
3. Obtain further information by seeing other employees and reviewing medical records
4. Obtain information on the industrial process
5. Develop better rapport with management and employees

Refer to Chapter 11 for more information on work-site visits (8,9).

Management Strategies

Wet Dressings

Absorbent material such as cotton dressings moistened with cool water or Burrow's solution (aluminum acetate diluted 1:40 in water) should be applied to the affected area four to six times a day. The effects of this treatment include bacteriostasis, gentle debridement, debris removal, and evaporative cooling to lessen pruritus (8,9).

Warm, moist dressings are useful in superficial and deep bacterial skin infections in debridement, surfacing of the infection, absorbing purulent material, and reducing pain and itching.

Emollients

Topical agents such as petrolatum (Vaseline) provide an occlusive film over inflamed skin, decrease fissuring, and reduce evaporation. They are most effective when applied after the skin as been soaked or washed in water (8,9).

Topical Steroids

Topical steroids have no effect on acute vesicular reactions but are useful in other inflammatory skin reactions. They are useful in eczematous lesions. Topical steroids come in four potency levels for use on various levels of the skin. For example, very high potency steroids are best used on thick-skinned

areas such as the palms and soles, while low-potency steroids should be used on the face, groin, and intertriginous areas. Once-a-day dosing is as effective as dosing two or three times a day, and occlusive dressings of plastic or a similar wrap will magnify the potency. Adverse effects include percutaneous absorption, skin atrophy, rebound papular dermatitis after use of medium high potency applications, and striae formation (26).

Systemic Steroids

Short courses of prednisone, in a dosage of 40 to 60 mg per day for 5 to 7 days, are indicated when the lesions are widespread, edematous, and vesicular or bullous (8,9).

Systemic Antihistamines

Systemic antihistamines counter histamine released from mast cells in the skin and mucous membranes. They are sedating, and workers should not operate equipment after taking them.

Diphenhydramine (Benadryl) is used in a dosage of 25 to 50 mg, three to four times daily. Hydroxyzine hydrochloride (Atarax) 25 mg three or four times a day is useful for reversing pruritus (8,9).

Doxepin (Sinequan) 10 to 30 mg at night is effective as an antipruritic but can cause anticholinergic effects. A 5% doxepin cream (Zonalon) is also effective (8,9).

Disease Complexes in Agriculture

Table 18.4 summarizes the clinical forms of occupational skin disease in agriculture.

Irritant Contact Dermatitis

Irritant contact dermatitis involves a nonimmunologic response to a skin irritant. Injury develops over days to months through disturbance of cell hydration and functions as a result of the defatting action of prolonged exposure to weaker irritants such as water, solvents, or soaps. More concentrated solutions cause a more immediate response. Xerosis dominates. Under excessively moist working conditions, these skin irritants can cause severe cell hydration and result in maceration, most often in the feet and groin (1,8,9).

Irritant contact dermatitis typically appears in exposed or contact areas, in thin skin more often than thick, and in areas around the belt or collar. The rash may be difficult to differentiate from the rash of allergic contact dermatitis. Acute lesions are painful, weepy, and vesicular, whereas chronic lesions are dry, erythematous, cracked, and lichenified. The lesions assume a

TABLE 18.4. Clinical forms of occupational skin disease in agriculture.

Irritant contact dermatitis	Squamous cell carcinoma (SCC)
Contact dermatitis	Actinic keratosis (AK)
Chemical skin burns	Melanomas
Allergic contact dermatitis	Ulcerations
Allergic contact dermatitis	Accidental
Acute and chronic urticaria	Intentional
Latex allergy	Granulomas
Photodermatitis	Animate agents
Phototoxic	Inanimate agents
Photoallergic	Infections
Follicular and acneiform dermatoses	Bacterial
Pigmentation disturbance	Viral
Hyperpigmentation	Mycotic
Hypopigmentation	Rickettsial
Neoplasms	Parasitic
Basal cell carcinoma (BCC)	Protozoan

clearly demarcated pattern and are often asymmetric and unilateral, for example in the distribution of a glove that became soaked in chemicals. Hardening or adaptation of the skin may occur as a result of repeated contact with moderate irritants (Table 18.5) (1,8,9).

Treatment begins with removal of clothing and decontamination with water. Definitive treatment includes wet dressings and topical and systemic steroids. Secondary infections may require systemic antibiotics (1,8,9).

TABLE 18.5. Differences between allergic and irritant contact dermatitis.

Feature	Irritant reaction	Allergic reaction
Appearance	Erythema Erosion without infiltration Glazed appearance on bulla without erythema	Polymorphic with erythema, edema, and vesicles
First manifestation	Immediately to 24 hours	5–14 days for first manifestation 24–72 hours following reexposure
Threshold	High	Low
Index of sensitization	Nearly 100%, depending on concentration	Variable, but usually fairly low
Transferable	No	Yes
Patch test	Not useful	Useful
Examples of causative substances	Soaps, solvents, acids, alkalis	Nickel, chrome, epoxy

Source: Reprinted from Zugerman (8), with permission.

Chemical Skin Burns

Severe skin irritations are a rare but serious hazard. On contact, strong acids, alkalis, and heavy metals may cause chemical burns. The skin reacts immediately, and a lesion appears quickly. These lesions may progress to erosions and necrosis (1,8,9).

Immediate removal from exposure, removal of contaminated clothing, and irrigation with water can limit the extent of injury. It is a mistake to treat alkali burns with acid or acid burns with an alkali because it will result in additional damage through an exothermic reaction. Burns are best treated with Silvadene dressings, and tetanus prophylaxis must be assured. Large or full-thickness burns may require hospitalization, especially if the patient has other systemic illness such as diabetes (8,9).

Allergic Contact Dermatitis

Allergic contact dermatitis is an immunologic cell-mediated response to an exposure to an antigenic substance. The most common sensitizing agents are medications, plants, insect and snake bites, and certain food products. The percentage of workers who react to these agents varies widely. For example, only 6% of persons react to nickel, whereas as many as 70% react to poison oak or poison ivy. From 10% to 17% of workers who use latex gloves react to latex. Sensitization to one chemical may induce a cross-sensitization or cross-reactivity to related chemicals (1,8,9,27).

The rash is usually pruritic and typically appears in areas exposed to the sensitizing agent. It usually has an asymmetric or unilateral distribution and is characterized by erythema, vesicles, and severe edema. Treatment typically includes topical and systemic steroids, antihistamines, and tricyclics. Desensitization serums to many substances commonly found in agriculture are available from allergists and supply companies (Figure 18.1) (1,8,9,18).

Urticaria

Acute and chronic urticaria and angioedema can result from exposure to a number of agricultural products. They may be caused by immunologic and nonimmunologic histamine releasers. Immunologic mechanisms involve type I (immunoglobulin G [IgG]-mediated), type II (cytotoxic antibody–mediated), or type III (immune complex–mediated) reactions. Nonimmunologic mechanisms usually involve substances such as aspirin that directly incite the release of histamine and other mediators from mast cells. Medications, foods, food additives, and the bites of insects and snakes have been implicated. Common food allergies include shellfish, fish, eggs, nuts, chocolate, berries, tomatoes, cheese, and milk (27).

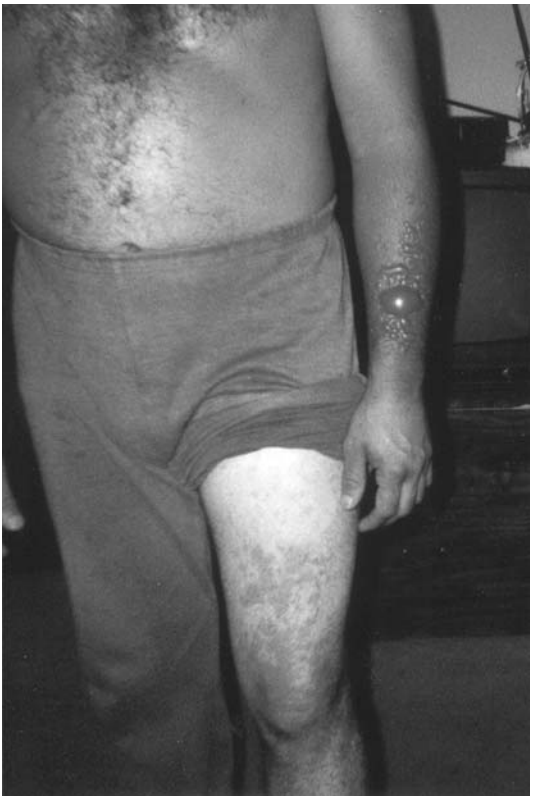


FIGURE 18.1. Allergic contact dermatitis from garlic in a production worker. (Photo by Dr. James E. Lessenger.)

There are four categories of urticaria:
1. Localized: a wheal and flare only where the chemical or substance touched
2. Angioedema: a generalized urticaria over the entire body
3. Pulmonary: manifested by wheezes
4. Anaphylaxis: manifested by a sudden onset of shock

Treatment for urticaria includes antihistamines, tricyclics, and systemic steroids (27).

Latex Allergies

Most of the use of natural rubber latex (NRL) is in the medical field where use increased dramatically as a response to the increased need for bloodborne pathogen control in the AIDS epidemic. Natural rubber latex is also used in worldwide agriculture to protect the hands of workers, especially for research, artificial insemination, and veterinary services (28–30).

The principal nonrubber components of NRL are proteins; 60% by weight of protein is bound to rubber, and 40% exists in a free aqueous phase. The product that arrives on the shelves in the form of gloves may have as many as 16 natural polypeptides with the ability to bind IgE antibodies (28–30).

Latex hypersensitivity reactions are categorized into two main types: (1) type IV or delayed (cell-mediated) hypersensitivity reactions, and (2) type I or immediate (IgE-mediated) anaphylactic reactions. Risk of sensitization is dependent on the frequency and intensity of NRL exposure. Atopy is a risk factor, as are allergies to foods such as banana, kiwi, avocado, and chestnut, which contain allergens that cross-react with antibodies to latex proteins. Typically the dermatitis is localized to the hand where the gloves are worn and is manifested by a polymorphic, erythemic rash with edema and vesicles. Chronic rashes may progress to maceration or lichenification with fissures. Along with hand dermatitis, the symptoms of asthma, rhinoconjunctivitis, hand urticaria, and general urticaria are seen in allergic individuals (28–30).

Patch and prick tests and a serum antibody test are available, but the diagnosis is primarily made by the clinical presentation. Prevention of occurrences entails offering alternative gloves of vinyl or nitrile to workers with a history of atopy or allergies to key foods. Treatment for the acute dermatitis consists of moist compresses and topical steroids. Research has documented that the purchase of powder-free NRL examination gloves significantly reduces the incidence of new cases of latex allergic dermatitis (28–30).

Photodermatitis

Adverse reactions to the sun's rays have become more commonplace because an increasing number of photosensitizers are entering our environment from industrial, cosmetic, and pharmaceutical sources. Two types of photosensitivity can occur: phototoxic and photoallergic. Clinically, these reactions usually resemble sunburn (31–33).

Phototoxic reactions may be induced by endogenous or exogenous chemicals. Endogenous photosensitizers made by the body include porphyrin molecules. Exogenous photosensitizers may arrive on the skin through topical applications or may be distributed through the body by the blood flow. Topical photosensitizers are found in cosmetics, medications, plant, and industrial and air pollutant emissions. Plant sensitizers include celery, carrots, grasses, and lime. Systemic photosensitizers are primarily medications (31–33).

Acute and chronic phototoxic reactions may occur. The acute response is characterized by erythema and edema followed by hyperpigmentation and desquamation. The end point of chronic damage may be cutaneous cancer formation as a result of nucleic acid and cytoplasmic molecular injury. Treatment consists of removal of the offending agent and systemic steroids (31–33).

Photoallergy is uncommon and acquired through altered reactivity to an antigen. The immune response may be antigenic or cell mediated and presents with urticaria or eczema. Examples of substances causing photoallergic reactions include musk ambrette (after-shave), hydroxychloroquine, ketoprofen, and celecoxib. Treatment is removal of the offending substance and systemic steroids (31–33).

Follicular and Acneiform Dermatoses

Exposure to solvents and oils results in the mechanical blockage of the pilosebaceous units and leads to "oil acne." "Coal-tar acne" is produced by exposure to coal tar and shares the same causes and presentations as oil acne. Exposure to halogenated hydrocarbons can cause a diffuse, papular acneform rash called *chloracne* (34–36).

In oil acne and coal-tar acne, comedos, pustules, and papules are typically present over inflamed and erythemic skin. Typical areas of exposure and disease are the hands and arms. Occupational acne may aggravate existing acne, usually on the face and neck, or be confused with adolescent acne. Secondary infection from bacterial folliculitis is common. Frequent cleaning and avoidance of the offending substance is critical. Infections respond to antibiotics (34–36).

Chloracne is also seen in people exposed to dioxins, a by-product in the manufacture of herbicides. Removal from exposure typically resolves the condition (34–37).

Pigmentation Disturbances

Acquired pigmentary changes are common among agriculture workers and fall naturally into the categories of hyper- and hypopigmentation. As opposed to tattoos and stains, pigmentary disturbances are caused by an increase or decrease of melanin in the skin. Stains typically arise from handling natural products such as nut husks and hemp. The psychosocial implications of these disorders can be substantial. It is important to diagnose hereditary causes of pigmentation changes through careful history taking, including a family history (18,19,38–40).

Hyperpigmentation

In agriculture, an increase in melanocytes in the skin is caused by physical and chemical causes. Physical causes include trauma, repetitive friction, chronic sun exposure, and burns. Burns can be chemical, radiological, or thermal. Chemical causes include tars and pitch, and psoralens from plants such as celery and limes (19,38–40).

The most commonly used treatment is topical hydroquinone. Other phenolic agents, such as *N*-acetyl-4-cystaminylphenol (NCAP), are currently

being studied and developed. Nonphenolic agents, which include tretinoin, adapalene, topical corticosteroids, azelaic acid, arbutin, kojic acid, and licorice extract, are also used for hyperpigmentation disorders (18,19,38–40).

Hypopigmentation

Physical agents that cause a decrease in melanin include burns (chemical, radiological, and thermal) and trauma. Chemical causes include postinflammatory changes after contact dermatitis, phenolics, and catecholics (alkyl phenols), such as tertiary butyl phenol, tertiary butyl catechol, and hydroquinone. Licorice extract also causes the disorder. The treatment includes psoralens (18,19,38–40).

Cutaneous Neoplasms

Agricultural occupational skin cancers are malignancies that result from exposure to carcinogenic forces present in agriculture. Of all occupational cancers, 75% are skin cancers, and 60% of those are basal cell carcinomas (BCCs), 34% are squamous cell carcinomas (SCCs), and 6% are mixed. Actinic keratoses (AKs) are precancerous lesions caused by excessive sun exposure. Melanomas may occur but typically appear in older persons, and their exact rate in agriculture is unknown. In Finland, lip cancer (BCC and SCC) is extremely common but cancers of the head aren't, presumably due to wearing hats (Table 18.6) (1,8,9,37,41,42).

Causes of Agricultural Skin Cancers

Fair skin, blond hair, and blue eyes predispose to the appearance of skin cancers in Caucasian people. The elevated levels of melanin in dark-skinned people offer an incomplete protective effect. The most common types of cancer that affect the Caucasian population are BCC and SCC (43).

There are five recognized causes of agricultural skin cancers:

1. Chemical carcinogens
2. Cocarcinogens or promoters
3. Physical carcinogens
4. Ionizing radiation
5. Nonionizing radiation (41,43,44)

Chemical Carcinogens

Coal-tar, mineral oils, pitch, soot, and asphalt are common chemical carcinogens. Chemicals that contain 4- to 5-ring aromatic hydrocarbons such as benzene and pyrene are potent carcinogens. Arsenic used in sheep dip has caused skin cancer in sheepherders. Used as a wood preservative for vine trellises in some parts of the world, arsenic can cause skin cancer in vineyard workers (1,41).

TABLE 18.6. Diagnostic findings in agricultural skin cancers.

Type of tumor	Location	Color	Morphology	Metastasis	Treatment
Basal cell carcinoma (BCC)	Chronically sun-exposed areas	Pearly gray	Circumscribed or slightly diffuse Morpheaform, nodular, infiltrating, or superficial	Slow but relentless growth, rarely metastases	Cryotherapy Curettage and electro-desiccation excision (Mohs' surgery)
Squamous cell carcinoma (SCC)	1. Sun exposed. 2. Secondary to scarring Process	Erythemic	Keratotic papule or nodule that may ulcerate	Slow and relentless, metastasis occurs	Same
Actinic keratosis (AK)	Pale sun-exposed skin	White keratin	Rough scaly, usually <less than >1cm	Doesn't metastasize, can evolve into BCC	Topical 5-fluorouracil Cryotherapy Curettage Electro-desiccation Dermabrasion Laser resurfacing
Melanomas	Sun-exposed skin, history of sunburns	Variable, dark brown to red to black	Asymmetric lesions, border irregular, color variability		Wide excision (Mohs) Further treatment as direction by the stage

Source: Data from Lazarus et al. (16), Callen et al. (17), Lebwohl et al. (18), and Maibach and Zhai (19).

Cocarcinogens or Promoters

These substances accelerate the cancer after it is induced, typically a 4- to 5-ring hydrocarbon or a noncarcinogenic chemical such as sulfur (used as a pesticide in grapes, citrus, and other fruits) (1,41).

Physical Carcinogens

Mechanical trauma causing chronic irritation, heat, and scars from chemical or thermal burns comprises the physical causes of skin cancer (1,41).

Ionizing Radiation

Seen rarely in agriculture, exposure to radiation caused by nuclear accidents, nuclear attacks, or accidental exposure to nuclear materials can lead to dry skin, thickening, hyperkeratosis, ulceration, and cancer (1,41).

Nonionizing Radiation

The sun, with mid-UV rays (290 to 320 nm), is a potent cause of skin cancers and actinic keratoses. Typically BCC is more common than SCC; melanoma rarely presents. Chemical and ultraviolet B (UVB) carcinogenesis have an additive effect (1,41,43).

Prevention

Prevention consists of avoidance of exposure, good hygiene practices, covering of skin surfaces, and sun block on those skin surfaces that can't be covered. However, care must be taken because some sunscreens can increase the penetration of some herbicides (44,45).

Diagnosis

In farming communities, community-based screening programs have been found effective in discovering agricultural skin cancers at an early stage. Newer approaches involving instrument-assisted screening and detection methods are under development (45,46).

Clinical diagnosis of skin cancers is based on the morphology of the lesion, area of skin where it is presenting, history of growth, and biopsy results (24,47).

Management

Surgery is the most popular treatment for BCC and SCC; cryotherapy is the most common for AK. Excision completely removes the skin cancer but can leave unsightly scars. Other techniques for removal include laser removal techniques, carbon dioxide resurfacing of photo-damaged skin, cryotherapy techniques, topical antimetabolites, electrodesiccation, and irradiation. Treatment of melanomas may require a complicated combination of excision, adjunctive immunotherapy or chemotherapy, and irradiation (47,48).

Ulcerations

Topical exposure to arsenic used in vineyards and calcium compounds used as micronutrients (Chapter 14) are common causes of ulcerations in agriculture. The diagnosis is made by the characterized scalloped appearance of the skin, although a biopsy may be necessary to exclude other etiologies. Secondary infections may occur and may necessitate systemic or topical antibiotics. Treatment is by removal of the offending agent, wet dressings, and emollients (49).

Chronic skin ulcers caused by *Mycobacterium ulcerans* (Buruli ulcer disease) are common in people who work in aquatic environments such as rice paddies and fish farms. Snails transitorily harbor *M. ulcerans* (50).

Granulomas

Acquired, noninfectious granulomas of the skin can have animate or inanimate causes. The most common animate granuloma is pyogenic granuloma, a polymorphous, irregular tumor that arises out of burned, abraded, or otherwise damaged skin. Pyogenic granulomas can be mistaken for BCC. Treatment is excision followed by electrodesiccation (49).

The most common inanimate cause of granuloma is foreign bodies. Foreign-body granulomas can be caused by almost any foreign body that gets lodged in the dermis and causes a foreign-body inflammatory reaction. Examples in agriculture are thorns from citrus trees and splinters from lumber. Treatment is excision, and antibiotics may be necessary for secondary infections (49).

Infections

In agriculture, people work close to water, animals, crops, natural fertilizers, and the soil, all of which serve to carry infectious diseases that can infect the skin. Persons with immunological disease, malnutrition, diabetes, and severe systemic disease are at risk for any kind of a infectious disease.

Bacterial Infections

Staphylococci and Streptococci

These gram-positive bacteria cause infection through contamination of cuts, burns, puncture wounds, and abrasions. All occupations are at risk, but those who work with meat are found to be particularly affected. Treatment is cleansing the wound and oral antibiotics (51).

Anthrax

Anthrax is associated with people who handle wool, hides, or sheep. *Bacillus anthracis* is a gram-positive, spore-forming rod distributed worldwide. Animals are infected by ingestion of spores while feeding on contaminated soil. The spores can survive for years in the soil or in contaminated animal material, such as lamb's wool (51–53).

Infection in humans typically occurs at sites of skin trauma. The lesion starts as a painless, pruritic papule that vesiculates, becomes necrotic, and ulcerates, leaving a back eschar surrounded by edema. Local lymphadenopathy, low-grade fever, and malaise are frequently found, but may not be present. Most cases are self-limiting; however, systemic antibiotic treatment is recommended to prevent the progression to a systemic disease. Diagnosis can be made by direct Gram-stain smear, culture, polymerase chain reaction, serology testing, or by the identification of spores in biopsy material. Treatment is typically with penicillin antibiotics or tetracyclines. Ciprofloxacin is recommended for

prophylaxis if exposure is suspected. A killed anthrax vaccine is available that is effective in reducing the chance of developing the disease, but significant side effects prevent its widespread use on whole populations. Prevention is through livestock vaccination, reduction in soil contamination, decontamination of hides and wool, and early isolation and treatment of suspected cases (51–53).

Brucellosis

In production agriculture, farmers, veterinarians, abattoir workers, and meat packers are at risk. *Brucella* is a gram-negative bacterium with worldwide distribution. Three types exist: *B. suis*, found in pigs; *B. abortus*, found in cattle; and *B. melitensis*, found in sheep and goats. Infection is acquired by contact with contaminated animals or by ingesting infected milk or cheese (19,51).

Brucellosis begins as a febrile illness with malaise and weight loss. The most common findings are hepatomegaly, splenomegaly, lymphadenopathy, and osteoarticular involvement. Cutaneous manifestations are rare and nonspecific. Diagnosis is made by culture and serologic testing. Treatment is with doxycycline or rifampicin for 6 weeks. Prevention is through animal vaccination and control programs (51).

Erysipeloid (Fish-Handler's Disease)

Erysipeloid is found in hunters, fishermen, butchers, farmers, and poultry dressers. The infection is caused by the gram-positive bacterium *Erysipelothrix rhusiopathiae*, which infects fish, shellfish, mammals, and poultry. Most cases consist of a localized, bright red, well-demarcated cutaneous infection, most often involving the hands. A diffuse cutaneous form as well as a systemic infection with septicemia and endocarditis can also occur. The diagnosis requires a culture of the skin. In septicemia, blood cultures may be positive. Most cutaneous infections are self-limiting. Treatment is recommended to reduce the risk of septicemia and endocarditis. The penicillins and cephalosporins are the first-line treatment. Prevention is achieved through strict hygiene of work environments (51,54).

Fish Tank Granuloma

Mycobacterium marinum is an acid-fast, nontuberculous mycobacterium that causes a cutaneous lesion on traumatized skin following exposure to contaminated water. People who work in fisheries are most at risk. The most common source is fish tank exposure. Most cases are a red, painless papule at the site of inoculation that may become verrucous or ulcerated. The diagnosis is made by culture. Most cutaneous infections are self-limiting; rifampicin, minocycline, clarithromycin, and ciprofloxacin are the drugs most commonly prescribed. Prevention is achieved through hygiene and the use of disinfectants (50,51,54).

Rickettsial Infections

Rickettsia are obligate intracellular microorganisms that multiply within the endothelial cell cytoplasm. Most are transmitted by blood-sucking insects and mites and affect farmers, trappers, and hunters (51).

Marine (endemic) typhus is caused by *Rickets typhus* and is transmitted by rat and cat fleas. A fever, headache, and a generalized, erythemic papular rash develop. Antibiotics shorten the duration of the illness. Scrub typhus is caused by *Orientia tsutsugamushi* and is transmitted by mites that live on field rodents. A fever, eschar, lymphadenopathy, hepatosplenomegaly, and an erythemic, evanescent rash occur. It is potentially fatal without treatment. Rocky Mountain spotted fever is caused by *Rickettsia rickettsii* and infects humans through ticks. It causes fever, malaise, headache, gastrointestinal bleeding, and a petechial rash. It can be fatal without treatment. Malaysian rubber estate workers have tested for antibodies against *R. typhi, O. tsutsugamushi,* and TT 118 spotted fever group rickettsiae, presumably due to the large number of rats and rodents that live in the groves (51).

Diagnosis of *Rickettsia* infections is through the typical clinical presentation or indirect immunofluorescence antibody testing. Treatment is with doxycycline, tetracycline, or chloramphenicol (51).

Viral Infections

Orf

Orf (ecthyma contagiosum), caused by a paravaccinia subgroup of poxviruses that commonly infects sheep and goats, is common among veterinarians, farmers, and sheep herders. Transmission occurs through contact between the broken skin of humans and the pustular dermatitis that develops around the mouth and feet of infected animals. The infection begins with a red papule with surrounding erythema, which sometimes ulcerates before resolving. The first infection results in lifelong immunity. The problem is commonly self-diagnosed and underreported, and resolves spontaneously without treatment. Diagnosis is confirmed by viral culture, electron microscopy, and polymerase chain reaction (PCR) (51).

Human Papilloma Virus (HPV)

The wart causing HPV-7 is responsible for "butchers' wart" found in butchers, meat handlers, and fish handlers. Risk factors include trauma, low working temperatures, and humidity. It is thought to be due to the exposure of skin to infected meat and fish. Diagnosis can be confirmed by histology and is prevented by protective gloves and automated processing equipment. While the warts eventually spontaneously resolve, they can be unsightly, and periungal warts can be painful. Treatment includes salicylic acid–based topical plasters or paints, tape occlusion, and cryotherapy (51).

Milker's Nodules

Milker's nodules are caused by the infection of dairy workers and veterinarians by a paravaccinia virus that is transmitted by direct contact from infected cow's udders to humans. The painful nodules that develop resemble orf and become crusted and resolve. Erythema multiforme and erythema nodosum can sometimes occur as secondary eruptions. Diagnosis can be confirmed by viral culture or histology. The use of gloves and automatic milking machines has made this disease less common in countries where such equipment is used (51).

Fungal Infections

Dermatophytosis (Barn Itch)

A dermatophyte fungus can penetrate the keratinized layer of the skin, hair, and nails. The most common features of the fungous infection are scaling and erythema of the skin. In hairy areas, alopecia can develop. Inflammatory changes with boggy swelling and pruritus (kerion) can occur, especially on the scalp and beard. The diagnosis is made by Wood's light, KOH preparations under microscopy, and fungal cultures (55).

Miscellaneous Fungal Infections

Tinea pedis is common to farmers where their feet are exposed to humid or wet environments without protective boots. Treatment is with topical or oral antifungal agents. Animals can infect humans with dermatophytes. *Trichophyton verrucosum* infects cattle, horses, sheep, goats, dogs, donkeys, farm buildings and straw; *T. mentagrophytes* can be transmitted by cattle and domestic animals; *Microsporum canis* is common in domestic animals, especially cats; and *M. nanum* infects pigs. *M. gypseum* infects soil, leading to infection in unprotected farmers (51,55).

Parasitic Infections

Scabies

Common to medical personnel, home care workers, and sex workers, scabies is also common to people who live in rural areas and practice poor hygiene. The mite *Sarcoptes scabiei* burrows into skin causing papules, eczematous rashes, and excoriations. The disease is often confused by agricultural workers with rashes due to pesticides and other chemicals. The diagnosis is by visualization of eggs and parts of the mite on a KOH preparation. Treatment with a topical permethrin treatment is usually curative, although more than one treatment may be necessary (19).

Protozoa

Mucocutaneous leishmaniasis is transmitted by sand flies and is endemic in tropical regions. It presents as a chronic, nonhealing nodular ulcer with an

acral distribution. Diagnosis is made by smear microscopy, culture, histology, and PCR. Uncomplicated, localized cutaneous leishmaniasis can be left to heal spontaneously. Severe, disfiguring, and nonhealing lesions should be treated. Pentavalent drugs are commonly used (19,51).

Helminths

Larva Migrans

Larva migrans, called *creeping eruption* in England and by various other names in other countries, is caused by various animal nematodes, the most common being the hookworm *Ancylostoma braziliense*. These nematodes live in the intestines of cats, dogs, and other similar animals. Their ova are released in the animal's feces, where they hatch to form infective larvae. Transmission to humans occurs when contact is made with contaminated soil, particularly sandy beaches (19,51).

The larvae penetrate intact skin and produce a serpiginous, cutaneous eruption that is pruritic and can be observed to progress at up to 1 cm a day. Complications include impetigo and, rarely, Loeffler's syndrome. Treatment includes topical or oral thiabendazole, cryotherapy, albendazole, or ivermectin. Preventive measures include wearing proper footwear and treating household and farm animals (19,51).

Cercarial Dermatitis

Called *swimmer's itch* in England and by other names in the water-rich countries where it is found, cercarial dermatitis is caused by the cercariae of trematodes (*Schistosoma* and *Trichobilharzia*) that live in fresh and salt water. Their primary hosts are water birds that release ova in their feces. These ova hatch into larvae that infect water snails. Under optimal conditions of sunlight and temperature, thousands of cercariae are released and reinfect more water birds. When the cercariae penetrate human skin, they die in the epidermis within a few hours. A monomorphic, pruritic, maculopapular skin eruption follows mainly on exposed skin. Treatment is symptomatic. Paddy field, pond, and aquarium workers are at risk (19,51).

References

1. Hoga DJ, Lane P. Dermatologic disorders in agriculture. Occup Med 1986;1:285–300.
2. McCurdy SA, Wiggins P, Schenker MB, et al. Assessing dermatitis in epidemiologic studies: occupational skin disease among California grape and tomato harvesters. Am J Ind Med 1989;16:147–57.
3. Park H, Sprince NL, Whitten PS, Burmeister LF, Zwerling C. Farm-related dermatoses in Iowa male farmers and wives of farmers: a cross-sectional analysis of the Iowa Farm Family Health and Hazard Surveillance Project. J Occ Environ Health 2001;43:364–69.

4. Kaufman JD, Cohen MA, Sama SR, Shields JW, Kalat J. Occupational skin diseases in Washington State, 1989 through 1993: using workers' compensation data to identify cutaneous hazards. Am J Public Health 1998;88:1047–51.
5. Cole DC, Carpio F, Math JJM, Leon N. Dermatitis in Ecuadorian farm workers. Contact Dermatitis 1997;37:1–8.
6. Gamsky TE, McCurdy SA, Wiggins P, Samuels SJ, Berman B, Shenker MB. Epidemiology of dermatitis among California farm workers. J Occup Med 1992;34:304–9.
7. Vitasa BC, Taylor HR, Strickland PT, et al. Association of nonmelanoma skin cancer and actinic keratoses with cumulative solar ultraviolet exposure in Maryland watermen. Cancer 1990;65:2811–7.
8. Zugerman C. Dermatology in the workplace. Am Fam Physician 1982;26:103–9.
9. Peate WF. Occupational skin disease. Am Fam Physician 2002;66:1025–32.
10. Schenker MB, Orenstein MR, Samuels SJ. Use of protective equipment among California farmers. Am J Ind Med 2002;42:455–64.
11. Meekonnen Y, Agonafir T. Pesticide sprayers' knowledge, attitude and practice of pesticide use on agricultural farms of Ethiopia. Occup Med (Lond) 2002;52:311–5.
12. Now AV, Maeda DN, Weaseling C, Partaken TJ, Saga MP, Miser G. Pesticide-handling practices in agricultural Tanzania: observational data from 27 coffee and cotton farms. Int J Occup Environ Health 2001;7:326–32.
13. McCauley LA, Michaels S, Rothlein J, Muniz J, Lasarev M, Ebbert C. Pesticide exposure and self-reported home hygiene: practices in agricultural families. AAOHN J 2003;51:113–9.
14. Wollenberg A, Zoch C, Wetzel S, Plewig G, Przybilla B. Predisposing factors and clinical features of eczema herpeticum: a retrospective analysis of 100 cases. J Am Acad Dermatol 2003;49:198–205.
15. Stolz R, Hinnen U, Elsner P. An evaluation of the relationship between "atopic skin" and skin irritability in metalworker trainees. Contact Dermatitis 1997;36:281–4.
16. Lazarus GS, Goldsmith LA, Tharp M. Diagnosis of Skin Disease. Philadelphia: FA Davis, 1980.
17. Callen JP, Greer KE, Hood AF, Paller AS, Swinyer LJ. Color Atlas of Dermatology. Philadelphia: WB Saunders, 1993.
18. Lebwohl MG, Heymann WR, Berth-Jones J, Coulson I. Treatment of Skin Diseases. New York: Mosby, 2002.
19. Maibach HI, Zhai H. Dermatotoxicology, 6th ed. Washington, DC: CRC Press, 2004;296:212–9.
20. Dickel H, Bruckner TM, Erdmann SM, et al. The "strip" patch test: results of a multicentre study towards a standardization. Arch Dermatol Res 2004.
21. Belsito DV. Patch testing with a standard allergen ("screening") tray: rewards and risks. Dermatol Ther 2004;17:231–9.
22. Ortiz KJ, Yiannias JA. Contact dermatitis to cosmetics, fragrances, and botanicals. Dermatol Ther 2004;17:264–71.
23. Ale SI, Maibach HI. Reproducibility of patch test results: a concurrent right-versus-left study using TRUE test. Contact Dermatitis 2004;50:304–12.
24. Trigg SD. Biopsy of hand, wrist and forearm tumors. Hand Clin 2004;20:131–5.
25. Asawanonda P, Taylor CR. Wood's light in dermatology. Int J Dermatol 1999;39:801–7.

26. Webster GF. Topical medications: a focus on antifungals and topical steroids. Clin Cornerstone 2001;4:33–8.
27. Burrall BA, Halpern GM, Huntley AC. Chronic urticaria. West J Med 1990;152:268–76.
28. Hunt LW, Fransway AF, Reed CE, Miller LK, Jones RT, Swanson MC, Yunginger JW. An epidemic of occupational allergy to latex involving health care workers. J Occup Environ Med 1995;37:1204–9.
29. Allmers H, Schmengler J, Skudlik C. Primary prevention of natural rubber latex allergy in the German health care system through education and intervention. J Allergy Clin Immunol 2002;110:318–23.
30. Allmers H, Brehler R, Chen Z, Raulf-Heimsoth M, Fels H, Bauer X. Reduction of latex aeroallergens and latex-specific IgE antibodies in sensitized workers after removal of powdered natural rubber latex gloves in a hospital. J Allergy Clin Immunol 1998;102:841–6.
31. Lisi P, Assalve D, Hansel K. Phototoxic and photoallergic dermatitis caused by hydroxychloroquine. Contact Dermatitis 2004;50:255–6.
32. Yazici AC, Baz K, Ikizoglu G, Kokturk A, Uzumlu H, Tataroglu C. Celecoxib-induced photoallergic drug eruption. Int J Dermatol 2004;43:459–61.
33. Chobot V, Vytlacilova J, Jahodar L. Phototoxic activity and the possibilities of its testing. Cent Eur J Public Health 2004;12:S31–3.
34. Kiec-Swierczynska M. Occupational dermatoses and allergy to metals in polish construction workers manufacturing prefabricated building units. Contact Dermatitis 1990;23:27–32.
35. Ancona AA. Occupational acne. Occup Med 1986;1:229–43.
36. Proudfoot AT. Pentachlorophenol poisoning. Toxicol Rev 2003;22:3–11.
37. Bodner KM, Collins JJ, Bloemen LJ, Carson ML. Cancer risk for chemical workers exposed to 2,3,7,8–tetrachlorodibenzo-p-dioxin. Occup Environ Med 2003;60:672–5.
38. Halder RM, Richards GM. Topical agents used in the management of hyperpigmentation. Skin Therapy Lett 2004;9:1–3.
39. Ongenae K, VanGeel N, DeSchepper S, Vander Haeghen Y, Naeyaert JM. Management of vitiligo patients and attitude of dermatologists towards vitiligo. Eur J Dermatol 2004;14:177–81.
40. Gellin GA, Maibach HI, Misiaszek MH, et al. Detection of environmental depigmentating substances. Contact Dermatitis 1979;5:201–13.
41. Ward EM, Burnett CA, Ruder A, Davis-King K. Industries and cancer. Cancer Causes Control 1997;8:356–70.
42. Lindquist C, Teppo L, Pukkala E. Occupations with low risk of lip cancer show high risk of skin cancer of the head. Community Dent Oral Epidemiol 1081;9:247–50.
43. Epstein JH. Photocarcinogenesis: a review. NCI Monograph 1979;50:13–25.
44. Robinson JD, Silk KJ, Parrott RL, Steiner C, Morris SM, Honeycutt C. Healthcare providers' sun-protection promotion and at-risk clients' skin-cancer-prevention outcomes. Prev Med 2004;38:251–7.
45. Mullan PB, Gardiner JC, Rosenman K, Shy Z, Swanson GM. Skin cancer prevention and detection practices in a Michigan farm population following an educational intervention. J Rural Health 1996;12(4 suppl):311–20.
46. Linde KG. Screening and early detection of skin cancer. Curr Oncol Rep 2004;6:491–6.

47. Edligh RF, Becker DG, Long WB, Masterson TM. Excisional biopsy of skin tumors. J Long Term Eff Med Implants 2004;14:201–14.
48. Orringer JS, Johnson TM, Kang S, et al. Effect of carbon dioxide laser resurfacing on epidermal p53 immunostaining in photodamaged skin. Arch Dermatol 2004;140:1073–7.
49. Luba, Bangs SA, Mohler AM, Stulberg DL. Common benign skin tumors. Am Fam Physician 2003;67:729–38.
50. Marsollier L, Severin T, Aubry J, et al. Aquatic snails, passive hosts of *Mycobacterium ulcerens*. Appl Environ Microbiol 2004;70:6296–8.
51. Harries MJ, Lear JT. Occupational skin infections. Occup Med 2004;54:441–49.
52. Carter T. The dissemination of anthrax from imported wool: Kidderminster 1900–14. Occup Environ Med 2004;61:95.
53. Irmak H, Buzgan T, Karahocagil MK, et al. Cutaneous manifestations of anthrax in Eastern Anatolia: a review of 39 cases. Acta Med Okayama 2003;57:235–40.
54. Van Seymortier P, Verellen K, De Jonge I. *Mycobacterium marinum* causing tenosynovitis: "fish tank finger." Acta Orthop Belg 2004;70:279–82.
55. Schwartz ME. Barn itch. Am Fam Physician 1983;27:149–53.

19

Agricultural Respiratory Diseases

Robert Bhavesh J. Pandya

Key words: dusts, gases, pesticides, fertilizers, solvents

Agricultural areas have potentially significant sources of exposure to respiratory irritants and allergens associated with respiratory diseases. From an occupational and environmental perspective on a global scale, exposures to organic and inorganic dusts, biological material such as endotoxin and mold, pesticides, and chemicals are prevalent in agriculture and associated with a wide variety of respiratory symptoms and diseases. Agricultural activities such as fieldwork, planting and harvesting, grain handling, and work in silos, animal stalls, and dairy barns can generate significant amounts of respirable dust. Many respiratory exposures, like total dust concentration in fields, can be higher in agriculture than in other industries, and exposure levels may often exceed general industry standards for nuisance dusts. Despite generally lower rates of cigarette smoking in agriculture and farm workers, they have an increased prevalence of respiratory illnesses compared to the general population (Table 19.1) (1–10).

In developed countries, recent technological advances in agriculture have improved working conditions, yet paradoxically have increased other exposures such as concentrated indoor exposures to organic dust in confined animal feeding operations. In addition, engineering controls are often insufficient, and respiratory protection is needed but often underutilized by agricultural workers. In developing countries, significant overall exposures remain more widespread as agricultural practices and regulations are not standardized, although the majority of the working population participates in some type of agricultural work. Information regarding disease burden and prevalence is not easily available; statistics may underestimate disease prevalence because of underreporting or unavailability of reliable data. This chapter reviews respiratory illnesses associated with specific agricultural exposures, outlines the medical evaluation for respiratory diseases, highlights evolving research areas, and discusses strategies for prevention (1–3,7,8).

Several specific respiratory illnesses and syndromes are related to occupational and environmental exposures to agricultural areas. For those uninitiated in farm medicine, the atypical sources of toxic gas inhalation may come

TABLE 19.1. Agricultural respiratory diseases.

Exposure type	Sources	Environments	Respiratory illnesses
Organic dusts	Grain, hay, endotoxin, silage, cotton, animal feed, microorganisms	Animal confinement areas, barns, silos, harvesting and processing operations	Asthma, asthma-like syndrome, ODTS,[1] HP, chronic bronchitis
Inorganic dusts	Silicates	Field work, harvesting /tiling of soil	Pulmonary fibrosis, chronic bronchitis
Gases	Ammonia, hydrogen sulfide, nitrogen oxides, methane, CO	Animal confinement facilities, manure pits, silos, fertilizers	Asthma-like syndrome, tracheobronchitis, silo-filler's disease, pulmonary edema
Chemicals: Pesticides	Organophosphates, paraquat, fumigants	Applicators, field work	Bronchospasm, pulmonary edema, pulmonary fibrosis
Fertilizers	Anhydrous ammonia	Application in fields, storage containers	Mucous membrane irritation, tracheobronchitis
Disinfectants	Chlorine, quaternary compounds	Dairy barns, hog confinement areas	Respiratory irritant, bronchospasm
Solvents	Diesel fuel, pesticide solutions	Farm vehicle exhaust, storage containers	Mucous membrane irritation, chronic effects
Welding fumes	Ozone, metals	Welding operations	Bronchitis, metal fume fever, emphysema
Zoonotic infections	Microorganisms	Animal husbandry, veterinary services, animal droppings	Q fever, psittacosis, hantavirus pulmonary syndrome, anthrax

[1]HP, hypersensitivity pneumonitis; [2] ODTS, organic dust toxic syndrome.
Source: From Kirkhorn and Garry (7), with permission from Environmental Health Perspectives.

as a surprise. Even grain storage and manure can produce toxic substances in the right circumstances.

Toxic Gas Inhalation

Silo Filler's Disease

Farms with large numbers of livestock typically rely on a large storage container called a silo to store animal feed. A variety of relatively airtight structures can serve for animal feed storage, including upright metal tower silos, in-ground pits, and even huge plastic bags. In the silo, recently harvested grains are tightly compressed to squeeze out most of the air. The remaining oxygen is consumed rapidly by actively metabolizing plant cells. As the silo becomes anaerobic, rising amounts of organic acids are formed, resulting in

lowering of the pH (acidification) with suppression of microbial overgrowth and prevention of spoilage. As a result, nitrogen oxides (nitric oxide, NO, or nitrogen dioxide, NO_2) are generated during fermentation of silage. Nitrogen oxides (NOx) are dangerous chemical gases released from reactions between nitric acid and organic materials. They are severe respiratory irritants of low solubility that penetrate to the lower respiratory tract. When levels of NOx rise in a closed tower silo, the levels of NO_2/NOx may rise progressively in the following 1 to 4 days. During this period, the silo becomes a major hazard for any worker without respiratory protection who enters the silo or works in buildings connected to the base of the silo. Fatal exposures by inhalation of silo gas can occur in this setting. Acute high-level exposure can be a cause of acute hemorrhagic pulmonary edema and death. In addition to the potential for exposure to fatal asphyxia secondary to NO_2 and other oxides of nitrogen, less severe exposure to nitrogen oxides produces transient pulmonary decompensation, cough, dyspnea, and headaches. Long-term pulmonary consequences can occur secondary to fibrotic scarring (7,8,11,12).

The generation of toxic silo gases can occur unpredictably despite adherence to usual work practices. Although the potential for silo gas formation exists with any type of ensiled feed, the risk appears to be highest with corn silage (8,13).

Animal Confinement Gases and Other Gases

Animal confinement areas and larger confinement animal facility operations (CAFOs) consist of indoor areas that confine and feed animals and do not grow or store grain. Animals are typically gathered in large numbers to maximize efficiency of space and labor. This practice first became widespread in poultry farms but eventually has been used in other animal confinement areas, such as for raising swine, sheep, and young beef cattle. Animals typically receive all required care in the confinement areas, including feeding, washing, and veterinary services, and may spend their entire lives in these areas. The density of animals in these areas can vary, but generally they are very crowded. A concentrated animal feeding operation can house over 1000 animals (1).

Toxic inhalation exposures in animal confinement facilities are possible with exposures to gases produced from the manure pit. High levels of gases are generated as a by-product of animal waste, especially in high-density confinement facilities such as with swine. The major gases include ammonia, hydrogen sulfide (H_2S), carbon dioxide, and methane, which are all produced in manure pits (14,15).

Ammonia

Ammonia is highly water-soluble and associated with upper airway irritation producing immediate symptoms of burning of eyes, nose, and throat, accompanied by coughing. The odor of ammonia is detectable at 3 to 5 ppm and respiratory irritation at 50 ppm. Sinusitis, mucous membrane inflammation

syndrome, with massive inhalation exposures, and noncardiogenic pulmonary edema can result from exposure. Tolerance to ammonia can occur over time, leading to less irritant symptomatology with greater exposure. Possible effects of long-term exposure (i.e., greater than 2 hours per day for up to 6 years) include sinusitis, mucous membrane inflammation syndrome, chronic bronchitis, and asthma-like syndrome (7,16,17).

Anhydrous Ammonia

Anhydrous ammonia (NH_3) is also common in agriculture and is stored as a liquid and then injected into soil to add nitrogen as fertilizer. It is a highly irritating gas that is very water-soluble. Exposures have resulted in severe burns, laryngeal edema, as well as pulmonary effects including bronchiolitis obliterans and reactive airways dysfunction syndrome (18,19).

Hydrogen Sulfide

Hydrogen sulfide (H_2S) gas is produced from sulfur-containing compounds in manure contained within an anaerobic environment. It is a respiratory irritant at low concentrations and a chemical asphyxiant at high concentration. A concentration of 20 ppm produces mucous membrane irritation; levels of 100 ppm can cause lung injury and bronchiolitis. Higher concentrations may cause asphyxia via inhibition of cytochrome oxidase, similar to the effects of cyanide. Levels of 250 ppm can cause pulmonary edema, and unconsciousness and death can occur at 500 ppm. However, at levels of 150 ppm or higher, olfactory fatigue and paralysis occur. Exposed persons are not able to detect the presence of the gas, leading to fatal exposures. Agitation of manure during emptying of manure pits can generate concentrations of H_2S as high as 1000 ppm into breathing zones of humans and animals. Open-storage manure pits and lagoons are less dangerous than deep pits that are enclosed. Accidental death due to H_2S asphyxiation or cardiogenic pulmonary edema, although rare, can occur with exposures in swine or dairy confinement buildings with under-building manure pits (7,20,21).

Treatment of acute H_2S exposures is with nitrites, which facilitates removal of sulfides by inducing methemoglobinemia. However, nitrates may not be helpful after the acute injury period. Complete recovery may occur after exposure to H_2S although some have suggested the possibility of residual central nervous system toxicity (14,22,23).

Carbon Monoxide

Carbon monoxide (CO) is generated from the operation of gas-powered equipment such as kerosene heaters in insufficiently ventilated buildings. As the gas is invisible and odorless, toxic levels may develop in as little time as 3 to 5 minutes, resulting in poisoning. Higher-level exposures can result in coma, cardiac toxicity, respiratory arrest, and long-term neurologic sequelae and death (20,24).

Carbon Dioxide and Methane

Carbon dioxide (CO_2) and methane (NH_4), also generated from animal wastes, are simple asphyxiants. Unlike H_2S, they are generally not primary causes of adverse health effects. However, methane and carbon dioxide are hazardous when they displace enough oxygen to cause asphyxiation. At levels above 5%, methane can be a potential explosive hazard. CO_2 is also produced by animal respiration. Co_2 levels serve as an indicator of ventilation with acceptable levels typically below 5000 ppm (7,17).

Fumigants

Fumigants are chemicals used to eliminate pests and are applied to crops, grain, or grain storage facilities. Since they are volatile, rapid dissipation occurs and little or no trace is left on the crops or grains. Methyl bromide and phosphine are two common fumigants. Methyl bromide is very toxic and may cause pulmonary edema and hemorrhage after acute exposures. Phosphine is produced from aluminum phosphide pellets that are added to grain and is very reactive, unstable, and toxic. Some have suggested that fumigant exposures may lead to chronic lung disease (14,25,26).

Exposure to Dusts

Inorganic Dusts

Agricultural work is generally performed outdoors. Major outdoor work activities leading to dust and chemical exposure by farm workers include preparation of soil for field crops, growing, harvesting, transport, storage of agricultural products, and fieldwork activities such as plowing, tilling, and haying. Fieldwork also has the potential to expose agricultural workers to inorganic dusts as well as various pesticides and chemicals. Exposures may be particularly significant in dry, semiarid, and desert climates and under windy conditions. The bulk of inorganic dusts are composed of silicates. These include crystalline silica (quartz) and noncrystalline amorphous silica (diatomite). Dust samples from outdoor agricultural environments may be composed of approximately 10% to 20% or greater concentrations of crystalline silica. Workers performing fieldwork may develop clinically significant exposures to various silicates including respirable fibrous minerals and to nonfibrous silicate materials, including mica and clay silicates, known to cause pulmonary fibrosis (27–30).

Airborne mineral dust concentrations and exposure potential may vary with many environmental variables, such as regional geological and climate conditions, amount of rainfall, type of crops grown, and the specific agricultural practices employed. Aerosolized dusts with a median diameter of 4 to 5μm or less can penetrate deep into the respiratory system and have pathophysiological

effects after deposition in the gas-exchange areas of the terminal bronchioles and alveoli (12,17).

In general, inorganic dusts do not contribute to agricultural respiratory disease to the same degree as organic dusts. However, occupational exposures to mineral particles from inorganic dusts and crystalline silica may stimulate release of reactive oxygen species (ROS) in the lung. Reactive oxygen species may play a key role in the mechanisms of disease initiation and progression subsequent to inhalational exposures to these particles. In fact, multiple pathways may be facilitated to produce ROS, which may lead to inflammation, resulting in production of diseases such as pneumoconiosis and carcinogenesis (31).

Organic Dusts

Several work environments have the potential for organic dust exposure including agricultural fields, grain handling and storage areas, animal confinement areas, and dairy barns. Grain handling and storage has been associated with respiratory symptoms and illnesses (such as chronic cough, sputum production, chronic bronchitis, grain fever (organic dust toxic syndrome), and nasal and skin irritation in exposed workers. Similar findings were found in several global areas. Grain elevator workers frequently report symptoms such as cough, sputum production, wheezing, and dyspnea, and have obstructive or restrictive impairments on pulmonary function testing. Respiratory symptoms and worsening of ventilatory function have also been reported with workers exposed to dusts from soybeans and burned rice husk in rice farmers. Growing crops such as rice, soybeans, and flowers has been associated with lung disease (32–43).

Work in dairy barns is also related to respiratory illness. Hay and preserved grasses or corn (silage) are generally used to feed cows in dairy barns and may be a significant source of organic dust exposure to varying degrees based on the mechanism of preparation and storage. Rates of allergic alveolitis were found to be high in workers exposed to hay in small, tightly closed barns. Increased respiratory symptoms have been observed in workers in Finland who shake out hay to feed cows in dairy barns. Another source of exposure in the barn is the bedding chopper, which uses a series of rotating blades to cut bales of hay into smaller lengths, which are then blown into animals' stalls to serve as bedding. This practice can aerosolize hay and create significant amounts of respirable dust (44,45).

In addition, possible additive and/or synergistic toxic exposures and respiratory health effects may occur with dust exposure with coexistent toxic gases, especially in confined work spaces (12,19).

Major components of organic dusts include substances derived from bacterial and fungal organisms such as endotoxin from gram-negative bacteria, peptidoglycans from gram-positive bacteria, glucans, and mold and mycotoxins from fungi. Biologically active proteins of organic dusts may be aller-

genic and proinflammatory. Endotoxin from gram-negative bacteria has been particularly found to be an important causative agent in producing respiratory illness. Recent insights into the innate immune system from genetic research may help elucidate the biological mechanism(s) related to respiratory health effects from endotoxin and other inhaled toxins. The Toll-like group of receptors (TLRs) are receptors for specific components of pathogens such as lipopolysaccharide (LPS), peptidoglycan, and others. It appears that genetic variation in TLRs influences the response to inhaled endotoxin. Thus, variable pulmonary responses in individuals exposed to organic dusts may be due to polymorphisms in the TLR genes. For example, it has been demonstrated that common missense mutations in the Toll-like receptor 4 (TLR4) are associated with a blunted response to inhaled LPS (endotoxin). Consequently, some individuals may be more susceptible than others when exposed to organic dusts. Some authors have also suggested that grain dusts and extracts of grain dusts may play a role in activating inflammation in the lung independent of endotoxin, and that this mechanism may also involve the TLR receptors (46–50).

Mucous Membrane Inflammation Syndrome

Nasal, eye, and throat symptoms commonly found in animal confinement workers and other workers exposed to dusts and gases have been given the name *mucous membrane inflammation syndrome*. Nasal symptoms occur in up to 50% and sinusitis in 25% of swine confinement workers. Nasal lavages have demonstrated increased levels of interleukin-1α, interleukin-1β, and interleukin-6 (7,17)

Organic Dust Toxic Syndrome

Organic dust toxic syndrome (ODTS) describes a self-limiting noninfectious, febrile illness accompanied by malaise, chills, myalgia, nonproductive cough, dyspnea, headache, and nausea, which occurs approximately 4 to 12 hours after heavy exposure to organic dust with a high attack rate. Prior sensitization is not required as in hypersensitivity pneumonitis. Organic dust toxic syndrome is also known as silo-filler's disease, grain fever, precipitin-negative farmer's lung, toxic alveolitis, and pulmonary mycotoxicosis. Organic dust toxic syndrome is highly prevalent in swine confinement operations, with a prevalence of approximately 30% to 35%. However, ODTS has also been observed after unloading silos, removing grain from storage bins (especially with grain sorghum), and on mushroom farms. Estimates indicate that up to one third of farmers will experience an episode of ODTS at some time in their work lives. Other surveys indicate an incidence of 6% to 36% in farmers and agricultural workers at any given time (47–60).

Etiology

As organic dust is composed of a variety of respirable organic materials, it is not clear what specific entity is responsible for OTDS. Endotoxin has been suggested to be the primary cause of inflammation in ODTS. Inhalation of endotoxin can reproduce the symptoms of ODTS, and acute ODTS episodes occur in areas of high endotoxin levels. However, endotoxin-free grain extract also appears capable of inducing pulmonary inflammation. Others have suggested that other microbial sources, such as spores and glucan, are important in the pathogenesis (14,50,61–68).

Pathogenesis

Although it is unclear, ODTS does not appear to elicit a specific immune response to a specific antigen as may occur during an allergic response. Furthermore, sensitization does not occur in ODTS, and the condition is nonprogressive and resolves within several days. However, some individuals have developed respiratory failure secondary to having ODTS.

Clinical Presentation and Diagnosis

Approximately 4 to 12 hours after heavy exposure to organic dust, ODTS presents with fever, chills, malaise, nonproductive cough, dyspnea, myalgias, and headache. Leukocytosis may be found on a laboratory exam. Chest x-ray findings may be normal. Severe cases may present with infiltrates on chest x-ray and respiratory failure. Some authors have suggested an association of a history of ODTS symptoms with chronic bronchitis (43,69,70).

Management

Most cases of ODTS are treated with antipyretics and supportive care, although hospitalization may be required for severe cases. Preventive strategies such as use of respirators would help in work-practice situations where exposure to high levels of dust may occur (69).

Hypersensitivity Pneumonitis

Etiology

Also known as “farmer’s lung” and “extrinsic allergic alveolitis”, hypersensitivity pneumonitis (HP) is caused by exposures to specific fungi found in moldy hay, straw, and feed. In addition to moldy feed, exposure to moldy compost, wood chips, sugar cane (bagasse), composting in mushroom growing, and turkey farming can lead to HP. Hypersensitivity pneumonitis is

much less likely to occur in settings with organic dust exposure compared to ODTS. The overall prevalence of HP is variable and varies with climate.

Studies cite an incidence range from 2 to 3 cases per 10,000 farmers in Sweden, to 4.2 per 10,000 in Wisconsin, to 43.7 per 10,000 in France (45,71,72).

Pathogenesis

Hypersensitivity pneumonitis is a complex disease that has elements of an immunological and cell-mediated allergic response that develops in response to exposure to antigens produced by some species of thermophilic actinomycetes, such as *Micropolyspora faeni, Aspergillus,* and other common fungi found as contaminants of grain or hay (73–75).

Ongoing exposure to antigen in sensitized individuals may lead to either a production of antigen-antibody complex (suggesting a type III reaction), or a late-phase cell-mediated response with granuloma formation compatible with a type IV reaction. The immunological response in HP requires prior sensitization and involves recruitment and activation of alveolar neutrophils and macrophages and T-lymphocyte cells. It appears that genetic and environmental interaction plays an important role in HP.

Risk factors for HP appear to be a –308 polymorphism of the tumor necrosis factor-α (TNF-α) promoter gene and polymorphisms of the major histocompatibility complex (74).

Clinical Presentation

The acute presentation of HP occurs after a single large exposure to antigen. Acute symptoms commence typically after 4 to 6 hours of exposure and consist of fever, chills, malaise, chest tightness, cough, and dyspnea. Physical exam findings are nonspecific but may include inspiratory crackles on auscultation. Hypoxia may be found. It is important to note that if the individual is removed from exposure, symptoms often resolve within several days. Chest x-ray findings may demonstrate diffuse, ill-defined nodular opacities that can be normal. After severe acute exposures, bilateral infiltrates are seen on chest x-rays. A high-resolution computed tomography (CT) scan of the chest may demonstrate ground-glass changes, typically in the lower lobes; this is a good test to obtain for patients suspected of having HP. Other findings on CT are nonspecific and range from patchy airspace consolidation to rounded small opacities, centrilobular nodules, air trapping, fibrosis, and emphysema (37,75,76).

Hypersensitivity pneumonitis can also present with subacute symptoms or as a chronic process with periodic bouts of acute episodes. Subacute HP has a more gradual onset than the acute form, and weight loss appears to be a prominent feature of this form of HP. Pulmonary function tests will show restriction with decreased carbon monoxide diffusing capacity of the lungs (DLCO), chest x-ray findings may show infiltrates or be normal, and CT

scans may be helpful. Lymphocytosis can be seen with bronchoalveolar lavage (37).

Hypersensitivity pneumonitis can develop into a chronic form in a small percentage of cases. The disease may progress even though exposure to the causative agent has ended. When the exposure is prolonged and chronic, individuals may report malaise, fatigue, and cough that present gradually over days or even weeks. A chest x-ray may show reticular markings in chronic diseases. Repeated exposures to low levels of antigens in organic dusts can lead to insidious pulmonary function loss. Noncaseating granulomas with foreign-body giant cells are typically found on a lung biopsy in subacute and chronic cases. Emphysema can be an important sequela (77,78).

Diagnosis

A clinical prediction rule has been developed for identifying acute and subacute HP that consists of six predictors:

1. Good clinical and occupational or environmental history of likely or known exposure to offending antigens, i.e., measurement of microorganisms in the relevant environment
2. Serum precipitating antibodies to thermophilic bacteria
3. Recurrent episodes of symptoms
4. Finding of rales on lung exam
5. Symptom onset 4 to 8 hours postexposure
6. Weight loss (79)

Serum precipitins are present in about 90% in acute cases but tend to wane later in the course of disease. Serum precipitins have been described to specific agents causing HP. The majority of precipitins are IgG and IgA, but IgM precipitins have also been described (80–85). The prevalence of precipitins in exposed symptomatic and asymptomatic individuals varies depending on the number of antigens and how recent and severe the exposure to antigens. However, presence of serum precipitins does not always indicate disease. Asymptomatic exposed individuals can have positive serum precipitins with an estimated prevalence of 5% to 20%. Furthermore, absence of measurable serum precipitins does not rule out a diagnosis of HP because the correct antigen may not be available for testing, and the titer of antibodies can decline to nondetectable levels with chronic disease (86–88).

Management

Corticosteroids are the primary treatment for acute and subacute HP and will shorten the illness duration. However, steroids will not affect the outcome in terms of lung function. No clear guidelines appear to exist about dosing. Early recognition of the exposure sources and symptoms by agricultural

workers and health providers remains the foundation for prevention and control of HP (7,13,83).

Bronchitis

The prevalence of bronchitis is elevated in agricultural workers despite their lower rates of cigarette smoking compared to the general population and other occupational cohorts. Nonsmoking farming populations appear to have a prevalence range of 3% to 30% for chronic bronchitis. Up to 13% to 20% of hog confinement workers may report symptoms consistent with chronic bronchitis. Exposures to grain dust, swine confinement areas, and poultry farming appear to be associated with the highest risk for bronchitis in the agricultural population. Grain workers may develop a dose-related, acute cross-shift decline in peak flow and a gradual reduction in forced expiratory volume in 1 second (FEV_1) over the initial 2 weeks of exposure. Many workers also experience cough and dyspnea, which is initially reversible but recurs with seasonal reexposure to grain dust. With chronic exposure, approximately 20% of nonsmoking and up to 50% of smoking elevator workers develop cough and phlegm (84–91).

Etiology

Exposure to organic dusts in agricultural work areas appears to be a major risk factor for developing acute and chronic bronchitis. Organic dusts are mixtures of several entities including endotoxin, microbial products, and plant and soil particles, and may also include inorganic dusts. It is unclear which of these components is most correlated with respiratory illness, but endotoxin levels are more clearly associated with bronchitis than total dust levels (92).

Concentration and length of exposure to dusts may also be important factors. For instance, acute, high-level exposures to organic dusts may lead to ODTS; chronic, intermittent, lower level exposures may lead to bronchitis. Prior sensitization is not required for acute responses to organic dust exposure. For example, acute cough and signs of lower respiratory inflammation may develop with exposure to hog confinement areas by persons not previously exposed. Compared to previously unexposed nonfarmers, persons chronically exposed to swine confinement areas appear to have a reduced airway response, suggesting possible adaptive mechanisms. Having a history of HP or ODTS from work in animal confinement or greenhouses is a risk factor for chronic bronchitis (93–95).

Diagnosis

Chronic bronchitis is defined clinically as cough that is productive of at least 2 tablespoons of sputum on most days, for three consecutive months in 2

consecutive years, and in the absence of any other lung disease. Diagnosis of chronic bronchitis is based entirely on the history and a temporal association of symptoms with work exposures. Smoking workers are at increased risk of developing respiratory symptoms with exposure to other irritants, and a work-related contribution to their symptoms may be significant. Occupationally induced chronic bronchitis should be suspected in a nonsmoking worker exposed to high concentrations of an irritant at the workplace who has evidence of airway obstruction with no history of asthma (96).

Management

General management for patients with acute bronchitis is with symptomatic therapy such as nonnarcotic cough suppressants or decongestants. Attempting to limit exposures to dusts is the best treatment approach in managing patients with chronic bronchitis. Evidence suggests that the form of chronic bronchitis with airway obstruction seen in farmers may not respond to β-agonist bronchodilator medication. No clinical studies have been specifically done to assess therapeutics of treating chronic airway disease related to organic dust. Current medication regimens are based on studies related to chronic bronchitis secondary to cigarette smoking (97,98).

Asthma

Asthma is characterized by airway inflammation, increased airway responsiveness to a variety of stimuli, and generally reversible airway obstruction either spontaneously or with treatment (99–104). In occupational asthma, there is variable airway obstruction and/or airway hyperresponsiveness due to workplace exposure(s). There are two major types of occupational asthma:

1. Sensitizer-induced asthma, characterized by a variable time during which "sensitization" to a high or low molecular weight agent present at the work site occurs
2. Irritant-induced asthma

Reactive airways dysfunction syndrome is a type of irritant-induced asthma secondary to acute, high-level exposure to an irritant such as anhydrous ammonia on the farm. Work-aggravated asthma is defined as preexisting or concurrent asthma worsened by irritants in the workplace. Exposure to organic dust can aggravate preexisting asthma, through allergic or irritant mechanisms (13,96).

Epidemiological studies of adult farmers have shown prevalence rates for asthma equal to or lower than that of the general population. Recent prevalence rates for asthma in farmers are in the range of 3.7% to 11.8%. However, the prevalence of wheezing in farmers has been found to increase with cumulative years of farm work performed from a level of 1.5% among farm work-

ers with less than 1 year to 4.7% among those with more than 10 years of this work. Specific agricultural jobs, such as production related to livestock and work with farm machinery and equipment, are among occupations with significantly elevated mortality for asthma with a proportionate mortality ratio (PMR) of 1.51. In addition, agricultural production related to crops had a PMR of 1.10. Although agricultural work was associated with an elevated PMR for asthma mortality, agriculture was not among the primary three industries with the greatest number of work-related asthma cases in the areas that were surveyed (98–105).

Etiology

In the agricultural setting, etiologic factors for occupational asthma include organisms that create various high molecular weight antigens, pollens, and animal danders that can cause sensitization and subsequent IgE-mediated asthma. Farmers may also become allergic to components of organic dusts, including grain dust, pollens, and antigens from swine and storage mites. Certain exposures have been found to have an increased risk for asthma. Work in swine confinement areas, poultry operations, greenhouses, and in growing rice increases the risk of asthma. Some specific outbreaks have also been described, such as asthma caused by sensitivity to soybeans. The agricultural and farm environment is generally not a source of low molecular weight chemicals. However, some farmers may perform a significant amount of welding on the farm, and this may be a source of exposure (13,37,44,99,100).

In contrast, being raised on a farm is associated with a lower prevalence of asthma. Early-life exposure to organic dust may have a protective effect against developing asthma and atopy. It is not known if this protective effect is lost in adult farmers who also were raised on farms. Lower rates of asthma have been found in young adults who were raised on farms compared to young adults not raised on farms (101–105).

Diagnosis

Clinical findings include cough, breathlessness, chest tightness with respiration, and wheezing. These symptoms may be mild, moderate, or severe, and be either intermittent or persistent. The chest exam may be normal, even during persistent asthma. A forced expiratory maneuver may uncover wheezing (106).

Although patients with asthma can have normal pulmonary function, persistent asthma usually has a reduction in FEV_1. An inhaled bronchodilator may allow confirmation of the reversibility of the reduced FEV_1 by 12% or greater, a diagnostic characteristic of asthma. Across-shift spirometry, when available, can provide objective evidence of occupational asthma. A greater than 10% fall in FEV_1 across a work shift is suggestive of an asthmatic response (106). Monitoring at home or work with a peak expiratory flow rate

(PEFR) meter can substantiate a diagnosis of asthma by demonstrating an intra-day (a.m. to p.m.) variability in PEFR of 20% or greater. Attention should also be given to any work-related pattern of change in the PEFR.

Management

Once the diagnosis of occupational asthma is made, the primary intervention is to reduce or eliminate the worker's exposure to the offending agent. However, this option is limited in the agricultural setting as compared to other industrial workplaces (107).

Pharmacological treatment of asthma is predicated on the severity of disease and whether the asthmatic symptoms are intermittent or persistent. Intermittent asthma is treated with no daily medication except with an inhaled β-agonist as needed for symptoms; persistent asthma is treated with a daily inhaled corticosteroid medication along with an inhaled β-agonist as needed (106).

Asthma-Like Syndrome

Asthma-like syndrome (ALS) is a nonallergic respiratory condition that is clinically identical to asthma but is not associated with persistent airway inflammation or airway hyperreactivity. This illness is common in swine confinement workers, in whom the prevalence has been reported to be as high as 25%. Approximately 20% of pig farmers had nonproductive cough and 11% experienced wheezing in one study. Veterinarians are another occupational group at risk. Swine confinement workers have increased prevalence of bronchial hyperresponsiveness. There is evidence that exposure to endotoxin, dust, and ammonia in the hog barn environment plays a key role in causing asthma-like syndrome. Slight elevation in neutrophils, lymphocytes, and macrophages in the lower respiratory tract without an increase in eosinophils has been observed in subjects challenged with inhalation exposure to the hog barn setting. Inflammation has also been observed in the lower respiratory tract of hog farmers and increased numbers of lymphocytes and neutrophils (107–115).

Asthma-like syndrome can be difficult to document in the clinical setting. The pulmonary deterioration can often be detected only by cross-shift testing. The cross-shift decline in FEV_1 is generally less than 10% but can range from 10% to 15% and is associated with more than 6 years of exposure.

Ensuring adequate air quality in swine/hog confinement areas is a practical preventive measure to prevent asthma-like syndrome. Respirator use reduces lower respiratory tract inflammation. Treatment may utilize corticosteroids, but one study showed that these medications did not block the inflammatory response, which ensued after subjects were exposed to hog barn dust in an experimental setting. It is unclear whether chronic pulmonary disease can occur after developing this syndrome (116,117).

Respiratory Infections

The agricultural environment harbors a rich microbial reservoir that can lead to several human infections and zoonoses depending on the specific exposures and work activities. Examples include development of swine influenza in hog confinement workers, psittacosis in poultry workers, Q fever from aerosolization of *Coxiella burnetti* from infected goats, sheep, and cattle, causing atypical pneumonia, and infections with *Mycobacterium bovis*, which is endemic in farm animals (118).

Exposure to rodent urine, saliva, and droppings after aerosolization can lead to hantavirus pulmonary syndrome (HPS). This is caused by the sin nombre virus, a single-stranded RNA hantavirus from the Bunyaviridae family. Documented cases have been associated with agricultural activities such as handling grain and cleaning animal sheds. Cases have been reported from North, Central, and South America. The fatality rate can be as high as 30% to 40%. Symptoms of HPS include an initial febrile prodrome similar to a general viral syndrome. However, after about 3 to 5 days, rapid progression to pulmonary edema occurs, resulting in respiratory failure and need for mechanical ventilation. Ribavirin is investigational and of no proven benefit. Extracorporeal oxygenation has been used with some success (7,119).

Evaluation of Patients with Respiratory Disease

As with evaluation for most occupational and environmental illnesses, the evaluation of individuals presenting with respiratory symptoms entails a detailed history and physical examination, followed by appropriate imaging and diagnostic studies.

History

A detailed personal and occupational and environmental history, including a thorough review of job tasks, is essential to understand likely exposures in the agricultural setting. Work practices need to be adequately understood with attention to types, duration, and intensity of likely exposures, whether appropriate environmental and engineering controls are present, and if respiratory protective gear has been used for work activities. It also helps to ask the patient if coworker(s) have similar symptoms, as this may suggest a common workplace exposure or hazard (37,96,120,121).

If available, specific industrial hygiene data on the level of exposure and the agent to which the patient was exposed should be requested from the employer. Material Safety Data Sheets (MSDSs) can provide useful information about the important health, safety, and toxicological properties of the product's ingredients. Under federal law in the United States these must be furnished by the employer to the worker and health care provider upon

request. However, this information may be difficult to obtain in many agricultural areas of the world.

Information about the patient's social habits, such as cigarette smoking, hobbies, home, and living conditions, should be collected, as these factors outside of the work environment can contribute to or cause respiratory diseases (96).

Physical Examination

As respiratory diseases from agricultural exposures may present with nonspecific signs and symptoms, a complete physical exam is prudent rather than focusing only on findings suggested by the exposure history. Vital signs, presence of respiratory distress, if present, and the presence of clubbing or cyanosis should be recorded. Exam of the skin, eyes, and mucous membranes of the nasopharynx may reveal signs of inflammation or irritation. Oropharyngeal and nasal areas may reveal presence of ulcers or polyps. Lung exam should evaluate for presence of wheezing, rhonchi, or both (suggestive of airways disease) and for presence of rales or crackles (suggestive of presence of parenchymal lung disease). When crackles are heard, a cardiovascular system exam is important for evaluation for left ventricular heart failure. The presence of isolated right ventricular heart failure is suggestive of possible cor pulmonale, secondary to chronic severe lung disease with hypoxemia (119).

Diagnosis

A chest radiograph is usually part of the medical workup of suspected respiratory disease. However, a negative chest x-ray does not exclude significant lung damage. For example, immediately after toxic inhalational injuries, the chest x-ray is frequently normal. Furthermore, abnormalities on chest x-ray do not necessarily correlate with the degree of pulmonary impairment or disability, which are better evaluated by pulmonary function testing (PFT) and arterial blood gas evaluation (119).

Chest Computed Axial Tomography

A chest CT is better able to detect abnormalities of the pleura and mediastinal structures than a plain chest x-ray, in large part because it is more sensitive to differences in density. A chest CT may also be performed after administration of intravenous contrast material to gain better visualization of the pulmonary hila. A high-resolution CT (HRCT) is a more detailed exam than a conventional chest CT and obtains sharp interfaces between adjacent structures. A high-resolution CT appears to be more sensitive for a number of diffuse lung processes, such as emphysema and interstitial lung disease (76).

Pulmonary Function Testing

Pulmonary function testing is used to detect and quantify abnormal lung function. This exam consists of spirometry, measurement of lung volumes and diffusing capacity, gas exchange analysis, and exercise testing. Although a pulmonary function laboratory is needed to do most of this evaluation, spirometry can be done at most regional evaluation centers. Often, the most useful of all pulmonary function measures are those obtained from spirometry: FEV_1, forced vital capacity (FVC), and the FEV_1/FVC ratio. The forced expiratory flow (FEF) from 25% to 75% of the vital capacity (FEF 25 to 75) and the shape of the expiratory flow-volume curve are more sensitive findings for mild airway obstruction. Results of spirometry can be compared to predicted values from reference populations (adjusted for age, height, and sex) and expressed as a percentage of predicted value. The determination of obstructive, restrictive, or mixed ventilatory defects can be ascertained from the comparison of observed with predicted values. However, as the commonly used reference population consists entirely of Caucasians, there can be problems using predicted values when evaluating non-Caucasian patients. Generally, the predicted value is lowered by approximately 10% to 15% to adjust for the smaller lungs of non-Caucasians (97).

Several other factors may affect the accuracy of spirometric findings including patient cooperation, poor testing methods, and unreliable equipment.

Peak Expiratory Flow Rate

Measurement of peak flow is a commonly used single-breath test that reflects the degree of airway obstruction. Many portable units exist. Peak flow measurements are helpful in the diagnosis of occupational asthma to document delayed responses after the work shift has ended. However, a major limitation of this method is that patient self-recording is needed and results can be inaccurate or manipulated (97).

Bronchoprovocation Testing

This evaluation is helpful in making the diagnosis of occupational asthma. Pulmonary function responses to inhaled histamine or methacholine are measured and give an indication of the presence and degree of nonspecific airway hyperresponsiveness. A dose-response curve is constructed for repeated measurements of FEV_1 after progressively increasing the exposure doses of histamine or methacholine. The test is typically terminated after a 20% drop in FEV_1. In asthmatic subjects, a relatively low cumulative dose of methacholine induces the 20% in FEV_1 compared to normal subjects (97).

Evolving Areas of Research

Pesticide Exposure and Respiratory Health

Although there are few animal and human studies in the literature on this subject, exposure to pesticides in the course of agricultural activities can produce a range of respiratory illnesses including irritant-induced asthma and persistent wheeze. Case reports also exist regarding the respiratory health effects of pesticides in occupational cohorts exposed to organophosphates or paraquat. For example, depressions in acetylcholinesterase levels were found in Kenyan farmers exposed to organophosphate pesticides. A case series observed the development of persistent irritant asthma in individuals exposed to methylisothiocyanate during a metam-sodium pesticide spill in the Sacramento River in California. A study of grain farmers in Ohio found that increased cough was associated with mixing and applying pesticides more frequently. Among Iowa farmers, increased phlegm and wheeze was associated with insecticide application to animals, even after controlling for the animal exposures themselves. In aerial applicators, increased wheeze was found compared to control subjects (122–131).

The Agricultural Health Study is an ongoing study of licensed pesticide applicators consisting mainly of farmers in North Carolina and Iowa in the United States. In this cohort, 19% of farmers reported wheeze over the previous year, which is higher than the 12% background rate of wheeze in the general United States population. Eleven of 40 pesticides used by farmers were associated with wheeze and specific organophosphates (Parathion, malathion, chlorpyriphos), one thiocarbamate (s-ethyl-dipropylthiocarbamate), and herbicides (glyphosate), paraquat, and atrazine) were associated with wheeze (132,133).

Chronic low-level pesticide exposures may also result in respiratory illness. For instance, chronic low-level occupational exposures to paraquat in Nicaraguan banana farmers found an association of wheeze among highly exposed groups. Another study in South African farm workers found more arterial desaturation among people working with paraquat (134,135).

Rural populations may also be at increased risk for respiratory effects from pesticide exposures. In China, an increased prevalence of wheeze was found in persons who applied organophosphate and pyrethroid/pyrethrins insecticides in the home. In Ethiopia, insecticide use at home was associated with increased skin sensitivity and increased wheeze; malathion was the pesticide most often involved (136,137).

Some strategies to reduce the likelihood of respiratory exposures to pesticides among agricultural populations include choosing pesticides with lower volatility, lower concentrations of active ingredients, and using equipment designed to minimize exposures (138).

Exposure to Mold and Mycotoxins

The medical literature is sparse in regard to mold exposures and respiratory illness in agricultural workers. Sources of mold dust exposure in agricultural areas include hay, grain, silage, and bedding. Baled hay and straw have been found to contain and liberate the largest amounts of microbes such as mesophilic bacteria, xerophilic fungi, mesophilic fungi, thermotolerant fungi, and thermophilic actinomycetes. Hay, except when dried in storage, liberates great numbers of fungal spores (139).

Seasonal variability is an important factor in characterizing the amount and type of microbes in specific farm areas. A study showed a decreased amount of microbial contaminants during summer seasons in swine confinement areas. Another study in a turkey confinement house in Minnesota found the highest concentration of aspergillus (a fungal respiratory disease agent), dust, and ammonia in the winter months (140,141).

Inhalation of dust from complex organic materials may result in acute respiratory tract illness. Possible mechanisms include toxic and cellular reactions to microbial and other organic products or immunological responses after prior sensitization to an antigen. Mold exposure results in production of specific IgE and IgG in the lung. However, aside from the specific IgE and IgG responses, the in-vivo reactions to mold inhalation are poorly understood. Furthermore, it has been difficult to distinguish the health effects of mold and mycotoxins from those of endotoxins and other components of complex organic dust exposures. In immunocompromised individuals, such as post–organ transplant or HIV-infected patients, the potential for invasive systemic disease with fungi such as aspergillus is possible (142,143).

Respiratory Effects of Exposure to Diesel Exhaust

Many farm vehicles are powered by diesel fuel. Diesel exhaust contains many well-known air pollutants including nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and fine particulate matter smaller than 10 μm in diameter (PM10). In the Agricultural Health Study, the estimated prevalence of exposure to diesel fumes was 93% based on questionnaires administered to farmers. Diesel exhaust and diesel exhaust particles appear to play a role in respiratory and allergic diseases and have been associated with exacerbation of asthma.

References

1. Kirkhorn SR, Schenker MB. Current health effects of agricultural work: respiratory disease, cancer, reproductive effects, musculoskeletal injuries, and pesticide-related illnesses. J Agric Saf Health 2002;8:199–214.
2. Schenker MB, ed. American Thoracic Society. Respiratory health hazards in agriculture. Am J Respir Crit Care Med 1998;158(suppl 4):S1–S76.

3. Omland O. Exposure and respiratory health in farming in temperate zones: a review of the literature. Ann Agric Environ Med 2002;9:1136.
4. Singh AB, Singh A, Pandit T. Respiratory diseases among agricultural industry workers in India: a cross-sectional epidemiological study. Ann Agric Environ Med 1999;6:115–26.
5. Radon K, Monso E, Weber C, et al. Prevalence and risk factors for airway diseases in farmers: summary of results of the European farmers' project. Ann Agric Environ Med 2002;9:207–13.
6. Kimbell-Dunn MR, Fishwick RD, Bradshaw L, et al. Work-related respiratory symptoms in New Zealand farmers. Am J Ind Med 2001;39:292–300.
7. Kirkhorn SR, Garry VF. Agricultural lung diseases. Environ Health Perspect 2000;108(suppl 4):705–12.
8. Schenker MB. Agriculture. In: Harber P, Schenker MB, Balmes J, eds. Occupational and Environmental Respiratory Disease. St. Louis: Mosby, 1996:617–36.
9. Louhelainen K, Kangas J, Husman K, et al. Total concentrations of dust in the air during farm work. Eur J Respir Dis 1987;152(suppl):73–9.
10. Zejda JE, Hurst TS, Rhodes EM, et al. Respiratory health of swine producers: focus on young workers. Chest 1993;3:702–9.
11. Olson K. Nitrogen oxides. In: Olson K, ed. Poisoning and Drug Overdose. Stamford, CT: Appleton & Lange, 1999:234–5.
12. Douglas WW, Hepper NGG, Colby TV. Silo filler's disease. Mayo Clin Proc 1993;64:291–304.
13. Zwemer PL, Pratt DS, May JJ. Silo filler's disease in New York State. Am Rev Respir Dis 1992;146:650–3.
14. Spurzem JR, Romberger DJ, Von Essen SG. Agricultural lung disease. Clin Chest Med 2002;23:795–810.
15. Von Essen S, Donham K. Respiratory diseases related to work in agriculture. In: Langley R, Meggs W, McLymore R, et al., eds. Health and Safety in Agriculture, Forestry and Fisheries. Rockville, MD: Government institutes 1997:353–84.
16. Tharatt RS. Ammonia. In: Olson, K, ed. Poisoning and Drug Overdose. Stamford, CT: Appleton & Lange, 1999:67–8.
17. Von Essen SG, Donham KJ. Illness and injury in animal confinement workers. Occup Med 1999;14:337–50.
18. Flury KE, Dines DE, Rodarte JR, et al. Airway obstruction due to inhalation of ammonia. Mayo Clin Proc 1983;58:389–93.
19. Leduc D, Gris P, Lheureux P, et al. Acute and long term respiratory damage following inhalation of ammonia. Thorax 1992;47:755–7.
20. Center for Disease Control and Prevention Morbidity and Mortality Weekly Report. Fatalities attributed to entering manure waste pits—Minnesota, 1992. MMWR 1993;42:325–9.
21. Donham KJ, Knapp LW, Monson R, et al. Acute toxic exposure to gases from liquid manure. J Occup Med 1982;24:142–5.
22. Beck JF, Bradbury CM, Connors AJ, et al. Nitrite as antidote for acute hydrogen sulfide intoxication? Am J Ind Hyg Assoc 1981;42:805–9.
23. Reiffenstein RJ, Hulbert WC, Roth SH. Toxicology of hydrogen sulfide. Annu Rev Pharmacol Toxicol 1992;32:109–34.
24. Olson K. Carbon monoxide. In: Olson K, ed. Poisoning and Drug Overdose. Stamford, CT: Appleton & Lange, 1999.

25. Garry VF, Good PF, Mainvel JC, et al. Investigation of a fatality from nonoccupational aluminum phosphide exposure: measurement of aluminum in tissue and body fluids as a marker of exposure. J Lab Clin Med 1993;122:739–47.
26. Garry VF, Kelly JT, Sprafka JM, et al. Survey of health and use characterization of pesticide appliers in Minnesota. Arch Envrion Health 1994;49: 337–43.
27. Lee K, Lawson RJ, Olenchock SA, et al. Personal exposures to inorganic and organic dust in manual harvest of California citrus and table grapes. J Occup Environ Hygiene 2004;1:505–14.
28. Green FHY, Yoshida K, Fick G, et al. Characterization of airborne mineral dusts associated with farming activities in rural Alberta, Canada. Int Arch Occup Environ Health 1990;62:423–30.
29. Silicosis and Silicate Disease Committee. Diseases associated with exposure to silica and nonfibrous silicate minerals. Arch Pathol Lab Med 1988;112:673–720.
30. Sherwin RP, Barman JL, Abraham JL. Silicate pneumoconiosis of farm workers. Lab Invest 1979;40:576–82.
31. Vallyathan V, Shi X, Castranova V. Reactive oxygen species: their relation to pneumoconiosis and carcinogenesis. Environ Health Perspect 1998;106(suppl 5):1151–5.
32. Ye TT, Huang JX, Shen Y, et al. Respiratory symptoms and pulmonary function among Chinese Rice granary workers. Int J Occup Environ Health 1998;4:155–9.
33. Chan-Yeung M, Enarson D, Grzybowski S. Grain dust and respiratory health. Can Med Assoc J 1985;113:969–73.
34. Do Pico GA, Flaherty D, Bhansalo P, et al. Grain fever syndrome induced by airborne grain dust. J Allergy Clin Immunol 1982;69:435–43.
35. Rylander R. Pulmonary cell reactions and occupational lung diseases: revision of terminology. Am J Ind Med 1987;11:495–6.
36. Dosman JA, Cotton DJ, Graham BL, et al. Chronic bronchitis and decreased forced expiratory flow rates in lifetime nonsmoking grain workers. Am Rev Respir Dis 1980;121:11–16.
37. Becklake M, Broder I, Chan-Yeung M, et al. Recommendations for reducing the effect of grain dust on the lungs. Canadian Thoracic Society Standards Committee. Can Med Assoc J 1996;155:1399–403.
38. Zuskin E, Kanecljak B, Schachter EN, et al. Immunological and respiratory changes in soy bean workers. Int Arch Occup Environ Health 1991;63:15–20.
39. Zuskin E, Skuric Z, Kanceljak B, et al. Respiratory symptoms and ventilatory capacity in soy bean workers. Am J Ind Med 1988;14:157–65.
40. McCurdy SA, Ferguson TJ, Goldsmith DF, et al. Respiratory health of California rice farmers. Am J Respir Crit Care Med 1996;153:1553–9.
41. Golshan M, Faghihi M, Roushan-Zamir T, et al. Early effects of burning rice farm residues on respiratory symptoms of villagers in suburbs of Isfahan, Iran. Int J Occup Environ Health 2002;12:125–31.
42. Lim HH, Domala Z, Jorinder S, et al. Rice miller's syndrome: a preliminary report. Br J Ind Med 1984;41:445–9.
43. Monso E, Schenker M, Radon K, et al. Region-related risk factors for respiratory symptoms in European and California farmers. Eur Respir J 2003;21:323–31.

44. Dalphin JC, Pernet D, Reboux G, et al. Influence of mode of storage and drying of fodder on thermophilic actinomycete aerocontamination in dairy farms of the Doubs region of France. Thorax 1991;46:619–23.
45. Depierre A, Dalphin JC, Pernet D, et al. Epidemiological study of farmer's lung in five districts of the French Doubs province. Thorax 1988;43:429–35.
46. DeLucca AJ, Godshall MA, Palmgren MS. Gram-negative bacterial endotoxins in grain elevator dusts. Am Ind Hyg Assoc J 1984;45:336–9.
47. Jagielo PJ, Thorne PS, Watt JL, et al. Grain dust and endotoxin inhalation challenges produce similar inflammatory responses in normal subjects. Chest 1996;110:263–70.
48. Reynolds SJ, Donham KJ, Whitten P, et al. Longitudinal evaluation of dose-response relationships for environmental exposures and pulmonary function in swine production workers. Am J Ind Med 1996;29:33–40.
49. Aderem A, Ulevitch RJ. Toll-like receptors in the induction of the innate immune response. Nature 2000;406:782–7.
50. Arbour NC, Lorenz E, Schutte BC, et al. TLR4 mutations are associated with endotoxin hyporesponsiveness in humans. Nat Genet 2000;25:187–91.
51. Von Essen S, Robbins RA, Thompson AB, et al. Organic dust toxic syndrome: an acute febrile reaction to organic dust exposure distinct from hypersensitivity pneumonitis. J Toxicol Clin Toxicol 1990;28:389–420.
52. Brinton WT, Vastbinder EE, Greene JW, et al. An outbreak of organic dust toxic syndrome in a college fraternity. JAMA 1987;258:1210–12.
53. Von Essen SG, Romberger DJ. The respiratory inflammatory response to the swine confinement building environment: the adaptation to respiratory exposures in the chronically exposed worker. J Agric Saf Health 2003;9:183–96.
54. Tanaka H, Saikai T, Sugawara H, et al. Workplace-related chronic cough on a mushroom farm. Chest 2002;122:1080–5.
55. Seifert S, Von Essen S, Jacobitz K, et al. Organic dust toxic syndrome: a review. J Toxicol 2003;41:185–93.
56. Von Essen SG, Fryzek J, Nowakowski B, et al. Respiratory symptoms and farming practices in farmers associated with an acute febrile illness after organic dust exposure. Chest 1999;116:1452–8.
57. Malmberg P, Rask-Andersen A, Hoglund S, et al. Incidence of organic dust toxic syndrome and allergic alveolitis in Swedish farmers. Int Arch Allegy Appl Immunol 1988;87:47–54.
58. Husman K, Terho EO, Notkola V, et al. Organic dust toxic syndrome among Finnish farmers. Am J Ind Med 1990;17:79–80.
59. Simpson JC, Niven RM, Pickering CA, et al. Prevalence and predictors of work related respiratory symptoms in workers exposed to organic dusts. Occup Environ Med 1998;55:668–72.
60. Vogelzang PF, van der Gulden JW, Folgering H, et al. Organic dust toxic syndrome in swine confinement farming. Am J Ind Med 1999;35:332–34.
61. Rylander R, Bake B, Fischer JJ, et al. Pulmonary function and symptoms after inhalation of endotoxin. Am Rev Respir Dis 1989;140:981–86.
62. Hagmar L, Schultz A, Hallberg T, et al. Health effects of exposure to endotoxins and organic dust in poultry slaughter-house workers. Int Arch Occup Environ Health 1990;62:159–64.
63. Rask-Andersen A, Malmberg P, Lundholm M. Endotoxin levels in farming: Absence of symptoms despite high exposure levels. Br J Ind Med 1989;46:412–6.

64. Von Essen SG, O'Neill DP, McGranaghan S, et al. Neutrophilic respiratory tract inflammation and peripheral blood neutrophilia after grain sorghum dust extract challenge. Chest 1995;108:1425–33.
65. Malmberg P, Rask-Andersen A, Rosenthall L. Exposure to microorganisms associated with allergic alveolitis and febrile reactions to mold dust in farmers. Chest 1993;103:1202–9.
66. Douwes J, McLean D, van der Maarl E, et al. Worker exposures to airborne dust, endotoxin, and beta(1,3)-glucan in two New Zealand sawmills. Am J Ind Med 2000;38:426–30.
67. Young SH, Robinson VA, Barger M, et al. Acute inflammation and recovery in rats after intratracheal instillation of a 1,3 beta-glucan (zymosan A). J Toxicol Environ Health A 2001;64:311–25.
68. Yoshida K, Ando M, Araki S. Acute pulmonary edema in a storehouse of moldy oranges: a severe case of organic toxic dust syndrome. Arch Environ Health 1989;44:382–4.
69. Perry LP, Iwata M, Tazelaar HD, et al. Pulmonary mycotoxicosis: a clinicopathological study of three cases. Mod Pathol 1998;11:432–6.
70. Kuchuk AA, Basanets A, Louhelainen K. Bronchopulmonary pathology in workers exposed to organic fodder dust. Ann Agric Environ Med 2000;7:17–23.
71. Boyer RS, Klock LE, Schmidt CD, et al. Hypersensitivity lung disease in the turkey raising industry. Am Rev Respir Dis 1974;109:630–5.
72. Marx JJ, Guernsey J, Emanuel DA, et al. Cohort studies of immunologic lung disease among Wisconsin dairy farmers. Am J Ind Med 1990;18:263–8.
73. Roberts RC, Wenzel FJ, Emanuel DA. Precipitating antibodies in a Midwest dairy farming population toward the antigens associated with farmer's lung disease. J Allergy Clin Immunol 1976;57:518–24.
74. Agostini C, Trentin L, Facco M, et al. New aspects of hypersensitivity pneumonitis. Cur Opin Pulmon Med 2004;10:378–82.
75. Gurney JW. Hypersensitivity pneumonitis. Radiol Clin North Am 1992;30:1219–30.
76. Glazer CS, Rose CS Lynch DA. Clinical and radiological manifestations of hypersensitivity pneumonitis. J Thorac Imaging 2002;17:261–72.
77. Barbee RA, Callies Q, Dickie HA, et al. The long-term prognosis in farmer's lung. Am Rev Respir Dis 1968;97:223–31.
78. American Thoracic Society. Respiratory health hazards in agriculture. Am J Respir Crit Care Med 1998;158:S1–S76.
79. Lacasse Y, Selman M, Costabel U, et al. Clinical diagnosis of hypersensitivity pneumonitis. Am J Respir Crit Care Med 2003;168:952–8.
80. Pepys J, Jenkins P. Farmer's lung: Thermophilic actinomycetes as a source of "farmer's lung hay" antigen. Lancet 1963;2:607–11.
81. Ojanen T, Terho EO, Tukiainen H, et al. Class-specific antibodies during follow up of patients with farmer's lung. Eur Respir J 1990;3:257–60.
82. Ojanen TH, Terho EO, Mantyjarvi RA. IgG subclasses in farmer's lung. Eur J Respir Dis Suppl 1987;154:145–50.
83. Moncare S. Influence of corticosteroid treatment on the course of farmer's lung. Eur J Respir Dis 1993;64:283–93.
84. Organic dusts and lung diseases. Proceedings of an International Workshop. Skokloster, Sweden, October 24–27, 1988. Am J Ind Med 1990;17:1–148.

85. Babbott Jr FL, Gump DW, Sylwester DL, et al. Respiratory symptoms and lung function in a sample of Vermont dairymen and industrial workers. Am Rev Respir Dis 1980;70:241–5.
86. Dosman JA, Cotton DJ, Graham BL, et al. Chronic bronchitis and decreased forced expiratory flow rates in lifetime nonsmoking grain workers. Am Rev Respir Dis 1980;121:11–6.
87. Terho EO, Husman K, Vohlonen I, et al. Atopy, smoking, and chronic bronchitis. J Epidemiol Community Health 1987;41:300–5.
88. Zuskin E, Zagar Z, Schachter EN, et al. Respiratory symptoms and ventilatory capacity in swine confinement workers. Br J Ind Med 1992;49:435–40.
89. Vogelzang PFJ, van der Gulden JWJ, Tielen MJM, et al. Health-based selection for asthma, but not for chronic bronchitis, in pig farmers: an evidence-based hypothesis. Eur Respir J 1999;13:187–9.
90. James AL, Zimmerman MJ, Ee H, et al. Exposure to grain dust and changes in lung function. Br J Ind Med 1990;47:466–72.
91. Chan-Yeung M, Enarson D, and Kennedy S. The impact of grain dust on respiratory health. Am Rev Respir Dis 1992;145:476–87.
92. Schwartz DA, Donham KJ, Olenchock SA, et al. Determinants of longitudinal changes in spirometric function among swine confinement operators and farmers. Am J Respir Crit Care Med 1995;151:47–53.
93. Comier Y, Duchaine C, Israel-Assag E, et al. Effects of repeated swine building exposures on normal naïve subjects. Eur Respir J 1997;10:1516–22.
94. Palmberg L, Larson BM, Malmberg P, et al. Airway responses of healthy farmers and nonfarmers to exposure in a swine confinement building. Scand J Work Environ Health 2002;28:256–63.
95. Dalphin JC, Debieuvre D, Pernet D, et al. Prevalence and risk factors for chronic bronchitis and farmer's lung in French dairy farmers. Br J Ind Med 1993;50:941–4.
96. Balmes J, Scannell CH. Occupational lung diseases. In: LaDou J, ed. Occupational and Environmental Medicine, 2nd ed. Stamford, CT: Appleton & Lange, 1997.
97. Bailey TC, Little R. Infectious diseases. In: Lin TL, Rypkema SW, eds. The Washington Manual of Ambulatory Therapeutics. Philadelphia: Lippincott Williams & Wilkins, 2002:409.
98. Dalphin JC, Dubiez A, Monnet E, et al. Prevalence of asthma and respiratory symptoms in dairy farmers in the French province of the Doubs. Am J Respir Crit Care Med 1998;158:1493–98.
99. Kimbell-Dunn M, Bradshaw L, Slater T, et al. Asthma and allergy in New Zealand farmers. Am J Ind Med 1999;35:51–7.
100. Kronquist M, Johansson E, Pershagen G, et al. Risk factors associated with asthma and rhinoconjunctivitis among Swedish farmers. 1999;54:1142–9.
101. Riedler J, Braun-Fahrlander C, Eder W, et al. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. Lancet 2001;358:1129–33.
102. Ernst P, Cormier Y. Relative scarcity of asthma and atopy among rural adolescents raised on a farm. Am J Respir Crit Care Med 2000;161:1563–6.
103. Chrischilles E, Ahrens R, Kuehl A, et al. Asthma prevalence and morbidity among rural Iowa schoolchildren. J Allergy Clin Immunol 2004;113:66–71.

104. Kipelainen M, Terho EO, Helenius H, et al. Childhood farm environment and asthma and sensitization in young adulthood. Allergy 2002;57:1130–5.
105. Center for Disease Control and Prevention. National Institute for Occupational Safety and Health. Worker Health Chart Book, 2004. NIOSH Publication No. 2004–146. Washington, DC: NIOSH, 2004.
106. Grayson MH, Wedner HJ, Korenblat PE. Allergy and asthma. The Washington Manual of Ambulatory Therapeutics. Philadelphia: Lippincott Williams & Wilkins, 2002.
107. Donham KJ, Cumro D, Reynolds SJ, et al. Dose-response relationships between occupational aerosol exposures and cross-shift declines of lung function in poultry workers: recommendations for exposure limits. J Occup Environ Med 2000;42:260–9.
108. Hoppin JA, Umbach DM, London SJ. Animal production and wheeze in the Agricultural Health Study: interactions with atopy, asthma, and smoking. Occup Environ Med 2003;60:e3.
109. Kirychuk SP, Senthilselvan A, Dosman JA, et al. Respiratory symptoms and lung function in poultry confinement workers in Western Canada. Can Respir J 2003;10:375–80.
110. Radon K, Danuser B, Iversen M, et al. Respiratory symptoms in European animal farmers. Eur Respir J 2001;17:747–54.
111. Volgelzang PF, van der Gulden JW, Folgering H, et al. Longitudinal changes in bronchial responsiveness associated with swine confinement dust exposure. Chest 2000;117:1488–95.
112. Reynolds SJ, Donham KJ, Whitten P et al. Longitudinal evaluation of dose-response relationships for environmental exposures and pulmonary function in swine production workers. Am J Ind Med 1996;29:33–40.
113. Kirychuk SP, Senethilselvan A, Dosman JA, et al. Predictors of longitudinal changes in pulmonary function among swine confinement workers. Can Respir J 1998;5:472–8.
114. Larrson K, Elkund A, Malmberg P, et al. Alterations in bronchoalveolar lavage fluid but not in lung function and bronchial responsiveness in swine confinement workers. Chest 1992;101:767–74.
115. Pedersen B, Iversen M, Laarsen BB, et al. Pig farmers have signs of bronchial inflammation and increased numbers of lymphocytes and neutrophils in BAL fluid. Eur Respir J 1996;9:524–30.
116. Dossman JA, Senthilselvan A, Kirychuk SP, et al. Positive human health effects of wearing a respirator in a swine barn. Chest 2000;118:852–60.
117. Ek A, Palmberg L, Larrson K. Influence of fluticasone and salmeterol on airway effects of inhaled organic dust; An in vivo and ex vivo study. Clin Exp Immunol 2000;121:11–6.
118. Weber DJ, Rutala WA. Zoonotic infections. Occup Med 1999;14(2):247–84.
119. Hantavirus pulmonary syndrome. In: Chin J, ed. Control of Communicable Diseases Manual. Washington, DC: American Public Health Association, 2000.
120. Schenker MB, Orenstein MR, Samuels SJ, et al. Use of protective equipment among California farmers. Am J Ind Med 2002;42:455–64.
121. Wu JD, Nieuwenhuijsen MJ, Samuels SJ, et al. Identification of agricultural tasks important to cumulative exposures to inhalable and respirable dust in California. AIHA J 2003;64:830–6.

122. Weiner A. Bronchial asthma due to organic phosphate insecticides. Ann allergy 1961;19:397–401.
123. Deschamps D, Questel F, Baud J, et al. Persistent asthma after acute inhalation of organophosphate insecticide. Lancet 1994;344:1712.
124. Royce S, Wald P, Sheppard D, et al. Occupational asthma in a pesticides manufacturing worker. Chest 1993;103:295–6.
125. Draper A, Cullinan P, Campbell C, et al. Occupational asthma from fungicides fluazinam and chlorothalonil. Occup Environ Med 2003;60:76–7.
126. Honda I, Kogrogi H, Ando M, et al. Occupational asthma induced by the fungicide tetrochloropthalonitrile. Thorax 1992;47:760–1.
127. Cone JE, Wugofski L, Balmes JR, et al. Persistent respiratory health effects after a metam sodium pesticide spill. Chest 1994;106:500–8.
128. Ohayo-Mitoko GJA, Kromhout H, Simwa JM, et al. Self reported symptoms and inhibition of acetylcholinesterase activity among Kenyan agricultural workers. Occup Environ Med 2000;57:195–200.
129. Wilkins JR, Engelhardt HL, Rublaitus SM, et al. Prevalence of chronic respiratory symptoms among Ohio cash grain farmers. Am J Ind Med 1999;35:150–63.
130. Sprince NL, Lewis MQ, Whitten PS, et al. Respiratory symptoms: Associations with pesticides, silos, and animal confinement in the Iowa Farm Family Health and Hazard Surveillance project. Am J Ind Med 38:455–63.
131. Jones SM, Burks AW, Spencer HJ, et al. Occupational asthma symptoms and respiratory function among aerial pesticide applicators. Am J Ind Med 2003;43:407–17.
132. Hoppin JA, Umbach DM, London SJ, et al. Chemical predictors of wheeze among farmer pesticide applicators in the agricultural health study. Am J Respir Crit Care Med 2002;165:683–9.
133. Alavanja MC, Sandler DP, McMaster SB, et al. The Agricultural Health Study. Environ Health Perspect 1996;104:362–9.
134. Castro-Gutierrez N, McConnell R, Andersson K, et al. Respiratory symptoms spirometry and chronic occupational paraquat exposure. Scand J Work Environ Health 1997;23:421–7.
135. Dalvie M, White AN, Raine R, et al. Long-term respiratory health effects of the herbicide, paraquat, among workers in the Western Cape. Occup Environ Med 1999;56:391–6.
136. Zhang LX, Enarson DA, He GX, et al. Occupational an environmental risk factors for respiratory symptoms in rural Beijing, China. Eur Respir J 2002;20:1525–31.
137. Yemaneberhan H, Bekele Z, Venn A, et al. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. Lancet 1997;350(9071):85–90.
138. Dowling KC, Seiber JN. Importance of respiratory exposure to pesticides among agricultural populations. Int J Toxicol 2002;21:371–81.
139. Kotimaa MH, Oksanen L, Koskela P. Feeding and bedding materials as sources of microbial exposure on dairy farms. Scand J Work Environ Health 1991;17:117–22.
140. Duchaine C, Grimard Y, Cormier Y. Influence of building maintenance, environmental factors, and seasons on airborne contaminants of swine confinement buildings. AIHA J 2000;61:56–63.

141. Mulhausen JR, Mc Jilton CE, Redig PT, et al. Aspergillus and other human respiratory disease agents in turkey confinement houses. Am Ind Hyg Assoc J 1987;48:894–9.
142. Weber S, Kullman G, Petsonik E, et al. Organic dust exposures from compost handling: case presentation and respiratory exposure assessment. Am J Ind Med 1993;24:365–74.
143. Aspergillosis. In: Chin J, ed. Control of Communicable Diseases Manual. Washington, DC: American Public Health Association, 2000.

20

Renal and Hepatic Disease

Michael Nasterlack and Andreas Zober

Key words: liver disease, kidney disease, agrochemicals, biological hazards, organic solvents, infections

Generally speaking, the occurrence of liver or kidney disease is not particularly associated with agriculture. Nevertheless, life in rural settings in general, as well as work in agriculture in particular, is associated with a variety of health risks that can affect liver or kidney. These risks are not completely different from those in urban life but can be present to a greater or lesser degree. Environmental exposures on farms are typically characterized by biological hazards, including a higher infectious disease risk; by the use of agricultural chemicals, including fertilizers and biocides; and by exposures to solvents, fuels, paints, and welding fumes associated with maintenance and repair work. On the other hand, pollution by traffic exhausts, industrial emissions, and other effluents of civilization play a comparatively smaller role in a rural environment. Health risks associated with general lifestyle choices, such as smoking, alcohol consumption, and lack of physical exercise, are also present to a lesser extent on average than in urban settings. This association might not be true under all circumstances as with respect to alcohol consumption in wine-producing areas or to behavioral patterns in migrant farm workers as compared to farmers themselves. Diseases of poverty, such as malnutrition and infectious diseases not only put the farm worker at risk for hepatic and renal injuries, but also can cause diseases in their own right (1,2).

General Epidemiological Liver and Kidney Findings in Farmers

Cohort studies in farmers or agricultural workers have mostly been targeted at cancer outcomes; those focused on other health issues are scarce. The overall findings suggest that farmers and farm residents experience less cancer and more favorable mortality patterns, except from accidents, than their respective control groups. Liver cirrhosis as a cause of death was significantly

less than expected in New York farmers, and so was the incidence of liver and kidney cancer in several cohorts of farmers, agricultural workers, and licensed pesticides applicators in other studies (3–7).

One cohort study among farmers and agricultural workers from Italy found a small excess of kidney cancers based on five observations against the background of overall reduced cancer mortality. Studies in female farm residents have shown either insignificant elevations of liver cancer risk or no elevations at all, with kidney cancer risk being significantly reduced. In a large case-control study of hepatocellular carcinoma, cholangiocarcinoma, or combined hepatocellular and cholangiocarcinoma, male farmers were the only occupational group with an odds ratio significantly below unity. A few studies suggest that migrant farm workers may differ from farmers by experiencing excesses of cancers of the buccal cavity and pharynx, lung, and liver. This disease pattern, however, appears to be more closely related to lifestyle factors like smoking and alcohol drinking than to occupational exposures typically associated with farming (8–13).

Only few reports describe relevant disease patterns deviating from the above-mentioned findings. One was a cluster of 14 hepatic angiosarcoma cases in Egypt, 10 of which had "a definite history of a direct chronic recurrent exposure to agricultural pesticides of variable chemical nature." The authors' conclusion that "this significant increase . . . among farmers involved in pesticide spraying suggests that agricultural pesticides might play a role in the genesis of hepatic angiosarcoma" does not hold, however, against the lack of evidence in the rest of the available literature (14).

Elevated rates of liver cancer in rural populations in Fiji as compared to Tonga have been attributed to the higher prevalence of food contamination with aflatoxin in the former, reflecting different storage practices. Men who used mainly dichlorodiphenyl-trichloroethane (DDT) in an antimalarial campaign in Sardinia, Italy, during the late 1940s experienced an increased mortality from liver and biliary tract cancers. This increase, however, also occurred in nonexposed subjects and showed no dose response relation. The authors concluded that these cancers probably were unrelated to DDT and that other environmental exposures common to the Sardinian population accounted for the increase in risk (15,16).

In a report on a case series on end-stage renal disease (ESRD) in El Salvador, the authors described a group of patients with known risk factors for ESRD, basically diabetes mellitus, hypertension, and chronic consumption of nonsteroidal antiinflammatories. Another group had unusual characteristics that were not associated with the known risk factors. According to the authors they "identified an important group of patients with ESRD who seem to lack a cause for their disease. Their special characteristics make it possible to suspect a relationship with the occupational exposure to insecticides or pesticides." While this interpretation contrasts with the lack of similar findings in other rural populations from other regions, it is a perfect illustration of a widespread perception bias in parts of the epidemiological

literature on health risks associated with agriculture: health effects are readily attributed to agricultural chemicals, notably pesticides, without even trying to define what pesticides are, and without adequate consideration of other possible causes (17).

Chemical Exposures

Chemical exposures in agriculture and farming can be manifold and heterogeneous. This is especially true for the handling of pesticides, an exposure category often used in the occupational medical literature (see Chapter 16). Although liver and kidney damage from agrochemicals is noted with some regularity both in high-dose animal toxicology testing and in case reports from accidental or suicidal poisoning, these findings are hardly transferable to occupational or environmental human exposure situations. The reason for the findings in animals is that many of these chemicals through their metabolism may lead to adaptive responses such as enzyme induction, organ enlargement, and, finally, to overload phenomena at the highest doses that are not normally achievable in human workplaces. Consequently, a general risk increase for liver disease caused by agrochemicals is doubtful, and no reports are available regarding the general risk for kidney effects. However, in situations with poor occupational hygiene and lack of personal protective equipment, eventually aggravated by unfavorable climatic conditions, high exposures to agrochemicals with the occurrence of mostly acute adverse health effects are possible. Other chemical exposures in agriculture such as solvents may have well-known liver- or kidney-damaging properties associated with certain uses; however, their relevance for farmers and farm workers has rarely been assessed. Given these limitations, only some generic remarks on chemicals in farming can be made and some specific examples for toxic effects on liver or kidney can be given (18).

Pesticides

Pesticides are a heterogeneous group of chemicals that, by definition, are produced and used to exert biological activity. There are thousands of naturally occurring pesticides in all kinds of plants and, currently, some 500 different synthetic molecules in more than 5000 formulations. As diverse as their chemistry are their respective biological targets and modes of action. They are used as herbicides, fungicides, insecticides, acaricides, rodenticides, and microbicides. Against this background, it is impossible to give a summary evaluation of liver or kidney effects of these substances in farm workers or residents (see Chapters 13 and 16).

Most insecticides act primarily as neurotoxins, with much lower effective doses in insects than in mammals. They elicit symptoms in the central and

peripheral nervous system much earlier than in any other organ system. This explains why, except in cases of deliberate poisoning, as in suicide, manifest liver or kidney damage due to insecticide use hardly ever occurs in persons who handle them professionally. One exception to this statement may be lead arsenate, which was used as an insecticide in vineyards in the past and allegedly caused liver cirrhosis and liver cancer in wine growers. Such cases have been acknowledged as an occupational disease in Germany; however, some doubted the relevance of arsenic as the major culprit. Elevated liver enzyme activities in professional pesticide sprayers have occasionally been reported, whereas others did not confirm these findings (19–25).

Some fungicides act via inhibition of the P450 enzyme family and can thus interfere with xenobiotic metabolism in mammals. Although liver damage has been found after administration of fungicides in experimental animals, liver and kidney toxicity of most of these substances is insignificant in humans under normal circumstances. Notable exceptions from this rule happened in the past with the accidental consumption of wheat seedlings treated with hexachlorobenzene (HCB). Several thousand cases of hepatic porphyria occurred after incidences of mass poisoning in Iraq and Turkey. Of course, porphyria was neither the leading nor the most severe symptom of HCB poisoning (26,27).

Herbicides primarily target plant-specific enzymes and are thus generally of comparatively low toxicity to nontarget organisms. Acute intoxications mainly affect the central nervous system, with kidney effects being reported after long-term exposure to chlorophenoxy derivatives. From this group of substances, 2,4,5-T especially has been found to be contaminated with dioxin in the past, and a variety of health effects in former users have been attributed to it. The most exposed, however, were not farmers but American soldiers involved in the spraying of Agent Orange in Vietnam, and hepatic or renal disorders were not a major issue in these cases. The herbicide paraquat has become an infamous example of high mortality due to pulmonary fibrosis together with liver and kidney failure. Although such cases usually relate to either accidental or suicidal oral intake of larger quantities, one case of lethal paraquat poisoning in a Japanese worker with an occupational history of spraying paraquat in a greenhouse has been reported (28,29).

Solvents and Fuels

Although exposures to organic solvents and fuels are not specific for agricultural settings, they represent typical health risks for farmers. Solvents and fuels not only are used in repair and maintenance work, as in painters or cleaners, but also are often the basis for the preparation of pesticide solutions for spraying. Especially for sprayed solvents, exposure through inhalation or skin contact not only of vapors but also of aerosols is possible. Depending on the substance used, the hepatotoxic potency of the solvent can be more

relevant than that of the active ingredient pesticide. This aspect is often neglected in the discussion of health findings in pesticide sprayers, not least because of the difficulty of differentiating between the effects of single factors in complex mixtures. To enable an educated guess of the possible solvent-related health risk for farmers, experience from typically solvent-exposed professionals like degreasers, printers, painters, and paint manufacturers may serve as a model. Here, on average, subclinical effects have been described on liver and kidney function. However, except from some specific agents like *N,N′*-dimethylformamide or several chlorinated hydrocarbons, the hepatotoxicity and nephrotoxicity of organic solvents should not be overrated (30–34).

Many similar studies have not found any demonstrable solvent effect on liver and kidney even in comparatively highly exposed subjects, and liver-related findings often were more closely associated with individual alcohol consumption than with occupational solvent exposure. Taken together, the findings of slight effects on kidney and liver, if any, in heavily solvent-exposed workers other than farmers is consistent with the generally low reported rates of liver or kidney damage in farmers, who have much lower solvent exposure (35–38).

Biological Agents

If ever there is a "typical exposure" in agricultural settings, it is the close contact with biological agents, many of which are associated with an enhanced risk for infections. This link is most evident in cases of zoonoses, diseases that can be passed from animals, whether wild or domesticated, to humans. Although most zoonotic infections do not primarily affect liver or kidneys, some links can be established.

A two- to fivefold prevalence of hepatitis E antibodies, for example, has been found in North Carolina swine workers as well as in Moldavian swine farmers, suggesting that hepatitis E may be a zoonosis and specifically an occupational infection of livestock workers. Being in the vicinity of wildlife, including having close contact with free-roaming farm animals such as dogs, and in some regions also herding of sheep, goats, and cattle are associated with an increased risk for human alveolar echinococcosis, which typically forms hydatid cysts in the liver and caused up to 100% lethality in untreated patients before the 1970s (39–44).

Life in rural areas itself may be associated with lack of sanitation or unhygienic work practices, not only in developing but also in developed countries. One well-described risk factor for infectious disease in general, including liver or kidney disease, is the use of untreated waste water for irrigation, which increased the incidence of shigellosis, salmonellosis, typhoid fever, and infectious hepatitis by a factor of two to four in Israeli kibbutzim. In Turkey, this practice has been identified as a source of hepatitis E infection in farm

workers. Melioidosis is an infection, endemic in Southeast Asia, North Australia, New Guinea, and in tropical Africa, that primarily affects the lung but can subsequently lead to liver and kidney abscesses. Farmers and stockmen represented predisposed populations in North Queensland, which was attributed to their prolonged soil contact (45–47).

Noninfectious biological hazards through fungal growth on hay, grain, food, and feedstock also have to be taken into account. Again, liver and kidney are not the most important targets for associated health effects but can be affected in special cases. A case of acute renal failure (ARF) due to inhalation of ochratoxin A produced by a mold of the species *Aspergillus ochraceus* was reported from Italy. After working 8 hours in a granary closed for several months, a farmer and his wife suffered respiratory distress; the woman developed nonoliguric ARF, and biopsy revealed tubulonecrosis. A strain of *A. ochraceus* producing ochratoxin was isolated from the wheat (48).

Conclusion

Living on farms or doing farm work is associated with a number of health risks, some of which may also pertain to liver or kidney. However, apart from some specific but rare diseases or some unusual local clusters, liver or kidney disease in general is not a major cause of concern in rural settings. One cause for this reduced specific illness frequency as compared with urban populations is the reduced presence of some classical behavioral risk factors, notably smoking and alcohol consumption. The highest risks for liver and kidney disease in farming are due to biological hazards. Toxicological health risks, where present, are not primarily targeted at liver or kidney. This does of course not mean that there are no relevant toxicological risks present in agriculture. Occupational hygiene, including appropriate personal protective equipment, is essential in the handling of toxic chemicals in agriculture, as well as elsewhere.

References

1. Coble J, Hoppin JA, Engel L, et al. Prevalence of exposure to solvents, metals, grain dust, and other hazards among farmers in the Agricultural Health Study. J Exp Anal Environ Epidemiol 2002;12:418–26.
2. Olkinuora M. Alcoholism and occupation. Scand J Work Environ Health 1984;10:511–5.
3. Stark AD, Chang HG, Fitzgerald EF, et al. A retrospective cohort study of mortality among New York State Farm Bureau members. Arch Environ Health 1987;42:204–12.
4. Wiklund K, Dich J. Cancer risks among male farmers in Sweden. Eur J Cancer Prev 1995;4:81–90.
5. Blair A, Dosemeci M, Heineman EF. Cancer and other causes of death among male and female farmers from twenty-three states. Am J Ind Med 1993;23:729–42.

6. Wiklund K, Dich J, Holm LE, et al. Risk of cancer in pesticide applicators in Swedish agriculture. Br J Ind Med 1989;46:809–14.
7. Blair A, Malker H, Cantor KP, et al. Cancer among farmers: a review. Scand J Work Environ Health 1985;11:397–407.
8. Faustini A, Forastiere F, Di Betta L, et al. Cohort study of mortality among farmers and agricultural workers. Med Lav 1993;84:31–41.
9. Wang Y, Lewis-Michl EL, Hwang SA, et al. Cancer incidence among a cohort of female farm residents in New York State. Arch Environ Health 2002;57:561–67.
10. Wiklund K, Dich J. Cancer risks among female farmers in Sweden. Cancer Causes Control 1994; 5:449–57.
11. Dossing M, Petersen KT, Vyberg M, et al. Liver cancer among employees in Denmark. Am J Ind Med 1997;32:248–54.
12. Zahm SH, Blair A. Cancer among migrant and seasonal farmworkers: an epidemiologic review and research agenda. Am J Ind Med 1993;24:753–66.
13. Suarez L, Weiss NS, Martin J. Primary liver cancer death and occupation in Texas. Am J Ind Med 1989;15:167–75.
14. el Zayadi A, Khalil A, el Samny N, et al. Hepatic angiosarcoma among Egyptian farmers exposed to pesticides. Hepatogastroenterology 1986;33:148–50.
15. Lovelace CE, Aalbersberg WG. Aflatoxin levels in foodstuffs in Fiji and Tonga islands. Plant Foods Hum Nutr 1989;39:393–9.
16. Cocco P, Blair A, Congia P, et al. Proportional mortality of dichloro-diphenyl-trichloroethane (DDT) workers: a preliminary report. Arch Environ Health 1997;52:299–303.
17. Trabanino RG, Aguilar R, Silva CR, et al. [End-stage renal disease among patients in a referral hospital in El Salvador] [article in Spanish]. Rev Panam Salud Publica 2002;12:202–6.
18. Perger G. [Erkrankungen der Leber durch berufliche Exposition gegenüber Pestiziden.] Arbeitsmed Sozialmed Umweltmed 1998;33:548–56.
19. Hayes WJ, Laws ER, eds. Handbook of pesticide toxicology, v.1. San Diego: Academic Press, 1991.
20. Lüchtrath H. [Die Leberzirrhose bei chronischer Arsenvergiftung der Winzer.] Dtsch Med Wochenschr 1972;97:21–2.
21. Hossfeld C, Bartsch R, Beyer B, et al. [Aussagen zum Gesundheitszustand langjährig estizidexponierter Arbeitnehmer in Thüringer Obstbaubetrieben.] Arbeitsmed Sozialmed Umweltmed 2002;37:599–605.
22. Thiele E, Perger G, Möllmann A.[Expositionscharakteristik, präpathologische und pathologische Normabweichungen ausgewählter Laborparameter als Folge intermittierender Pestizidexposition.] Ergebn Exp Med 1985;46:456–8.
23. Morgan DP, Roan CC, Tucson A. Liver function in workers having high tissue stores of chlorinated hydrocarbon pesticides. Arch Environ Health 1974;65:14–7.
24. Straube E, Krüger E, Bradatsch M.Untersuchungen zur Bewertung der externen Belastung durch Pflanzenschutz-und Schädlingsbekämpfungsmittel beim beruflichen Einsatz im Freiland und in geschlossenen Räumen sowie zur Beanspruchung des Menschen.Greifswald: Druckhaus Panzig, 1998.
25. Hanusch A. Zur Untersuchung PSM-Exponierter. Z Gesamte Hyg 1978;24:544–7.
26. Solecki R, Pfeil R. Biozide und Pflanzenschutzmittel. In: Marquardt H, Schäfer SG, eds. Lehrbuch der Toxikologie. Stuttgart: Wissenschaftliche Verlagsgesellschaft, 2004:657–701.

27. Cripps DJ, Gocmen A, Peters HA. Porphyria turcica. Twenty years after hexachlorobenzene intoxication. Arch Dermatol 1980;116:46–50.
28. Michalek JE, Ketchum NS, Longnecker MP. Serum dioxin and hepatic abnormalities in veterans of Operation Ranch Hand. Ann Epidemiol 2001;11:304–11.
29. Kishimoto T, Fujioka H, Yamadori I, et al. [Lethal paraquat poisoning caused by spraying in a vinyl greenhouse causing pulmonary fibrosis with a hepatorenal dysfunction] [article in Japanese]. Nihon Kokyuki Gakkai Zasshi 1998;36:347–52.
30. Brautbar N, Williams J. Industrial solvents and liver toxicity: risk assessment, risk factors and mechanisms. Int J Hyg Environ Health 2002;205:479–91.
31. Michailova A, Kuneva T, Popov T. A comparative assessment of liver function in workers in the petroleum industry. Int Arch Occup Environ Health 1998;71:S46–9.
32. Boogaard PJ, Rocchi PS, van Sittert NJ. Effects of exposure to low concentrations of chlorinated hydrocarbons on the kidney and liver of industrial workers. Br J Ind Med 1993;50:331–9.
33. Nasterlack M, Frank K-H, Hacke W, et al. Die Heidelberger Malerstudie der ARGE Bau. Multidisziplinäre Querschnittsstudie zu Wirkungen berufstypischer Arbeitsstoffbelastungen auf die Gesundheit langjährig tätiger Maler. Arbeitsmed Sozialmed Umweltmed Sonderheft 1997;23:1–79.
34. Nasterlack M, Triebig G, Stelzer O. Hepatotoxic effects of solvent exposure around permissible limits and alcohol consumption in printers over a 4-year period. Int Arch Occup Environ Health 1994;66:161–5.
35. Rasmussen K, Brogren C-H, Sabroe S. Subclinical affection of liver and kidney function and solvent exposure. Int Arch Occup Environ Health 1993;64:445–8.
36. Rees D, Soderlund N, Cronje R, et al. Solvent exposure, alcohol consumption and liver injury in workers manufacturing paint. Scand J Work Environ Health 1993;19:236–44.
37. Lundberg I, Hakansson M. Normal serum activities of liver enzymes in Swedish paint industry workers with heavy exposure to organic solvents. Br J Ind Med 1985;42:596–600.
38. Zober A, Raithel H, Valentin H. Hinweise für die Sachaufklärung bei berufsbedingten toxischen Leberschäden. Arbeitsmed Sozialmed Präventivmed 1981;16:128–31.
39. Withers MR, Correa MT, et al. Antibody levels to hepatitis E virus in North Carolina swine workers, non-swine workers, swine, and murids. Am J Trop Med Hyg 2002;66:384–8.
40. Drobeniuc J, Favorov MO, Shapiro CN, et al. Hepatitis E virus antibody prevalence among persons who work with swine. J Infect Dis 2001;184:1594–7.
41. Uzunlar AK, Yilmaz F, Bitiren M. Echinococcosis multilocularis in southeastern Anatolia, Turkey. East Afr Med J 2003;80:395–7.
42. Saeed I, Kapel C, Saida LA, et al. Epidemiology of *Echinococcus granulosus* in Arbil province, northern Iraq, 1990–1998. J Helminthol 2000;74:83–8.
43. Auer H, Aspock H. Incidence, prevalence and geographic distribution of human alveolar echinococcosis in Austria from 1854 to 1990. Parasitol Res 1991;77:430–6.
44. Deplazes P, Eckert J. Veterinary aspects of alveolar echinococcosis: a zoonosis of public health significance. Vet Parasitol 2001;98:65–87.
45. Katzenelson E, Buium I, Shuval HI. Risk of communicable disease infection associated with wastewater irrigation in agricultural settlements. Science 1976; 194:944–6.

46. Ceylan A, Ertem M, Ilcin E, Ozekinci T. A special risk group for hepatitis E infection: Turkish agricultural workers who use untreated waste water for irrigation. Epidemiol Infect 2003;131:753–6.
47. Guard RW, Khafagi FA, Brigden MC, et al. Melioidosis in Far North Queensland. A clinical and epidemiological review of twenty cases. Am J Trop Med Hyg 1984;33:467–73.
48. Di Paolo N, Guarnieri A, Garosi G, et al. Inhaled mycotoxins lead to acute renal failure. Nephrol Dial Transplant 1994;9(suppl 4):116–20.

21

Disease and Injury Among Veterinarians

James E. Lessenger

Key words: job tasks, hazards, trauma, infectious diseases, dermatoses, allergies, cancer, pregnancy, AIDS

Veterinarians have a unique position in agriculture. Their scientific knowledge of animal anatomy, physiology, and health makes them indispensable to the production of food. They are also important in the early identification of risks and hazards to food, especially from disease. Their close working relationship with production agriculture and animals exposes them to unique risks that will be explored in this chapter. In veterinary medicine, the patient is the animal, whether it is a reptile, bird, amphibian, fish, or mammal. The client is the owner of the animal, typically a farmer, agribusiness owner, or laboratory manager.

The job tasks of veterinarians are highly variable, as summarized in Table 21.1. They are involved in the clinical diagnosis and treatment of animal diseases, sometimes requiring subspecialization. Veterinarians are also engaged in teaching and research, regulatory medicine including food safety and inspection, public health, the military, and private industry (1).

Veterinarians may work in an office, or in farms, ranches, paddocks, and laboratories. They face many hazards, and the number of occupational illnesses and injuries they suffer is also high. Table 21.2 summarizes the hazards, injuries, and illnesses experienced by veterinarians (2).

A descriptive study conducted from 1967 to 1969 of the basic health characteristics of 1100 veterinarians in Illinois documented that 87% had consulted a physician concerning their health within the previous 30 months. Within the previous 18 months, 47% had been vaccinated against tetanus. Over one third of the veterinarians had received their last tetanus inoculation because of an injury. Thirty-one percent had been tested serologically for zoonotic infections other than at a meeting of the state veterinary association, and 12% were allergic to an antimicrobial (3).

TABLE 21.1. Veterinary job tasks.

Clinical diagnosis and treatment of animals (may be limited to a specific family, genus, or species)
Internal medicine
Surgery
Toxicology
Laboratory animal medicine
Poultry production health
Theriogenology (study of blood lines and reproduction)
Anesthesiology
Behavioral psychology
Clinical pharmacology
Dermatology
Emergency and critical care
Microbiology
Nutrition
Ophthalmology
Pathology
Radiology
Dentistry
Zoological medicine
Teaching and research
Classroom teaching and research
Field and laboratory work
Regulatory medicine
Animal quarantine and inspection, development and testing of new animal vaccines, implementation and enforcement of humane laws
Public health
Epidemiology, environmental health, food and medicine safety, supervision of laboratory animals
Military
Research, clinical work, epidemiology, food inspection
Private industry
Development of new production methods, drugs, chemicals, and biological products

Source: Data from Hoblet et al. (1) and Jeyaretnam et al. (2).

Trauma

Veterinarians are in close contact with animals of different families, genera, and species. Many of these animals are large, unwieldy, and uncooperative during examination or treatment. It is quite common for veterinarians to receive bites, scratches, crush injuries, and low-back injuries from these animals. In Australia, 71% of veterinarians surveyed reported a lost time injury within the last 10 years from handling animals. In a survey of zoo veterinarians in the United States, 61.5% of respondents reported major animal-related injury and 55% reported low-back injury. Full-time zoo veterinarians were more likely to report back injury and inadequate knowledge of occupational hazards (2,4).

TABLE 21.2. Veterinary hazards, illnesses and injuries.

Hazard	Injury	Illness
Trauma	Bites, scratches	Infections
	Crushing	Tetanus
	Lifting	Rabies
	Repetitive motion	Tenosynovitis
	Motor vehicles accidents	
	Assault	
	Scalpel cuts	
Zoonotic diseases		Infectious diseases
Dermatoses		Allergic contact
		Infectious
Allergies		Dermatitis
Animal hair		Asthma
Airborne dust		Bronchospasm
Equipment		Sinusitis
Medications		
Environment		
Toxic exposures	Chemical burns	Hepatorenal disease
Medications		
Anesthetics		Myelodysplastic disease
Pesticides		
Chemicals		
Emotional problems		Suicide
		Anxiety
Radiation	Radiation burns	Myelodysplastic diseases
Ionizing	Actinic skin lesions	Basal cell carcinoma
Nonionizing		
Drug abuse		Drug addiction and associated diseases
Medications		
Alcoholism		
Cancer risk		
Radiation		
Chemicals		
Pregnancy risk		Abortion
Chemicals		Preterm births
Radiation		
Needle sticks	Puncture trauma	Tetanus
		Rabies
		Infections
		Injection injury

Source: Data from Jeyaretnam et al. (2).

A survey of veterinarians in Minnesota and Wisconsin revealed that 64.6% of respondents had sustained a major animal-related injury in their careers. Seventeen percent were hospitalized within the last year, 25.3% requiring a surgical procedure. Hand injuries were most common in a veterinarian's career (52.6%), followed by trauma to the arms (27.6%) and the head (20.8%). The thorax (8.3%), genitalia (3.9%), and intraabdominal viscera (2.8%) were injured less often. Operative procedures were frequently required

to treat veterinarian injury from animal patients. Thirty-five percent of veterinarians required treatment for suture of lacerations, 10% for reduction of fracture/dislocation, and 5% for dental work during their career. One craniotomy and one carotid artery repair were necessary. Mechanisms of injury were animal kick (35.5%), bite (34%), crush (11.7%), scratch (3.8%), and miscellaneous causes (14.9%), including the patient pushing, goring, head butting, running over, and falling on the veterinarian. Additional work-related hazards included zoonotic disease, autoinoculation of live brucella vaccine, and self-inflicted scalpel injuries from sudden patient movement. The most common animals involved were bovine (46.5%), canine (24.2%), and equine (15.2%). Lost days from work secondary to animal injury averaged 1.3 days in 1986 and 8.5 days during the veterinarian's career. Job-related automobile accidents also occurred. Veterinarians averaged more than 300 miles driven per week, and only 56% reported following the speed limit. Fifteen percent did not wear seat belts. Self-treatment of injuries was common (5).

Even though animal bites are common and a real risk for rabies exists, surveys have demonstrated a relatively low rate of rabies immunization in veterinarians and veterinary workers. The cost of preexposure rabies vaccine was found to be a major barrier, especially in young, part-time workers (6).

In a survey of all 1970 to 1980 female graduates of all United States veterinary colleges, 64.0% of all respondents reported one or more needle sticks after graduation. Substances most often injected include vaccines, antibiotics, anesthetics, and animal blood. The estimated overall needle stick injury rate was 9.3 sticks per 100 person-years of practice, comparable to reported rates among health care workers such as nurses, laboratory technicians, and hospital housekeeping staff. All-small-animal and mixed-practice veterinarians demonstrated the highest rates, with all-large-animal practitioners demonstrating a rate lower by 40% (7).

Infectious Diseases

Most zoonotic diseases in veterinarians are self-diagnosed and treated. See Chapters 27 and 29 for a more extensive discussion of the diagnosis and treatment of these diseases. Nonzoonotic diseases in veterinarians include coccidioidomycosis, histoplasmosis, malaria, and other diseases common to areas where they work (see Chapter 28). In addition, veterinarians are at risk for infections from mishandled biological material in laboratories.

A survey of 88 veterinarians employed at a faculty of veterinary science found that 63.6% of veterinarians interviewed had suffered from a zoonotic disease. Veterinarians predominantly involved in farm animal practice were three times more likely to have contracted a zoonotic disease than those working in other veterinary fields. Fifty-six percent of disease incidents were initially diagnosed by the veterinarians themselves. Fifty-three percent of

incidents required treatment by a medical practitioner, but the majority (61%) of incidents did not require absence from work. The incidence density rate for contracting a zoonotic disease was 0.06 per person year of exposure. Kaplan-Meier survival analysis estimated that the probability of having contracted a zoonotic disease was 50% after 11 years in practice. The risk of contracting a zoonotic disease appeared to be higher early in practice, and the most common mode of transmission was by direct contact (8).

Another risk to agriculture and the veterinary profession is the possibility of veterinarians acting as carriers of zoonotic illness and infecting herds that they may be examining or treating. Although the spread of zoonotic infections from humans to animals is rare, it does occur; rapid treatment and monitoring of veterinarians for infection may be necessary to protect herds (9).

Dermatoses

Researchers studying California veterinarians found a reported history of skin atopy in 11% and respiratory atopy in 63% of respondents. Dermatoses during their career were reported by 46% of respondents, and hand and/or forearm dermatitis was reported more than once during the past year by 22% of women and 10% of men. Dermatitis with work-related exacerbating factors was reported by 28%. Almost one in five veterinarians reported animal-related skin symptoms. Other aggravators were medications (2%), gloves (4%), and other chemicals (7%). Of those with animal-related dermatitis, 65% reported only one animal (dog, 66%; cat, 29%; horse, 9%; and cattle, 8%), and 66% reported the symptoms appeared in minutes after the contact. The risk factors for the appearance of hand/forearm dermatitis during the past 12 months and more than once during their career were history of skin atopy, childhood hand dermatitis, history of respiratory atopy, and female gender (10).

In a study of the Kansas Veterinary Medical Association, 24% of respondents reported noninfectious, recurrent/persistent hand or forearm dermatoses, of which 66% were work related. Large-animal veterinarians and persons with a history of atopy were more likely than their counterparts to attribute their dermatoses to work-related factors. Thirty-eight percent of respondents had contracted at least one infectious skin disease from an animal. Veterinarians who never or rarely use gloves during obstetric procedures were more likely to report work-related dermatoses than those who use gloves (11).

The use of latex gloves in veterinary practice is common, and latex allergies are a routine finding in veterinarians as well as in other health care fields (see Chapter 18).

In Poland, bull terrier seminal fluid was found as a source of contact urticaria and rhinoconjunctivitis. In Belgium, contact sensitivity was documented in health care workers, including veterinarians, to penicillins,

cephalosporins, and aminoglycosides. In Germany, itching, swelling, and urticaria on the hands on arms of veterinarians were found after contact with amniotic fluid of cows and pigs. Immunoglobulin G (IgG) levels were elevated, radioallergosorbent test (RAST) investigations were positive to amniotic fluid, and skin tests were also positive to amniotic fluid. In all these cases, the use of gloves, either latex or a substitute, was recommended (12–14).

Researchers in the Netherlands assessed the incidence of pustular dermatitis after deliveries in cattle and sheep. One or more episodes of pustular dermatitis on an arm after a delivery in cattle or sheep was noticed by 81.5% of the respondents. Sometimes it was associated with secondary symptoms such as headache, fever, and lymphadenitis. *Listeria monocytogenes* and *Salmonella dublin* were the agents cultured most often (15).

Allergic Exposures

Allergic exposures not affecting the skin impact primarily on the respiratory system, including the nasal passages, bronchial tubes, and lungs. Allergens may include organic dusts in the air; dust, hair, and dander from animals; veterinary pharmaceuticals; and farm chemicals. Allergic respiratory disease is discussed in Chapter 19 and allergic skin disease in Chapter 18.

Radiographers process x-ray films using developer and fixer solutions that contain chemicals known to cause or exacerbate asthma. In a Canadian study, radiographers' personal exposures to glutaraldehyde (a constituent of the developer chemistry), acetic acid (a constituent of the fixer chemistry), and sulfur dioxide (a by-product of sulfites, present in both developer and fixer solutions) were measured. Average full-shift exposures to glutaraldehyde, acetic acid, and sulfur dioxide were 0.0009 mg/m^3, 0.09 mg/m^3, and 0.08 mg/m^3, respectively, all more than one order of magnitude lower than current occupational exposure limits. Local exhaust ventilation of the processing machines and use of silver recovery units lowered exposures, whereas the number of films processed per machine and the time spent near the machines increased exposures. Developments in digital imaging technology provide options that do not involve wet-processing of photographic film and therefore could eliminate the use of developer and fixer chemicals altogether (16).

Hazardous Chemical Exposures

Veterinarians and their assistants may be exposed to anesthetic gases, pharmaceuticals (including antineoplastic agents), disinfectants such as phenol and formaldehyde, and sterilants such as ethylene oxide. Typical chemicals that veterinarians may come in contact with include dark room chemicals, formaldehyde, glutaraldehyde, halothane, iodine, methylated spirits, and pentobarbital (2,17).

Anesthetic Gases

Anesthetic gases have been associated with toxic and chromosomal effects on the users. Investigations have shown that many of the anesthesia machines used in veterinary medicine have leaks that contribute to operating room contamination. Many others do not have appropriate scavenging attachments to remove escaping gases. Personnel have been frequently observed carelessly using equipment or handling anesthetic agents in a manner contributing to excessive exposure. Proper maintenance of equipment and careful use of gaseous anesthetic agents can significantly reduce waste gas levels and exposure of personnel (18).

In Austria, operating room personnel exposed to an 8-hour time-weighted average of 12.8 ppm nitrous oxide and 5.3 ppm isoflurane had a mean frequency of sister chromatid exchanges significantly higher than controls (19).

In Colorado, a survey of veterinarians in an 11-county region indicated that inhalation anesthetics were used in 80.8% of the 210 practices. Exposures to waste anesthetics in veterinary practices were far less than reported in human hospitals. Waste anesthetic concentrations were affected by size of the patient, type of breathing system, and use of scavenging systems. Dilution ventilation had no effect on breathing zone concentrations. The endotracheal tube and occasionally the anesthetic machine were the major sources of leakage of anesthetic gases (20).

In Canada, concerns were raised by several workers from veterinary clinics in Manitoba regarding potential exposure to isoflurane and halothane during anesthetic administration. No guideline have been established for isoflurane by the American Conference of Governmental Industrial Hygienist (ACGIH) or a permissible exposure limit by the Occupational Safety and Health Administration (OSHA) or a recommended exposure limit (REL) by the National Institute for Occupational Safety and Health (NIOSH). The ACGIH threshold limit value (TLV) time-weighted average (TWA) for halothane is 50 ppm and NIOSH has established 2 ppm as a recommended level based on a 1-hour sampling; OSHA has established no guideline for halothane. All veterinary clinics inspected had installed the passive waste gas scavenging system. Veterinarians' personal exposures for isoflurane ranged from 1.3 to 13 ppm, and for their assistants, personal exposures ranged from 1.2 to 9 ppm. Veterinarians' personal exposures for halothane ranged from 0.7 to 12 ppm; for their assistants, personal exposures ranged from 0.4 to 3.2 ppm. One clinic had significant leaks in the anesthetic gas delivery lines. Personal halothane exposure for the veterinarian at this clinic was 7.2 to 65 ppm. Peak exposures were recorded when the cuffed endotracheal tube was removed from the animal. Equipment leaks were minimal when the system was maintained at its optimum operating condition (21).

Veterinary Pharmaceuticals

Many veterinarians compound and apply their own pharmaceuticals to their patients. Safety guidelines in both the manufacture and use of these

medications are less stringent than in humans, although the risk of injury to the people who come in contact with them is just as great. Substances in this group include antibiotics, immunizations, hormones, anesthetics, steroids, disinfectants, sterilants, prostaglandins, special feed formulas, and insecticides. A good example is the accidental injection of brucellosis vaccine into the hand of the veterinarian as he gives an injection to an animal. The veterinarian is faced with multiple exposures including infection, tetanus, toxic injection injury, and an immunological response. Aggressive treatment with antibiotics, steroids, and sometimes surgery is often delayed by the reluctance of veterinarians to admit their injuries and their tendency for self-treatment.

Pesticides

In a health and safety survey of all licensed pet groomers and pet-animal veterinarians in New Jersey, approximately 36% of the respondents indicated that during the 1994 flea season they had experienced at least one of the 17 symptoms associated with insecticide application. Central nervous system symptoms (headache, dizziness, or confusion) and skin symptoms (skin rash or numbness/tingling) were reported most frequently. Logistic regression results suggest that applications per season, years as an applicator, certain hygiene variables, certain classes of products, and status of applicator (lay person vs. veterinary) are potentially important risk factors (see Chapters 13 and 16) (22).

Emotional Problems

Stress in veterinarians is associated with the ordering of drugs, staff supervision, public relations, professional working hours, heavy responsibilities, and the fear of burglaries. While most veterinarians manage these stressors adequately, there is an ongoing problem of suicide, drug addiction, and "burnout" in the profession. Especially in small-animal veterinarians, the euthanasia of animals and the supervision of the slaughter of animals for public health reasons add further stress (see Chapter 22) (2).

In a study of 450 California veterinarians who died between January 1960 and December 1992, white male and female veterinarians had significantly elevated mortality from suicide. Significantly elevated rates were noted for suicide in veterinarians in the profession for less than 30 years (23).

Radiological Exposures

In the early years of veterinary and medical radiology, many severe radiation injuries occurred in radiologists. Unfortunately, there are still cases of skin lesions of the hands affecting veterinarians, mainly caused by careless handling during the imaging. Safety advice includes staying out of the primary

beam and being aware that lead gloves are no protection against primary rays. In contrast, the risk of placing the feet in the primary beam is relatively low. Monitoring of radiation shows that if veterinarians take appropriate precautions, there is no danger of radiation damage (24).

Drug Abuse

Especially in small practices, there is access to opiate analgesics, anesthetics (especially nitrous oxide, which is inhaled to produced a heightened sexual experience), and steroids that can be diverted for personal use by veterinarians or their staff. As with other agricultural occupations, veterinarians are susceptible to a number of agents in addition to those used in their offices, including amphetamines, barbiturates, hallucinogens, and alcohol (see Chapter 10) (2).

Cancer Risks

The incidence of cancer in veterinarians is generally low, in part due to the low prevalence of cigarette smoking in this group. However, they come into contact with several potentially carcinogenic exposures including radiation, anesthetic gases, pesticides, and zoonotic agents. Other sources of carcinogenic exposure are solar radiation, veterinary pharmaceuticals, and office and laboratory chemicals (25).

Veterinarians have elevated risks for several specific cancer types including leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, and cancers of the lip, stomach, prostate, brain, and connective tissue. Two major groups of risk factors have been proposed as causes of hematological malignancies in agricultural workers. The first group includes various agricultural chemicals. In particular, several studies have found increased risks of malignant lymphoma and soft tissue sarcoma in persons exposed to phenoxy herbicides. However, the evidence is inconsistent, and there is a wide variation in relative risk estimates. The second group of risk factors includes various animal viruses. There is currently little evidence concerning the zoonotic nature or human carcinogenicity of these viruses. However, an association has been suggested by recent evidence of increased risks of hematologic malignancies in abattoir workers, veterinarians, and meat inspectors. A third hypothesis, for which little evidence is currently available, is that agricultural work may involve prolonged antigenic stimulus leading to lymphoproliferation. The factors responsible for the increased risks for cancers other than hematologic malignancies are not well understood but may also involve exposure to chemicals or viruses (26).

Using the Swedish Cancer Environment Registry, researchers compared the incidence of cancer among male veterinarians with that in the rest of the population. Veterinarians experienced increased risk of esophageal, colon,

pancreatic, and brain cancers, and melanoma of the skin. The increased risks did not seem to be explained by the high socioeconomic status of this occupational group, and it was postulated that some of these results reflected the carcinogenicity of occupational exposures, including animal viruses, solar or ionizing radiations, and anesthetics (27).

A study of 450 California veterinarians who died between January 1960 and December 1992 demonstrated that in comparison to the California general population statistics, white male veterinarians had significantly elevated mortality from malignant melanoma of the skin, cancer of the large intestine, and rheumatic heart disease. Significantly elevated ratios were noted for deaths due to malignant melanoma of the skin and rheumatic heart disease in veterinarians in the profession 20 years or more; and cancer of the large intestine in veterinarians in the profession 30 years or more (23).

In the United States a cancer surveillance investigation using death certificates from 24 states for the period 1984 to 1989 was used to identify multiple myeloma and occupation associations. Women demonstrated significant excess risk among managers and administrators, post–secondary school teachers, elementary school teachers, social workers, other sales workers, waitresses, and hospital maids. Men showed significant risks among computer system scientists, veterinarians, elementary teachers, authors, engineering technicians, general office supervisors, insurance adjusters, barbers, electronic repairers, supervisors of extracting industries, production supervisors, photoengravers, and grader/dozer operators (28).

Studies of the Danish Cancer Registry on the possible association between exposures of parents at the time of conception and cancer in their offspring have provided no clear answer. Significantly increased risks for renal cancer (mainly Wilms' tumor) and for osteogenic and soft tissue sarcomas were observed in children in association with mothers' employment in medical and dental care. The risk for cancers at all sites was significantly elevated in children of female nurses and of male and female physicians, dentists, dental assistants, veterinarians, and pharmacists combined. Handling of drugs and exposure to anesthetics and infections during pregnancy are suggested to be potential risk factors. The suggestion in earlier studies that exposures to hydrocarbons and lead are risk factors for childhood cancer could not be supported by the analysis (29).

Causes of death among 5,016 white male veterinarians were compared to a distribution based on the general U.S. population. Proportions of deaths were significantly elevated for cancers of the lymphatic and hematopoietic system, colon, brain, and skin. Fewer deaths were observed than expected for cancers of the stomach and lung. Although socioeconomic and methodological factors may be involved, the patterns suggest that sunlight exposure is responsible for the excess of skin cancer among veterinarians whose practices are not exclusively limited to small animals, and ionizing radiation exposure contributes to the excess of leukemia among veterinarians practicing during years when diagnostic radiology was widely used (30).

Risks to Pregnancy

In a major needle-stick study, one accidental self-injection of a prostaglandin compound resulted in a spontaneous abortion, heightening awareness that occupational needle sticks may also represent a serious human reproductive health hazard (7).

In a survey of 2,997 female graduates from United States veterinary colleges between 1970 and 1980, absolute and relative risks of preterm delivery (PTD) were highest for veterinarians employed in exclusively equine clinical practice. Occupational involvement with solvents among exclusively small animal practitioners was associated with the highest relative risk of PTD. Overall absolute risks of PTD and small for gestational age births among cohort members were much lower in comparison with the general female population (31).

Another study of female pregnancies concluded that veterinarians employed in all-equine practices were at highest relative risk of spontaneous abortion when compared with pregnancies reported by unemployed veterinarians. Agent-specific relative risk estimates ranged from 0.7 to 1.1, suggesting little or no excess risk. When analyses were restricted to small-animal practitioners, there was a weak association between miscarriage risk and job-related exposure to ionizing radiation (32).

Antineoplastic Medications

Antineoplastic medications such as mitotane (Lysodren), chlorambucil (Leukeran), and azathioprine (Imuran) are usually teratogenic but can also be mutagenic, carcinogenic, and abortigenic. The principle governing working with cytotoxics is to keep exposure as low as possible. This may necessitate premix syringes and bottles prepared at a pharmacy under special mixing hoods, personal protective equipment, and isolation procedures. The clients and other people close to the patient are also potentially at risk and should be told of this and informed about drug administration and the disposal of feces, vomit, urine, saliva, and blood that may contain the active pharmaceutical. The prescription and/or administration of cytotoxic drugs, including those that are used as immunosuppressive agents in veterinary medicine, should be restricted to specialist veterinarians who have adequate knowledge and appropriate facilities to work with these agents (33,34).

AIDS-Infected Persons in the Veterinary Workplace

The American Veterinary Association had reminded veterinarians that acquired immune deficiency syndrome (AIDS) is a human disease and that human immunodeficiency virus (HIV) does not infect animals other than nonhuman primates. Veterinarians and their employees are no more at risk by reason of their employment than are workers in offices. Cautions for

health care workers do not generally apply to animal health care workers, but they are good rules to follow if it is necessary to render first aid for human injuries in the workplace (35).

Persons infected with the AIDS virus may be more susceptible to zoonotic transmission due to their immunocompromised status. Animal-associated pathogens of concern to immunocompromised persons include *Toxoplasma gondii*, *Cryptosporidium* spp., Salmonella spp., Campylobacter spp., *Giardia lamblia*, *Rhodococcus equi*, *Bartonella* spp., *Mycobacterium marinum*, *Bordetella bronchiseptica, Chlamydia psittaci,* and zoophilic dermatophytes. However, with the exception of *Bartonella henselae* and zoophilic dermatophytes, infections in humans are more commonly acquired from sources other than pets, and the infectious disease risk from owning pets is considered low. Nonetheless, HIV-infected persons may still be advised not to own pets because of their compromised immune status and the possibility of contracting a zoonotic disease (36).

References

1. Hoblet KN, Maccabe AT, Heider LE. Veterinarians in population health and public practice: meeting critical national needs. J Vet Med Educ 2003;30(3):287–94.
2. Jeyaretnam J, Jones H, Phillips M. Disease and injury among veterinarians. Aust Vet J 2000;78(9):625–9.
3. Martin RJ, Habtemariam T, Schnurrenberger PR. The health characteristics of veterinarians in Illinois. Int J Zoonoses 1981;8(1):63–71.
4. Hill DJ, Langley RL, Morrow WM. Occupational injuries and illnesses reported by zoo veterinarians in the United States. J Zoo Wildl Med 1998;29(4)371–85.
5. Landercasper J, Cogbill TH, Strutt PJ, Landercasper BO. Trauma and the veterinarian. J Trauma 1988;28(8):1255–9.
6. Trevejo Rt. Rabies pre-exposure vaccination among veterinarians and at-risk staff. J Am Vet Med Assoc 2000;217(11):1647–50.
7. Wilkins JR 3rd, Bowman ME. Needlestick injuries among female veterinarians: frequency, syringe contents and side-effects. Occup Med (Lond) 1997;47(8):451–7.
8. Gummow B. A survey of zoonotic diseases contracted by South African veterinarians. S Afr Vet Assoc 2003;74(3):72–6.
9. Deutz A, Kofer J. Swine and wild pigs as carriers of zoonoses. Berl Munch Tierarztl Wochenschr 1999;112(8):305–10.
10. Susitaival P, Kirk J, Schenker MB. Self-reported hand dermatitis in California veterinarians. Am J Contact Dermatol 2001;12(2):103–8.
11. Tauscher AE, Belsito DV. Frequency and etiology of hand and forearm dermatoses among veterinarians. Am J Contact Dermat 2002;13(3):116–24.
12. Krakowiak A, Kowalczyk M, Palczynski C. Occupational contact urticaria and rhinoconjunctivitis in a veterinarian from bull terrier's seminal fluid. Contact Dermatitis 2004;50(6):385.
13. Gielen K, Goossens A. Occupational allergic contact dermatitis from drugs in healthcare workers. Contact Dermatitis 2001;45(5):273–9.
14. Kalveram KJ, Kastner H, Forck G. Detection of specific IgE antibodies in veterinarians with contact urticaria. Z Hautkr 1986;61(1–2):75–8,81.
15. Visser IJ. Pustular dermatitis in veterinarians following delivery in domestic animals: an occupational disease. Ned Tijdschr Geneeskd 1996;140(22):1186–90.

16. Teschke K, Chow Y, Brauer M, et al. Exposures and their determinants in radiographic film processing. AIHA J (Fairfax, Va) 2002;63(1):11–21.
17. Meggs WJ. Chemical hazards faced by animal handlers. Occup Med 1999; 14(2):213–24.
18. Short CE, Harvey RC. Anesthetic waste gases in veterinary medicine: analysis of the problem and suggested guidelines for reducing personnel exposures. Cornell Vet 1983;73(4):363–74.
19. Hoerauf K, Lierz M, Wiesner G, et al. Genetic damage in operating room personnel exposed to isoflurane and nitrous oxide. Occup Environ Med 1999;56(7):433–7.
20. Wingfield WE, Ruby DL, Buchan RM, Gunther BJ. Waste anesthetic gas exposures to veterinarians and animal technicians. J Am Vet Med Assoc 1981;178(4):399–402.
21. Korczynski RE. Anesthetic gas exposure in veterinary clinics. Appl Occup Environ Hyg 1999;14(6):384–90.
22. Bukowski J, Brown C, Korn LR, Meyer LW. Prevalence of and potential risk factors for symptoms associated with insecticide use among animal groomers. J Occup Environ Med 1996;38(5):528–34.
23. Miller JM, Beaumont JJ. Suicide, cancer, and other causes of death among California veterinarians, 1960–1992. Am J Ind Med 1995;27(1):37–49.
24. Hartung K. Radiation exposure of the hands and feet during x-ray studies in small animals. Tierarztl Prax 1992;20(2):187–93.
25. Fritschi L. Cancer in veterinarians. Occup Environ Med 2000;57(5):289–97.
26. Pearce N, Reif JS. Epidemiologic studies of cancer in agricultural workers. Am J Ind Med 1990;18(2):133–48.
27. Travier N, Gridley G, Blair A, Dosemeci M, Boffetta P. Cancer incidence among male Swedish veterinarians and other workers of the veterinary industry: a record-linkage study. Cancer Causes Control. 2003;14(6):587–93.
28. Figgs LW, Dosemeci M, Blair A. Risk of multiple myeloma by occupation and industry among men and women: a 24–state death certificate study. J Occup Med 1994;36(11):1210–21.
29. Olsen JH, de Nully Brown P, Schulgen G, Jensen OM. Parental employment at time of conception and risk of cancer in offspring. Eur J Cancer 1991;27(8):958–65.
30. Blair A, Hayes HM Jr. Mortality patterns among US veterinarians, 1947–1977: an expanded study. Int J Epidemiol 1982;11(4):391–7.
31. Wilkins JR 3rd, Steele LL. Occupational factors and reproductive outcomes among a cohort of female veterinarians. Am Vet Med Assoc 1998;213(1):61–7.
32. Steele LL, Wilkins JR 3rd. Occupational exposures and risks of spontaneous abortion among female veterinarians. Int J Occup Environ Health 1996;2(1):26– 36.
33. Pellicaan CH, Teske E. Risks of using cytostatic drugs in veterinary medical practice. Tijdschr Diergeneeskd 1999;124(7):210–5.
34. Valanis B, Vollmer WM, Steele P. Occupational exposure to antineoplastic agents: self-reported miscarriages and stillbirths among nurses and pharmacists. J Occup Environ Med 1999;41(8):632–8.
35. Tennyson AV. AVMA guidelines for dealing with AIDS-infected persons in the veterinary workplace. J Am Vet Med Assoc 1989;195(2):190–3.
36. Grant S, Olsen CW. Preventing zoonotic diseases in immunocompromised persons: The role of physicians and veterinarians. Emerg Infect Dis 1999;5(1):159–63.

22

The Mental Health of Agricultural Workers

Joseph D. Hovey and Laura D. Seligman

Key words: stress, anxiety, depression, suicide, coping

Because of the difficulties intrinsic to agricultural work, it might be conjectured that agricultural workers are at risk for mental health problems. Relatively little research has examined the mental health of agricultural workers, however, and much of the research that has been conducted on the topic is dated. Despite the scattered nature of this research, the image that has emerged reveals a population at risk for the development of mental health difficulties.

This chapter reviews the literature on stress and mental health of farm owners, farm operators, and farm workers; highlights a model of stress and coping; and gives recommendations for future research.

Model of Stress and Coping

Individuals experience stress when faced with demands that require them to change in some manner. The state of stress has two components: the stressor and the stress response. A stressor is the source of the demand. It is the external or internal event that creates the demand. The stress response is composed of cognitive, affective, and physiological elements. For example, the stress response may involve levels of worry that may compromise an individual's ability to concentrate; feelings of apprehension, tension, and panic; and physiological reactions such as an accelerated heart rate, perspiration, tense muscles, and shallow breathing (1).

The severity of the stress that is experienced by individuals is influenced by the manner in which individuals cognitively appraise both the stressors and their capacity to effectively react to the stressors. Those individuals who appraise a stressor as more threatening are more likely to experience a greater stress response than individuals who sense that they have the capacity to respond constructively to the stressor. Thus, two individuals may experience the same stressor but experience different levels of stress.

Coping refers to individual's efforts to manage the stressors and/or stress. Two commonly mentioned categories of coping strategies are problem-focused coping and emotion-focused coping. Problem-focused coping occurs when individuals change the relationship between them and the environment. For example, individuals who experience stress stemming from their job may choose to change jobs.

Emotion-focused coping, on the other hand, refers to a change in the meaning of the relationship between the individual and the environment. In reaction to stressors that cannot be physically eliminated, such as the death of a loved one or the experience of chronic physical pain, an individual may rely on the emotional support of others, cognitively reframe his or her reaction to the situation, develop a healthy sense of humor, or develop more effective relaxation techniques. All of these would be considered forms of emotion-focused coping.

Figure 22.1 depicts this model of stress and coping. People first appraise the stressor event in light of their past experiences. For example, their inability to effectively cope with a stressor may negatively influence their appraisal when they encounter a similar stressor in the future. If they appraise the situation as threatening, then a stress reaction occurs, quickly followed by coping. After the coping responses are activated, there may be either a reduction in the level of stress or, in the case of severe or unrelenting stress, a reduction in the effectiveness of these particular coping strategies (a breaking-down in coping) and thus a further increase in stress. As will be discussed later, severe or unrelenting stress may have major mental health implications for some individuals. The model implies that people actively interact with their environments. The broken arrow in Figure 22.1 represents the notion that coping has an ongoing influence on an individual's experience of stress and vice versa.

Mental Health of Farmers

This section discusses the mental health of agricultural workers who own or operate their own farms. These individuals, in comparison to hired

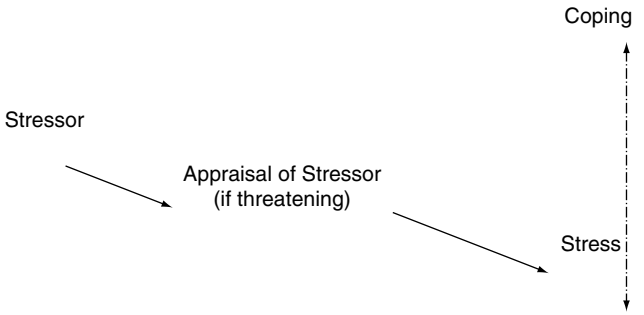


FIGURE 22.1. Model of stress and coping.

agricultural workers, play a major decision-making role in the operation of their farms. For the purposes of this chapter, when discussing individuals in this role, we will use the term *farmers*.

External Stressors

Demands stemming from outside the individual have a potential impact on an individual's internal state. Financial and economic difficulties are perhaps the most common type of external stressors experienced by farmers. In a study of farmer couples in Minnesota, Rosenblatt and Keller (2) found that greater economic loss, greater economic vulnerability as measured by economic indices, and patterns of blaming one's spouse for economic difficulties were related to increased stress. The farmers' perception of loss may be more significant than the actual amount of loss. For example, a farmer who loses 30 acres of a farm of 120 acres because of drought may experience more stress than a farmer who loses 250 of 1000 acres. Blaming a spouse for economic difficulties may occur as part of a farmer's attempt to cope. In trying to answer the question of why, a common attribution is that someone else (in this situation, the spouse) is responsible for the difficulties. This type of cognition may result in temporary relief, but it may eventually create tension within the marriage and create more stress in the long run.

In a sample from Iowa, Swisher et al. (3) found that, in comparison to men who did not farm, farm men reported significantly higher rates of financial losses, cuts in wages or salary, increases in debt loads, and limitations by banks on the sizes of loans. This study is one of the few studies that has directly explored the role of coping in farmers. In addition to the use of family support, the authors found that male farmers tended to utilize downward social comparisons (i.e., comparing themselves to others who were worse off) to cope with distress associated with financial and job-related stressors. The authors conjectured that the strategy of downward comparisons can enhance a farmer's sense of self. These comparisons remind farmers that things can be worse and that others have faced similar difficulties and have survived them. They also serve to reduce the stigma that is often experienced with economic difficulties, and they promote external attributions that are less threatening to self-efficacy.

Other studies have yielded purely descriptive findings. The purpose of these studies was to identify stressors that were commonly experienced by farmers. Murray (4), for example, explored the occurrence of stressors in a sample of dairy farmers in Pennsylvania. Over 90% of the farmers reported experiencing stressors in the following categories: financial management, business management, awareness of new technology, knowledge of law concerning agriculture, infrequent days off, and physical injuries/accidents. Weigel (5) found that Iowa farmers identified machinery breakdown, disease outbreak, accidents, and government regulations as stressors.

Rosenblatt and Anderson (6) reviewed factors related to tension and stress in farm families. In addition to the stressors already mentioned, they cited difficulties related to unpredictable weather, geographical isolation, high accident rates, invariant work demands, and seasonal variations in work demands and income. Invariant work demands represent heavy periods of work that are rarely interrupted by nonwork activities. This lack of flexibility often leads to stress and fatigue. Seasonal variations in work requirements represent the pattern of work in which farmers move back and forth between invariant work demands to periods in which the farmers have no pressing work demands. Such variations can result in stress emanating from, for example, a lack of togetherness time for farm families during heavy work periods and stress due to spending too much time with family members during the off-seasons.

Several researchers have documented a relationship between pesticide exposure and the experiences of stress and depression (7–11). This relationship is important to note because researchers have found an extremely high incidence of pesticide exposure in farmers. For example, Calvert et al. (9) found that agricultural workers were 35 times more likely to become exposed to pesticides in comparison to nonagricultural workers.

A common way to cope with external stressors is through the use of problem-focused coping strategies. The effectiveness of such coping methods may be limited for some farmers, however. In their discussion of rural psychology, Lefcourt and Martin (12) concluded that although farmers often experience a sense of competence and control in the daily actions of farming, they are likely to feel powerless in response to forces outside of the farming world such as the government and the economy. This is a form of learned helplessness, which has been shown to increase the risk for anxiety and depression (13).

Table 22.1 lists the stressors that are commonly experienced by farmers. Research exploring the full continuum of stress and coping is lacking. For example, few or no studies have assessed interactions between stress and coping in farmers, the direct impact of external stressors on stress and coping, or the influence of different types of coping on distress. Many of the studies reviewed thus far were conducted during the farming crisis in the 1980s. There is some question, therefore, about how exactly these findings generalize to today's farming environment.

Internal Stressors

Interpersonal conflict, along with role-related stressors, are the most commonly cited internal sources of stress for farmers. For example, Murray (4) examined the experience of stressors in Pennsylvania dairy farmers and found that most farmers stated that family conflict and problems with neighbors and other farmers were stressors. There appeared to be a link between these interpersonal stressors and economic concerns, depression,

TABLE 22.1. Stressors experienced by farmers.

External stressors
Economic factors (low income or poor cash flow, seasonal variations in income, increases in debt loads and limitations by banks on loan sizes, high interest rates on loans, conditions of market prices, potential or actual loss of the farm)
Structure of farming (long work hours, infrequent days off, high work load, seasonal variations in work demands, farming over long period of years, multitask nature of farming)
Physical hazards associated with farming (pesticide exposure, fertilizers, equipment, animals)
Health status (e.g., acute injuries, chronic health problems)
Lack of medical care and health insurance
Unpredictability of weather
Physical environment (terrain, size of farm, types of crops harvested)
Resource supplies (e.g., malfunctioning equipment, lack of labor equipment parts and animal chutes)
Geographical isolation
Internal stressors
Interpersonal stressors (e.g., interpersonal conflict with family, friends, and neighbors; divorce; social isolation)
Role strains (due to role incongruence, intergenerational transfer of farms, lack of equality and influence in farm activities)
Obligation to past, present, and future generations
Consideration of possible career change

and substance abuse. For some farmers, substance abuse may represent an unhealthy form of emotion-focused coping (see Chapter 10).

Berkowitz and Perkins (14,15) found that marital dissatisfaction and lack of their husband's support were related to increased psychosomatic stress symptoms in married dairy farmer women in New York State. Their findings suggest that effective marital support plays a primary role in reducing stress and promoting health in farmers. Similarly, Weigel and Weigel (16) found that greater perceptions of family satisfaction were related to decreased stress in Iowa farmers.

Weigel and Weigel (17) used factor analyses to identify stressors and coping strategies in two-generation farm families in Iowa. Their first analysis identified the stressor factors of lack of equality (not having an important role in the operation of the farm); lack of teamwork (difficulties family members had in communicating and working together); value differences (between generationals in the family); and competition (the stressors related to combining work and family roles on the farm). Their second analysis identified the coping factors of faith, fun and physical activities, talking with others, and avoidance of problem. Faith represented strategies that were used to cognitively reframe the stressors. Each of these four coping factors represents a form of emotion-focused coping in that they were utilized in the effort to better emotionally and cognitively deal with stressors, rather than to change potentially stressful situations.

As noted by Carruth and Logan (7), some farmer women assume increasing responsibilities both on and off the farm. This allows husbands or sons to hold more lucrative off-the-farm jobs, thus decreasing the economic vulnerability of the family. This type of role shift, however, may lead to greater fatigue for farmer women and increase their susceptibility to stress.

In an early study, Berkowitz and Hedlund (18) explored the influence of role incongruence on stress in 20 farm families in New York State. The authors defined role incongruence as the husband's and wife's incompatible expectations and perceptions of the wife's role. Interview data indicated that high stress levels were evident in 30% of the families. Role incongruence was present in 83% of the families that reported stress, and in 0% of the families without stress. According to the authors, many farmer wives perform major labor and management functions by acting as partners with their husbands in the operation of the farm. Thus, the ability to define mutually compatible roles for the wife as the family moves through its life cycle may be crucial for healthy family functioning.

Some researchers have examined role-related stress that is associated with the intergenerational transfer of farms. The transferring of farms may lead to stress because of a variety of reasons. Intergenerational transfers may involve issues of authority, control, and the dividing of tasks and income. Critical role transitions may include attempts within the family to accommodate the younger generation while phasing out the older generation. Moreover, while the younger generation may strive for self-respect, autonomy, and a fair share of responsibility, the older generation may strive to maintain decision-making responsibilities, emotional and physical territory, and the respect they believe is merited by greater experience. Elements of sibling rivalry and competition may also be evident (19,20).

Hedlund and Berkowitz (19) found that intergenerational transfers were disruptive in 30% of the families they interviewed. Russell et al. (20) examined coping strategies utilized in response to intergenerational transfer stress in farm families in Kansas. A factor analysis identified the coping strategies of individual coping (self-reliance, keeping problems to oneself), discussion, use of professionals/professional consultation, farm management strategies (including membership in farm organizations), and expression of anger. Family members, for example, reported that individual coping was most helpful in combating stress and that expressing anger was least helpful. Although, in comparison to their children, parents reported that the transfer decision was more difficult, they also reported higher psychological well-being than did their children. This suggests that the above coping strategies were relatively more effective for parents.

Heppner et al. (21) examined coping strategies in Missouri farmers who were considering making a change in their careers. Most of these farmers had lost or were in danger of losing their farms through bankruptcy. The authors found that, for both genders, those farmers who were stressed and depressed were more likely to use emotion-focused coping rather than

problem-focused coping in reaction to the stress linked to their possible career change.

Finally, Davis-Brown and Salamon (22) noted that the obligation to past, present, and future generations felt by some farmers compounds the stress engendered by other stressors.

Table 22.1 summarizes the internal stressors discussed in this subsection. It seems apparent that emotion-focused coping strategies may be more accessible, if not more effective, than problem-focused coping in dealing with farm-related distress.

Consequences of Stress

Many authors have pointed out the impact that severe stress and stressors have on the physical health of farmers. For example, in a sample of North Dakota farmers, Eberhardt and Pooyan (23) found that increased time pressures—the experience of having too much to do and too little time in which to do it—were significantly related to increased episodes of physical illness during the previous 2 years.

In regard to farm-related injuries and death, it has been estimated that 10% of agricultural workers experience a disabling injury every year and that nearly half of all survivors of farm trauma are permanently impaired. Moreover, according to the National Safety Council, agriculture has consistently ranked second to mining in the number of work-related fatalities in the United States over the past 20 years. For example, for the year 2003, the fatality rate for agriculture was 20.9 out of 100,000 workers. In comparison, the fatality rate for mining was 22.3 and the fatality rate for all work-related deaths was 1.5 (24,25).

The cognitive and physiological features of stress increase the risk for farm-related accidents. These include the diminished ability to concentrate on tasks, impaired decision making, carelessness, weakened immune system functioning, fatigue, direct physiological responses such as shakiness in the hands, and chronic strain and consequent physical effects such as back pain.

Several studies have found that stress is indeed associated with farm injuries. For example, Thu et al. (26) discovered that Iowa farmers who reported high stress levels were 3.5 times more likely to have experienced a disabling farm injury than were farmers without high stress levels. Reis and Elkind (27) found that farm families in eastern Washington State consistently reported stress as the fundamental cause of farm injury and that they readily perceived the potential harmfulness and daily risks of their occupation.

Stueland et al. (28) examined predictors of injuries in farmer women in central Wisconsin and discovered that the total number of hours worked significantly predicted the occurrence of injuries, with most injuries occurring in the barn. Many of these women had assumed increasing responsibilities in farm work as their husbands sought higher paying work off the farm, thus

increasing the women's chance for injuries. Changing role responsibilities thus appeared to have an indirect effect on farm injuries.

Swanson et al. (29) found that farm injuries in children, in combination with economic stressors, greatly increased the stress experienced by farm families. Similarly, Linn and Husaini (30) found that the number of chronic medical problems, in association with ineffective social support, significantly predicted depression in Tennessee farmers. Such findings point to a cycle of stress and injury that becomes circular. Stress itself may lead to illness and injury. However, once illness or injuries occur, these physical problems themselves become stressors, leading to more stress and an even higher risk for illness and injury. Acute or chronic physical problems can layer themselves on top of other stressors to exacerbate an already stressful picture. Interestingly, farmers often coped by passively waiting until their problems went away.

Carruth and Logan (7) examined predictors of depression in women farmers in southeast Louisiana. Odds ratios indicated that those women who experienced poor health were eight times more likely to experience depressive symptoms than were women with good health; those with long-term exposure to perceived hazards such as pesticides and tractor use were six times more likely to experience depression; those who had recently experienced farm-related injuries were 2.5 times more likely; those who had been engaged in farming for over 20 years were 1.5 times more likely; and those who were divorced were five times more likely. The authors concluded that farmer women are at particularly high risk for depression due to their juggling of a multitude of farm and family responsibilities. These responsibilities add to feelings of isolation and loneliness in creating a depressive outlook.

Although several of the above studies focused on depression, there is much evidence that depression and anxiety often coexist. Thus it can be argued that farmers who experience severe stress are also at risk for anxiety disorders (31).

For some farmers, severe stress and depression in farm workers may lead to an increased risk for suicide. Gunderson et al. (8) studied suicide rates for the period of 1980 to 1988 among farmers in Wisconsin, Minnesota, North Dakota, South Dakota, and Montana. The suicide rate for farmers was 48.1 per 100,000 individuals. This rate is more than twice as high as the overall suicide rate for adults in the United States. Firearms and poisoning by gas were the most preferred methods of suicide. The authors attributed the elevated suicide risk in farmers to geographical and social isolation, medical underutilization, chronic diseases, disabling injuries, pesticide use and consequent depression, and access to lethal methods.

Stallones (32) compared suicide rates among farmer men in Kentucky, nonfarmer men in Kentucky, and men in the United States for the period of 1979 to 1985. Farmers had a higher suicide rate (42.2/100,000) in comparison to nonfarmers in Kentucky (30.1/100,000) and men in the United States (19.2/100,000). Stallones conjectured that hazardous work environments; increasing social and geographical isolation due to the ongoing decrease of

rural residents; the changing economic environment in agriculture, including unemployment and the decreased ability to run heavy equipment required by increased mechanization on farms; and the lack of emergency medical care and mental health services in rural areas contribute to suicide risk in farmers.

Mental Health of Hired Farm Workers

A hired farm worker is an agricultural worker who is hired to work on a farm that someone else owns. Hired farm workers are usually hired contractually on a piecework basis—the more fruit they pick, for example, the more money they are paid.

The population of hired farm workers is composed of both migrant and seasonal farm workers. Migrant farm workers are individuals who migrate from one place to another to earn a living in agriculture. Seasonal farm workers, in contrast, earn a living in agriculture but live in one location throughout the year. Migrant farm workers generally live in the southern half of the United States during the winter months and migrate north before the planting or harvesting seasons. The population of migrant farm workers is ethnically diverse, with ethnic composition differing according to region of the country. For example, the majority of migrant farm workers in the Midwest stream are of Mexican descent, and many of these individuals are immigrants.

In a sample of Mexican-American farm workers in central California, Vega et al. (33) found that a environmental stressors and reduced physical health status were related to high levels of psychological distress as measured by the Health Opinion Survey, a measure of general psychopathology. In addition, they found that individuals aged 40 to 59 years reported elevated distress in comparison to other age groups. They conjectured that middle age is an especially high-risk period for farm workers since significant occupational and life hazards exist to progressively degrade farm workers' health and functional capacities. Vega et al. concluded that the high frequencies of environmental stressors and hazardous working conditions experienced by Mexican American hired farm workers place them at extraordinary psychological risk.

Hovey and Magaña (34–37) studied Mexican migrant farm workers in Ohio and Michigan. They found that the farm workers experienced relatively high levels of anxiety and depression. Nearly 40% of the farm workers revealed significant depression on the Center for Epidemiologic Studies–Depression Scale (CES-D). Typically about 20% of individuals from the general population have depression on the CES-D. About 30% of the farm workers demonstrated anxiety on the Personality Assessment Inventory (PAI). Typically about 16% of the general population indicates anxiety on the PAI. The authors found that high acculturative stress, low self-esteem, family dysfunction, ineffective social support, low religiosity, and a lack of control

and choice in the decision to live a migrant farm-worker lifestyle were significantly associated with greater anxiety and depression. It thus appears that positive self-esteem, effective family and social support, and religiosity may serve to help migrant farm workers cope against anxiety and depression.

In addition to collecting quantitative data such as the above, Hovey and his research team (38,39) collected interview data from each participant in their effort to explore the experience of being a migrant farm worker. As part of each interview, the interviewer probed for information regarding stress and coping by asking the farm workers about their perceptions of the difficulties that they had encountered as migrant farm workers. The interviews were conducted in an open-ended format so as to generate data in the participants' own words. Through the use of content analyses, the narrative data were organized thematically. These analyses resulted in the identification of 23 stressor categories that represent the stressors that the farm workers commonly experienced. These are listed in Table 22.2.

The narrative data also suggested that many migrant farm workers utilize an inactive coping style. The migrant farm workers frequently perceived the stressors of rigid work demands, poor housing conditions, hard physical labor, exploitation, and unpredictable work as external, uncontrollable, and unchangeable. Their perceptions ("This is how life is . . . we just put up with it") appear to reflect the chronic nature of their stresses. Given this chronicity, some migrant farm workers have difficulty identifying immediate mechanisms for coping, which may lead to a learned helplessness similar to that mentioned earlier for farmers. This inability to avert ongoing stress creates an increased susceptibility for anxiety and depression (38,39).

Implicit in the stress model is the notion that two migrant farm workers, for example, may experience the same stressor(s) with equal frequency and duration, yet may not experience the same severity of stress. This is because one of the farm workers may appraise the stressor(s) as relatively more threatening, thus inducing more stress.

To more precisely explore the relationship of migrant farm worker stress to anxiety, depression, and other mental health indicators, Hovey (40) developed the Migrant Farm Worker Stress Inventory (MFWSI). The MFWSI measures both the type of stressors experienced by migrant farm workers and the severity of stress experienced in response to the stressors. Respondents rate each of the 39 items on a five-point scale (0 = "have not experienced"; 1 = "not at all stressful"; 2 = "somewhat stressful"; 3 = "moderately stressful"; 4 = "extremely stressful"). The MFWSI items are listed in Table 22.3. Possible overall MFWSI scores range from 0 to 156.

After its validation, Hovey (41–43) utilized the MFWSI in a large-scale project that examined the mental health of migrant farm workers in western Colorado. Data particular to the scale itself are summarized in Table 22.3. The mean scores and standard deviations of each item are given, according to gender. Gender differences were evident for several items. For example,

Table 22.2. Stressors experienced by migrant farm workers.

- Being away from family or friends
- Hard physical labor/physical pain related to farm work
  - Difficulties due to the actual work itself:
    - Difficult physical nature of work
    - Physical pain and health consequences related to work
    - Not having enough water to drink while in the fields
- Rigid work demands
  - Difficulties associated with the structure of the work environment:
    - Long hours
    - No days off
- Unpredictable work or housing/uprooting
  - The unpredictable nature of finding work or housing
  - The feeling of instability due to constantly being uprooted
- Poor housing conditions
- Low family income/poverty/poor pay
- Limited access to health care
- Language barriers
- Geographical and social isolation
  - Being physically isolated
    - Difficult to meet people
    - No place for grocery shopping
- Emotional isolation
  - Inability to confide in others
  - Keeping feelings inside rather than sharing feelings with others
- Lack of transportation/unreliable transportation
- Education of self or children
- Discrimination from society
- Exploitation by employer

women were more likely to feel worried about being deported and not having a work permit. Men, on the other hand, were more likely to feel unsettled and to worry about transportation and the structural demands of farm work. The table also rank-orders each of the 39 items. Language difficulty is the highest endorsed stressor for women (fourth for men), whereas being away from family members is the highest endorsed stressor for men (second for women). In regard to overall MFWSI scores, greater migrant farm worker stress was heavily linked to lower self-esteem and social support and greater hopelessness, anxiety, depression, and suicidality.

Hovey's overall work in the area of farm-worker mental health suggests that migrant farm-worker stress—defined as the stress resulting from the stressors associated with the migrant farm-worker lifestyle—increases the risk for hopelessness, anxiety, depression, and suicide. His work has also identified possible coping resources including family support, social support, self-esteem, religiosity, and hopefulness for the future. Healthy usage of these

TABLE 22.2. Stressors experienced by migrant farm workers. (continued)

- Lack of day care and supervision of children
  - Worries over not having anyone to supervise their children while they worked
- Socialization of children
  - Worrying about possible negative influences in the social environment of their children
    - Drug use
    - Fewer moral values of friends of children
- Loss of spouse
  - The spouse no longer being in the home
    - Death of spouse
    - Spouse leaving
    - The spouse being kicked out of the home
- Domestic abuse/poor spousal relations
- Undocumented status
- Acculturating to new environment
  - Lack of familiar foods
  - Lack of Spanish-language media
- Migration experience
  - Stressors related to the migration experience itself
    - Owing money to individuals who helped them cross the border
    - Dangerous situations such as swimming across polluted waters or walking extremely long distances in the desert to avoid being caught by immigration authorities
- Paperwork for social services
- Responsibilities specific to being a woman
  - Duties that some view as belonging solely to women
    - Husband not helping with childcare and household duties because it is the responsibility of the woman

Source: Data from Hovey and Magaña (38) and Magaña and Hovey (39).

coping strategies may influence one's appraisal of stressors and lead to reductions in stress, anxiety, and depression (44).

Clinical Implications

Although much work remains to be done in terms of elucidating the phenomenology, risk factors, and effective treatments for mental health problems in agricultural workers in the United States, the current literature does provide some guidance for physicians serving this population. First, it is important for physicians to understand the link between the physical symptoms (including those that result from pesticide exposure) that farmers and farm workers may present with and common mental health problems faced by these groups. Because physical health problems and injuries are a major source of stress for farmers and farm workers and can lead to secondary

Table 22.3. Migrant Farm Worker Stress Inventory (MFWSI): mean stressor scores and stressor rankings from Western Colorado.

Item numbers and stressors	Female rank	F for females	Male rank	M for males
(01) I have difficulty communicating in the English language.	1	2.93	4	2.48
(08) It is difficult to be away from family members.	2	2.91	1	3.29
(37) I have difficulty understanding others when they speak English.	3	2.79	7	2.41
(06) I worry about not having medical care.	4	2.77	5	2.45
(05) I have not been able to buy things because of lack of money.	5	2.70	2	2.98
(38) I worry about my children's education.	6	2.64	9	2.34
(14) I worry about not having a permit to work in this country.	7	2.57*	20	1.68
(39) It bothers me that other people use drugs.	8	2.38	3	2.61
(30) I worry about being deported.	9	2.35*	29	1.39
(31) Migrating to this country was difficult.	10	2.07*	28	1.44
(25) It bothers me that other people drink too much alcohol.	10	2.07	14	1.98
(23) It is difficult to be away from friends.	12	1.98	13	2.10
(29) I sometimes have difficulty finding a job.	13	1.84	14	1.98
(26) I sometimes worry because I do not have reliable transportation.	14	1.71	9	2.34*
(09) I have had to adjust to the different foods in this country.	14	1.71	8	2.37*
(18) I find it difficult to talk about my feelings to other people.	16	1.70	19	1.73
(13) Sometimes I don't feel at home.	17	1.54	17	1.79
(07) At times I have to work long hours.	18	1.46	11	2.26*
(35) It is difficult to complete the social services paperwork.	19	1.38	24	1.60
(02) I have to work in bad weather.	20	1.36	12	2.22*
(03) There are not enough Spanish radio or television shows in area.	20	1.36	22	1.65
(11) Because I feel isolated, I find it hard to meet people.	22	1.34	23	1.64
(20) I worry about not having day care for children while working.	22	1.34	35	0.83

mental health issues, it is important for physicians to routinely screen for mental health difficulties as part of the physical exam. This can be done relatively quickly either with a brief interview during the course of the exam or with one of several paper-and-pencil screening instruments (e.g., the Beck Depression Inventory and the Beck Anxiety Inventory). Because of the increased risk for suicide observed in this population, it is advisable for physicians to include at least a few brief general mental health screening questions even in routine physical exams. Moreover, the risk for suicide, coupled with the risk for substance abuse disorders, should be considered when decisions are made regarding pharmacological treatments.

TABLE 22.3. Migrant Farm Worker Stress Inventory (MFWSI): mean stressor scores and stressor rankings from Western Colorado. (continued)

Item numbers and stressors	Female rank	F for females	Male rank	M for males
(24) I worry about the values that my children are being exposed to.	24	1.32	27	1.46
(21) Because of FW, I don't have time to get things done outside work.	25	1.25	18	1.78
(17) I worry about my relationship with my partner.	26	1.18	25	1.50
(16) Sometimes I have difficulty finding a place to live.	27	1.12	16	1.90*
(10) Due to following FW, sometimes I do not feel settled.	28	1.02	6	2.43*
(27) There are no stores nearby.	29	0.98	21	1.66*
(15) Sometimes I feel that my housing is inadequate.	30	0.93	25	1.50*
(32) Sometimes I feel that the conditions of the bathroom are bad.	31	0.91	30	1.24
(04) Because of the physical nature of FW, I have health problems.	32	0.89	33	0.95
(19) There is not enough water to drink when I am working.	33	0.75	35	0.83
(22) My life has become more difficult because my partner is gone.	34	0.71	31	1.10
(33) I worry about whom my children are spending time with.	35	0.65	32	1.00
(28) I have experienced discrimination in this country.	36	0.58	33	0.95
(36) I don't get enough credit from other family members for my work.	37	0.55	35	0.83
(12) I have been taken advantage of by my employer, supervisor, landlord.	38	0.52	38	0.76
(34) I have been physically or emotionally abused by my partner.	39	0.47	39	0.37

FW, farm work; M, mean; SD, standard deviation; *, significant gender difference.
Source: Data from Magaña and Hovey (39).
Note: $N = 98$ (57 females; 41 males). Possible range for each item is 0 to 4. Possible range for overall scale is 0 to 156. Overall M for MFWSI = 63.7 (SD = 30.4); for females (M = 61.0; SD = 30.2); for males (M = 67.4; SD = 30.7); $t = 1.02$, 2–tailed $p = .31$.

Additionally, individuals with disorders such as major depression, generalized anxiety disorder, and panic disorder frequently become fully cognizant of the physical manifestations of these disorders before attending to the psychological symptoms. Therefore, primary care physicians, rather than psychiatrists or psychologists, often provide the first line of treatment for these individuals. Physical symptoms can include tachycardia, breathing difficulties, sleep and appetite disturbances, as well as gastrointestinal and sexual symptoms. Once a physiological basis for these symptoms has been ruled out, a thorough psychiatric assessment should be requested.

When mental health treatment is indicated, economics and time pressures—either because of work-load demands or the need to migrate for work—can present significant obstacles. Many of the most effective treatments for disorders such as anxiety and depression are cognitive-behavioral therapies, which are relatively time-limited. These treatments cut down on both the time required for and expense associated with treatment. Moreover, many state-of-the-art treatments are primarily available through university psychology departments and medical centers, often with sliding scale fees. It is important for referring physicians to note that these treatments, with their focus on skill building and on immediate issues, may be more palatable than traditional psychotherapy to individuals from this population. Since this is not often the stereotype many laypeople have of psychotherapy, physicians may need to educate patients about cognitive-behavioral therapies in order to increase the likelihood that patients will follow through on referrals for mental health treatments.

Conclusion

The manifestation of stressors and associated coping strategies appears to vary according to whether individuals own or operate farms or whether individuals are hired as farm workers. It is apparent that farmers are at risk for the development of stress and other mental health difficulties such as anxiety, depression, and suicide.

Almost all of the studies on the mental health of hired farm workers have been conducted in the last 6 years. Although this literature is more scant than the farmer literature in terms of quantity, the research on stress and mental health in migrant farm workers has been conducted in a methodologically rigorous manner.

Many of these studies produced descriptive findings. Less common were studies that attempted to look at stress, coping, and mental health in a theoretical context. Prospective research is thus necessary to assess the interaction of stress and coping in agricultural workers over time. Also needed is research that looks at the interplay of mental health and physical health over time, given that the literature suggests that severe stress has a negative impact on both facets of health. Intensive, longitudinal work in the area will provide for the type of applied knowledge that will help in the generation of mental health interventions for agricultural workers.

References

1. Lazarus RS. Stress and Emotion: A New Synthesis. New York: Springer, 1999.
2. Rosenblatt PC, Keller LO. Economic vulnerability and economic stress in farm couples. Family Relations 1983;32:567–73.

3. Swisher RR, Elder GH, Lorenz FO, Conger RD. The long arm of the law: how an occupation structures exposure and vulnerability to stressors across role domains. J Health Soc Behav 1998;39:72–89.
4. Murray JD. The small farm: economic and emotional stress. Rural Community Mental Health Newsletter 1995;12:12–13.
5. Weigel R. Stress on the Farm—An Overview. Ames, IA: Iowa State University Cooperative Extension Service, 1981.
6. Rosenblatt PC, Anderson RM. Interaction in farm families: Tension and stress. In: Coward RT, Smith WM, eds. The Family in Rural Society. Boulder, CO: Westview Press, 1981.
7. Carruth AK, Logan CA. Depressive symptoms in farm women: effects of health status and farming lifestyle characteristics, behaviors, and beliefs. J Community Health 2002;27:213–28.
8. Gunderson P, Donner D, Nashold R, Salkowicz L, Sperry S, Wittman B. The epidemiology of suicide among farm residents or workers in five north-central states, 1980–1988. Am J Prev Med 1993;9(suppl 1):26–32.
9. Calvert GM, Plate DK, Das R, et al. Acute occupational pesticide-related illness in the U.S., 1998–1999: Surveillance findings from the SENSOR-pesticides program. Am J Ind Med 2004;5:14–23.
10. Flower KB, Hoppin JA, Lynch CF, et al. Cancer risk and parental pesticide application in children of Agricultural Health Study participants. Environ Health Perspect 2004;112:631–5.
11. Goldman L, Eskenazi B, Bradman A, Jewell NP. Risk behaviors for pesticide exposure among pregnant women living in farmworker households in Salinas, California. Am J Ind Med 2004;45:491–9.
12. Lefcourt H, Martin R. Locus of control and the rural experience. In: Childs A, Melton G, eds. Rural Psychology. New York: Plenum Press, 1983.
13. Peterson C. The future of optimism. Am Psychologist 2000;55:45–55.
14. Berkowitz AD, Perkins HW. Stress among farm women: work and family as interacting systems. J Marriage Family 1984;46:161–6.
15. Berkowitz AD, Perkins HW. Correlates of psychosomatic stress symptoms among farm women: a research note on farm and family functioning. J Human Stress 1985;11:76–81.
16. Weigel DJ, Weigel RR. Family satisfaction in two-generation farm families: the role of stress and resources. Family Relations 1990;39:449–55.
17. Weigel RR, Weigel DJ. Identifying stressors and coping strategies in two-generation farm families. Family Relations 1987;36:379–84.
18. Berkowitz AD, Hedlund DE. Psychological stress and role congruence in farm families. Cornell J Social Relations 1979;14:47–58.
19. Hedlund D, Berkowitz AD. The incidence of social psychological stress in farm families. Int J Sociology Family 1979;2:233–45.
20. Russell CS, Griffin CL, Flinchbaugh CS, Martin MJ, Atilano RB. Coping strategies associated with intergenerational transfer of the family farm. Rural Sociology 1985;50:361–76.
21. Heppner PP, Cook SW, Strozier AL, Heppner MJ. An investigation of coping styles and gender differences with farmers in career transition. J Counseling Psychol 1991;38:167–74.
22. Davis-Brown K, Salamon S. Farm families in crisis: an application of stress theory to farm family research. Family Relations 1987;36:368–73.

23. Eberhardt BJ, Pooyan A. Development of the farm stress survey: Factorial structure, reliability, and validity. Educational and Psychological Measurement 1990;50:393–402.
24. Thu KM. The health consequences of industrialized agriculture for farmers in the United States. Human Organization 1998;57:335–41.
25. National Safety Council. Injury Facts, 2004 ed. Itasca, IL: National Safety Council, 2004.
26. Thu KM, Lasley P, Whitten P. Stress as a risk factor for agricultural injuries: comparative data from the Iowa Farm Family Health and Hazard Survey (1994) and the Iowa Farm and Rural Life Poll (1989). J Agromed 1997;4:181–91.
27. Reis TJ, Elkind PD. Influences on farm safety practice in Eastern Washington. In: Donham KJ, Rautiainen R, Schuman RH, Lay JA, eds. Agricultural Health and Safety: Recent Advances. New York: Haworth Medical Press, 1997.
28. Stueland DT, Lee B, Nordstrom D, Layde PM, Wittman LM, Gunderson PD. Case-control study of agricultural injuries to women in central Wisconsin. Women's Health 1997;25:91–103.
29. Swanson JA, Sachs MI, Dahlgren KA, Tinguely SJ. Accidental farm injuries in children. Am J Disabled Children 1987;141:1276–9.
30. Linn JG, Husaini BA. Determinants of psychological depression and coping behaviors of Tennessee farm residents. J Community Psychol 1987;15:503–12.
31. Seligman LD, Ollendick TH. Comorbidity of anxiety and depression in children: an integrative review. Clin Child Family Psychol Rev 1998;1:125–44.
32. Stallones L. Suicide mortality among Kentucky farmers, 1979–1985. Suicide and Life-Threatening Behavior 1990;20:156–63.
33. Vega W, Warheit G, Palacio R. Psychiatric symptomatology among Mexican American farmworkers. Soc Sci Med 1985;20:39–45.
34. Hovey JD, Magaña C. Acculturative stress, anxiety, and depression among Mexican immigrant farmworkers in the Midwest United States. J Immigrant Health 2000;2:119–31.
35. Hovey JD, Magaña CG. Cognitive, affective, and physiological expressions of anxiety symptomatology among Mexican migrant farmworkers: predictors and generational differences. Community Mental Health J 2002;38:223–7.
36. Hovey JD, Magaña C. Exploring the mental health of Mexican migrant farmworkers in the Midwest: psychosocial predictors of psychological distress and suggestions for prevention and treatment. J Psychol 2002;136:493–513.
37. Hovey JD, Magaña C. Psychosocial predictors of anxiety among immigrant Mexican migrant farmworkers: implications for prevention and treatment. Cultural Diversity and Ethnic Minority Psychology 2002;8:274–89.
38. Hovey JD, Magaña C. Suicide risk factors among Mexican migrant farmworker women in the Midwest United States. Arch Suicide Res 2003;7:107–21.
39. Magaña CG, Hovey JD. Psychosocial stressors associated with Mexican migrant farmworkers in the Midwest United States. J Immigrant Health 2003;5:75–86.
40. Hovey JD. Correlates of migrant farmworker stress among migrant farmworkers in Michigan. Migrant Health Newsline 2001;18:5–6.
41. Hovey JD. Mental health and substance abuse. In: National Advisory Council on Migrant Health, ed. Monograph Series No. 4: Migrant Health Issues. Bethesda, MD: Bureau of Primary Health Care, 2001;4:19–26.
42. Hovey JD. The mental health status of migrant farmworkers in the Midwest United States: What we know, and what we need to do. In: Partida S, ed.

Proceedings of the 2000–2001 Migrant Farmworker Stream Forums. Washington, DC: U.S. Department of Health and Human Services, 2001.
43. Hovey JD, Gibbs D. Suicide risk among Latino/a farmworkers in Colorado. Poster presented at the annual conference of the American Association of Suicidology, Santa Fe, 2003.
44. Hovey JD, Smith ZF, Yzquierdo E. An assessment of the mental health of farmworkers in western Colorado: implications for prevention and treatment. Paper presented at the annual Public Health in Colorado Conference, Pueblo, 2002.

23

Neurotoxicity of Chemicals Commonly Used in Agriculture

Nikita B. Katz, Olga Katz, and Steven Mandel

Key words: assessment, wild plants, rodenticides, heavy metals, organochlorides, organophosphates

A multitude of chemical agents used in agriculture are known to have significant toxicity, many of them specifically developed to be toxic to animals. This chapter concentrates on the neurological consequences of occupational exposure to these and other common agents, including insecticides, pesticides, heavy metals, and volatile organic and plant toxins.

A physician in rural practice should be acquainted with the strategies for providing emergency care, especially after acute exposure to potent toxins. Acute exposure is suggested by a set of symptoms that include rapidly developing fatigue, dizziness, nystagmus, disorientation, confusion, hallucination, as well as other neurological presentations (e.g., symptoms of intracranial hypertension such as headache, nausea, or vomiting), muscle fasciculations, seizures, or coma (1).

A possibility of occupational exposure must be considered in all agricultural workers and their families; however, those who work in a confined space with little or no means of personal protection, who lack the necessary training or sufficient knowledge of the native language, or lack access to industrial hygiene data should be considered likely candidates for a detailed evaluation.

Often patients provide the best clues by attributing their medical condition to a specific agent or to the possibility of exposure. Patients may complain that their symptoms were preceded by the presence of a chemical smell or a spill of a chemical. They may also note that their symptoms get worse at the end of the shift, workweek, or season. This "undulating" presentation when symptoms are less acute during the weekend or time-off periods may be of special significance as it may allow gauging of personal susceptibility to a specific agent (2,3).

Occupational exposure may be suspected if the patient presents with reversible, static, or progressive neurological symptoms after removal from exposure, symptoms that occur slowly, especially if these symptoms are attributable to central nervous system (CNS) changes such as headache,

confusion, disorientation, and behavior or memory changes. Slow onset of peripheral neuropathy, often presenting with numbness in the feet and hands, pain, weakness, or difficulty walking is also highly suggestive of occupation-related toxicity. In the majority of cases, severity of symptoms may be directly related to the length of employment in the field or in processes that expose workers to toxic agents (4,5).

Both clinical and subclinical dysfunction is often noted by abnormal neurophysiological, neuropsychological, or neuroimaging testing results. Detailed evaluation of patients whose occupational or environmental history is deemed significant is warranted as it provides a snapshot of the patient's condition against which future changes can be judged.

In all cases strive to achieve unhindered communication with both the patient and the employer. Assistance of qualified interpreters may be needed and chemical names may differ significantly among languages (e.g., nitrogen is "azote" in several European languages). When evaluating the patient, consider both common and rare agents, keeping in mind that what may be rare in an urban/suburban setting may be common in the rural and agricultural setting.

Algorithm to Assess for Neurotoxic Illness

Step One: Background History

Assess for:

1. Significant medical and family histories, noting issues such as education, fluency in language, instruction about and adherence to use of personal protection equipment (see Chapter 6)
2. Residence history of the patient and cohabitants, and health problems in relatives and cohabitants
3. Current and historical medication, recreational drug use, and use of dietary supplements

Step Two: Potential Toxic Agents

Obtain:

1. A personal narrative through spontaneous communications and guided by open-ended questions about the patient's perception of occupational hazards and toxic chemicals he or she might have been exposed to
2. Material Safety Data Sheets (MSDS) for all chemicals of concern from the employer
3. Identification and comparison of chemical agents that may contribute to a patient's presentation, both past and present
4. Additional reference information as necessary

Step Three: General Medical Examination

Proceed with systemic examination, including a detailed assessment of skin and its derivatives (hair, nails), the lymph system, and dental health. Obtain past medical records as necessary.

Step Four: Neurological Examination and Confirmatory Testing

Check for mental status changes, seizure-like presentations, brainstem signs (e.g., nystagmus), motor and sensory neuropathies, and changes in reflexes. If appropriate, identify soft neurological signs for the purposes of later monitoring. Separately address cerebellar signs (ataxia, dystaxia, or dysmetria), as they may shed light on the identity of certain toxic agents. Exclude common diagnoses and differentiate between possible contributing factors such as peripheral neuropathy in patients with both chemical exposure and diabetes or alcoholism.

Neurophysiological testing provides irreplaceable data useful for assessment of the current condition and for neurological monitoring. Additional information should be obtained from imaging and neuropsychological tests, as appropriate. Industrial hygiene tests may be necessary, especially if legal issues are anticipated.

Step Five: Determine the Diagnosis and Extent of Injury

Determine if:

1. The dose and duration of exposure are consistent with the described dysfunction
2. The proposed mechanism for the exposure-induced dysfunctions

Step Six: Reevaluation Strategy

1. Decide on the need for reevaluation, its frequency and possible markers or end points
2. Discuss the reevaluation schedule and educate the patient about symptoms and manifestations that are consistent with both improvement and worsening of the condition
3. Alert the patient to possible situations, symptoms, and manifestations that warrant emergency care

Neurotoxicity of Wild Plants

Many plants cause nonspecific gastrointestinal upset. Among significantly toxic plants are philodendron, holly, dumbcane, poison ivy, pothos (devil's

ivy), English ivy, yew, rhododendron (azalea), and eucalyptus. Poison hemlock ingestion is suggested when gastrointestinal upset is accompanied by the early onset of increased secretions followed by syndromes such as respiratory difficulty, altered mental status, and seizures. Plant ingestion alone is unlikely to cause isolated altered mental status except in cases of exposure to water hemlock and chinaberry plants (6).

Water Hemlock (Cicuta maculata)

Water hemlock *(Cicuta maculate)* and most other species of *Cicuta* are similar in appearance and grow to heights of 6 feet. These plants are found in wetlands throughout the United States. Cicutoxin is distributed throughout the plant, with the highest concentration in the tuberous roots. One mouthful of root is sufficient to kill an adult (as documented by, among others, Plato). Toxicity has also been documented after dermal contact (7).

Cicutoxin ingestion produces symptoms in 15 to 60 minutes. Muscarinic actions manifest as abdominal pain, vomiting, diarrhea, trismus, and hypersalivation. More central effects manifest as CNS depression, respiratory distress, and possibly tonic-clonic seizures. Death is usually secondary to respiratory arrest. Treatment is mostly supportive, as anticholinergics have not been shown effective in animal models (7).

Chinaberry (Melia azedarach)

Chinaberry *(Melia azedarach)* is a tree with serrated leaves, long leaflets, and scented, purple flowers arranged in clusters. The toxic agent is concentrated in the berries that are yellow, contain smooth black seeds, and persist after the leaves are shed. Chinaberry trees grow in the South from Florida to Hawaii. Ingestion of as few as six to eight berries has been reported to cause fatalities (8).

In patients who ingest the berries, a prolonged latency period is followed by development of mental confusion, ataxia, dizziness, and stupor. Some patients may develop intense vomiting and bloody diarrhea, which results in hypovolemic shock. Respiratory depression, seizures, and paralysis also have been reported (8).

The treatment is primarily symptomatic in nature. Gastric decontamination may benefit by reducing the absorbed dose. Benzodiazepines remain the mainstay of management of seizures induced by plant alkaloids.

Neurotoxicity of Rodenticides

Rodenticides are a heterogeneous group of compounds that exhibit markedly different toxicities to humans and rodents. Table 23.1 lists the effects and neurological presentations for different examples. According to the Toxic

TABLE 23.1. Effects of specific rodenticides.

Chemical (brand name)	Effects	Possible neurological presentation
Sodium monofluoroacetate	Poisons the Krebs cycle	Dizziness, weakness, nausea
N-3-pyridylmethyl-Np-nitrophenyl urea [PNU] (Vacor)	Destroys the pancreatic beta cell	Dizziness, weakness, nausea
Strychnine	Antagonist of glycine at the postsynaptic spinal cord motor neuron	Seizure-like, extensor posturing with risus sardonicus
Barium compounds	Causes potassium redistribution (intracellular influx), may lead to hypotonia	Headache, weakness, nausea, shortness of breath, brain anoxia
Yellow phosphorus	Causes chemical burns, hemolysis	Agitation, weakness
Arsenic compounds	React with sulfhydryl groups of multiple enzymes	Nausea, vomiting, weakness
Zinc phosphide	Causes hemolysis	Nausea, vomiting, weakness
Bromethalin	Identified as a mitochondrion poison (uncouples oxidation)	Nausea, vomiting, weakness
Norbormide	Causes ischemia (via vasoconstriction)	Dizziness, seizure-like presentation possible
Warfarin-like anticoagulants and brodifacoum	Cause hemorrhages	Multiple dose- and organ-dependent complaints

Source: Data from Feldman (1), Carod Artal (6), and Van Sittert and Tuinman (9).

Exposure Surveillance System (TESS) of the American Association of Poison Control Centers (AAPCC), 20,300 human exposures to rodenticides were reported in 1 year (1998) (9,10).

Management of toxicity induced by rodenticides is toxin-specific and usually involves emergency care for acute exposure. Strychnine may be of special interest to a physician, due to its unique and well-studied mechanism of toxicity. This plant alkaloid is no longer widely used in the United States but is more widely used in the developing countries. Consider strychnine toxicity if an individual presents with generalized seizure-like appearance, with or without loss of consciousness. Of note is the fact that strychnine may be used as an adulterant in street drugs, especially those sold as lysergic acid diethylamide (LSD) (9).

Neurotoxicity of Heavy Metals

Nearly all organ systems are affected in heavy metal toxicity, most commonly the nervous, gastrointestinal, hematopoietic, renal, and cardiovascular systems. To a lesser extent, lead toxicity involves the musculoskeletal and reproductive

systems. The organ systems affected and the severity of the toxicity vary with the particular heavy metal involved, the age of the individual, and the level of exposure (11).

Heavy metals bind to sulfhydryl groups in proteins, resulting in alterations of enzymatic activity; however, specific metals also have unique mechanisms of toxicity that may explain the variety of presentations (11).

Encephalopathy is one of the leading causes of mortality in patients with heavy metal poisoning and is especially common in cases of lead poisoning. Neuropathies are also common, often presenting a challenge to diagnose and necessitating extended diagnostic studies (12).

Lead Toxicity

Lead disrupts the normal physiological effects of calcium, causing inappropriate release of neurotransmitters, and interferes with excitatory neurotransmission by glutamate, especially the *N*-methyl-D-aspartate (NMDA) receptor, which is blocked selectively by lead. Disruption of NDMA-mediated long-term potentiation is believed to be responsible for the cognitive manifestations of lead toxicity, especially in children. At higher blood levels, lead disrupts the function of endothelial cells in the blood–brain barrier, causing subsequent hemorrhagic encephalopathy, seizures, and coma (see Chapter 9 for biological monitoring) (13,14).

Mental status examination may detect changes in more severe cases of lead toxicity, while detailed neuropsychological testing is often needed to diagnose the less obvious cases. In both children and adults, impaired fine-motor coordination or subtle visual-spatial impairment may be seen, while chronic distal motor neuropathy with decreased reflexes and weakness of extensor muscles and relatively spared sensory function is more common in adults (15).

In addition to common environmental sources of lead (paint and leaded gasoline), identification of some of the sources of lead may present a challenge, since cosmetics ("surma" or kohl in the Middle East), folk remedies (often applied to the umbilical stumps of infants), and even alternative medical remedies may contain lead. A puzzling use of lead acetate is as an aphrodisiac, which has been reported historically and in some areas of Latin America (15).

Laboratory Tests and Studies

Blood lead levels higher than 10 μg/dL are considered toxic, but no level of lead, no matter how minute, is considered safe. A complete blood count (CBC) with peripheral smear may demonstrate basophilic stippling of the red blood cells (RBCs), a finding also observed in arsenic toxicity, sideroblastic anemia, thalassemia, and normocytic or microcytic anemia (11,12,15).

Cerebral edema and microhemorrhages may be seen on magnetic resonance imaging (MRI) in patients presenting with encephalopathy. Patchy calcifications, although not specific, are seen on MRIs of patients with chronic lead exposure. In adults, neurophysiological testing may be helpful if symptoms of lead-induced neuropathy are seen (15).

Management

The key to treating lead toxicity is removal of the offending agent and reducing the total body load. Chelation agents [calcium disodium ethylenediaminetetraacetic acid ($CaNa_2$ EDTA), dimercaprol, 2,3-dimercaptosuccinic acid (DMSA)] are used to reduce the body stores of lead. Treatment for acutely ill patients includes whole-bowel irrigation with polyethylene glycol electrolyte solution if radiographic evidence of lead toxicity is present (15).

A water-soluble, oral chelating agent, DMSA (succimer, Chemet®), is appropriate for use with blood lead levels ranging from 40 to 70 µg/dL. It is contraindicated in children with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency or those allergic to sulfa drugs. D-penicillamine (Cuprimine) is a second-line oral chelating agent, although it is not approved by the U.S. Food and Drug Administration (FDA) for use in lead poisoning (15).

Calcium disodium ethylenediaminetetraacetic acid ($CaNa_2$ EDTA) is a parenteral chelating agent that is administered intravenously to patients with blood lead levels in the range of 40 to 70 µg/dL who do not respond to succimer or cannot take it. In addition, it is used immediately before oral succimer in patients with blood lead levels higher than 70 µg/dL (15).

Dimercaprol [British antilewisite (BAL)] is another parenteral chelating agent recommended by some authors as an agent of first choice. With high blood lead levels (> 100 µg/dL), it is used in conjunction with $CaNa_2$ EDTA (16).

Mercury Toxicity

The clinician needs to distinguish between toxicity of the inorganic compounds (elemental mercury and the ions: mercuric and mercurial) and the toxicity of organic compounds (alkyls of mercury: methylmercury). Organic methylmercury toxicity causes prominent neuronal loss and gliosis in the calcarine and parietal cortices and cerebellar folia, as seen in cases of Minamata disease. Inorganic mercury causes cerebral infarctions as well as systemic features, such as pneumonia, renal cortical necrosis, and disseminated intravascular coagulopathy. Inorganic mercury impairs adenosine diphosphate (ADP)-dependent protein genesis in animal models, while organic mercury compounds may induce excitotoxicity and dysregulation of the nitric oxide system with subsequent cerebellar damage in rodents (17–19).

Patients presenting with gait ataxia, tremulousness, hearing loss, visual field constriction, dysarthria, and distal limb sensory loss, coupled with

cognitive and emotional dysfunction should be evaluated for mercury toxicity, although none of these symptoms is specific (18).

Organic mercury toxicity, seen in Minamata disease and in patients consuming grains contaminated with mercury-based fungicides, often leads to hearing loss and visual field impairments. Distal sensory loss, uncoordinated limb movements, resting tremors, gait ataxia, and a positive Romberg sign are associated with both inorganic and organic types of toxicity. Impairments in the frontal lobe domains (emotional and cognitive) observed with neuropsychological testing are somewhat more characteristic of acute inorganic mercury toxicity, although this presentation (the "Mad-Hatter" syndrome) is possible in all cases (19–23).

Laboratory Tests and Studies

A 24-hour urine specimen should be obtained for measurement of inorganic mercury levels, while whole blood mercury levels should be measured for alkyls of mercury (organic mercury). Blood and urine levels of mercury should not exceed 10 ng/mL (see Chapter 9). Hair levels are more useful in cases of organic mercury poisoning and should not exceed 2 ng/mL (24).

Electrophysiological studies are necessary and often demonstrate a sensorimotor neuropathy, typically axonal. Visual-evoked potential studies may also present with abnormalities. The utility of MRI appears to be primarily for ruling out other causes of symptomatic presentations, while sural nerve biopsies in patients with Minamata disease caused by organic mercury toxicity indicated preferential loss of large myelinated nerve fibers (19,20,25).

Management

Administration of chelating agents that contain thiol groups is the accepted standard of care. For acute, inorganic toxicity, dimercaprol (BAL) has been recommended traditionally, but oral agents are gaining prominence. Chelation with DMSA (Succimer) has been shown to result in increased mercury excretion compared to *N*-acetyl-D,L-penicillamine in adults with acute mercury vapor exposure. DMSA is generally well tolerated in adults and children (16).

Chelation removes only a small portion of the toxin, especially in cases of organic mercury poisoning. The placebo response has been observed in patients concerned with the occupational exposure in dentistry, and there is a general paucity of studies showing neurological improvement following any kind of chelation therapy (25,26).

Arsenic Toxicity

Arsenic toxicity may be mistaken for Guillain-Barré syndrome, as it presents with paresthesias and numbness in a symmetric stocking-glove distribution and muscle weakness. Arsenic-induced neuropathy may persist after exposure

stops, but long-term exposure may present with a sensory neuropathy that resembles alcoholic neuropathy. Burning paresthesias in glove and stocking distribution, early loss of stretch reflexes, and later weakness are also seen. In severe cases, flaccid paralysis may appear in the lower extremities and then the upper extremities, again resembling Guillain-Barré syndrome (27–29).

Laboratory Tests and Studies

A 24-hour urine specimen should be obtained for measurement of arsenic levels, as well as a CBC with peripheral smear. Analysis of hair and fingernail clippings is less useful as there is a significant risk of environmental contamination (27-29).

Management

Chelation therapy with BAL, DMSA, or d-penicillamine is the primary treatment of arsenic toxicity. Removal of the offending agent and aggressive gastric decontamination aids in reducing ongoing absorption of arsenic. Hemodialysis may be beneficial in patients with acute renal failure (16,27–29).

Thallium Toxicity

Thallium poisoning induces a painful sensory neuropathy, particularly at the soles and palms, which may be followed by lower extremity weakness, ataxia, confusion, hallucinations, convulsions, and coma. Neuro-ophthalmic symptoms such as diplopia, abnormal color vision, and impairment of visual acuity may develop early, while dermatologic manifestations such as alopecia, rashes, palmar erythremia, and Mees lines in the nails and gums may be delayed by several weeks. Electrodiagnostic findings include an axonal sensorimotor neuropathy with nerves innervating the feet most significantly involved (30).

Management

Gastrointestinal decontamination, activated charcoal, and Prussian blue (potassium ferric hexacyanoferrate) are recommended in thallium ingestions. Activated charcoal and Prussian blue bind thallium decrease the enterohepatic recycling, and enhance fecal elimination of the metal. Prussian blue binds more thallium than charcoal on a gram-bound per gram-agent basis and should be used instead of charcoal if possible. Prussian blue is available only as a laboratory reagent in the United States and Canada, and is not approved by the FDA as a pharmaceutical agent. Prolonged neurological exposure to thallium, especially in cases of acute poisoning when proper diagnosis is not established and detoxification is delayed almost universally leads to long-term and/or irreversible neurological sequelae (30,31).

Neurotoxicity of Volatile Organic Compounds

Volatile organic compounds (VOCs), such as solvents, esters, hydrocarbons, aromatic compounds, and other organic chemicals, are characterized by low boiling temperature and higher volatility (Table 23.2). They are ubiquitous in agriculture, providing power for vehicles and used in every technological process. Volatile organic compound toxicity is divided into clinical syndromes based on the organ system: the lungs are affected most commonly, but instances of neurological, cardiac, gastrointestinal, renal, hematological, and skin pathology are also well documented. Three factors affect the selectivity and severity of toxic effects: the identity of the VOC, the dose, and the route of exposure (Table 23.2) (32–34).

Almost all VOCs are strongly lipophilic and attracted to neural tissue. Demyelinating peripheral polyneuropathy is associated with exposure to 6-carbon aliphatic hydrocarbons (n-hexane, methyl-n-butyl-ketone) that are metabolized into a compound that interferes with axonal transport. Long-term workplace exposure or inhalant abuse (solvent sniffing) may result in chronic headaches, cerebellar ataxia, and encephalopathic findings of cognitive and psychopathic impairment (34).

Butane, benzene, toluene, and xylene are CNS depressants, have a disinhibiting euphoric effect, and are used as agents of abuse. Patients present with symptoms of CNS disinhibition, such as dizziness, slurred speech, ataxia, and obtundation. Ventilatory drive may be compromised. The initial

TABLE 23.2. Chemicals found in specific products.

Product	Solvents
Balsa wood cement	Ethyl acetate
Contact adhesives	Toluene, hexane, esters
Tire adhesive	Toluene, xylenes
PVC cement	Trichloroethylene
Air freshener, deodorants, fly spray, hair lacquer, spray paints, aerosol packages	Halons (chloro-fluoro-organic compounds), butane, dimethyl ether, methylbutyl ketone
Anesthetics/analgesics	Nitrous oxide, ether, chloroform
Commercial dry cleaning, domestic spot remover	1,1,1-Trichloroethane, tetrachloroethylene, trichloroethylene
Fire extinguishers	Bromochlorodifluoromethane, halons 11 and 12
Cigarette lighters	n-Butane, isobutane, propane
Nail/varnish remover	Acetone and esters
Paints/paint thinners	Butanone, esters, hexane, toluene, xylene
Paint stripper	Dichloromethane, toluene
Surgical plaster/chewing gum removers	Trichloroethylene
Paint thinners	1,1,1-Trichloroethane, toluene, hexane, methyl n-butyl ketone

PVC, polyvinyl chloride.
Source: Data from Feldman (1), Ford (3), and LaDou (4).

TABLE 23.3. Toxic effects of various volatile organic compounds.

Specific compound	Signs and symptoms
Aliphatic hydrocarbons	Dizziness, syncope, giddiness, hypotension, cerebral ischemia, headache, tachycardia
n-Butyl, isobutyl, and amyl nitrite	Increased intraocular pressure, confusion, sudden death, convulsion, coma
Naphtha, kerosene	Irritation of mucous membranes, nausea, ataxia, dizziness, hallucinations
Gasoline	Respiratory arrest, syncope, death, myoclonia, chorea, encephalopathy, tremor, pulmonary hemorrhage and edema, pneumonitis, plumbism, anemia, lead encephalopathy, confusion, dementia, cerebral edema, peripheral and cranial neuropathies, paresthesias, proteinuria, hematuria
n-Hexane	Eye and nasopharynx irritation, dizziness, giddiness, nausea, headache, CNS depression, peripheral neuropathy, anemia, basophilic stippling, bone marrow depression, fatal overdose
Benzene	Irritation of conjunctivae and visual blurring; irritation of mucous membranes; dizziness; headache; unconsciousness; convulsions; tremors; ataxia; delirium; tightness in chest; irreversible brain damage with cerebral atrophy; fatigue; vertigo; dyspnea; respiratory arrest; cardiac failure and ventricular arrhythmias; leukopenia; anemia; thrombocytopenia; petechiae; blood dyscrasia; leukemia; bone marrow aplasia; fatty degeneration and necrosis of liver, heart, adrenal glands; fatal overdose
Naphthalene	Irritation and injury of conjunctivae and corneas, perspiration, nausea, vomiting, headache, cataracts, hemolytic anemia (greater in G-6-PD deficiency), hepatic necrosis, hematuria, jaundice, proteinuria, oliguria, anemia, excitement, confusion, convulsions, coma, dermatitis, fatal overdose
Styrene	Irritation of mucous membranes, CNS depression and narcosis, fatal overdose
Toluene	CNS depression, syncope, coma, cardiac arrhythmias and sudden death, ataxia, convulsions, rhabdomyolysis, increased creatine phosphokinase, abdominal pain, nausea, vomiting, hematemesis, peripheral neuropathy, paresthesias, encephalopathy, optic neuropathy, cerebral ataxia, distal renal tubular acidosis, hyperchloremia, hypokalemia, azotemia, hypophosphatemia, hematuria, proteinuria, pyuria, hepatosplenomegaly, lymphocytosis, macrocytosis, basophilic stippling, hypochromia, eosinophilia, EEG abnormalities, decreased cognitive function, fatal overdose

presentation may mimic alcohol intoxication. In some patients, an initial component of CNS stimulation may present as agitation, tremor, or seizure (Table 23.3) (35–37).

A physician dealing with the predominantly rural population may expect to see intermediate and long-term, low-level exposures that can lead to reversible and nonreversible neurological abnormalities. In some cases exposures that caused long-term neurotoxic effects have been estimated

TABLE 23.3. Toxic effects of various volatile organic compounds. (continued)

Specific compound	Signs and symptoms
Xylene	Irritation to eye and mucosa; CNS depression and narcoses; reversible corneal damage; death; pulmonary edema and hemorrhage; fatty degeneration of heart, liver, and/or adrenal glands; abnormal liver function tests
Esters	Irritation of eyes, skin, and mucous membranes; CNS depression; liver and kidney necrosis; fatal overdose
Glycols	Oxalosis, impaired renal and liver function, stupor, coma, convulsions, irreversible brain damage, pulmonary edema, respiratory failure, nausea, vomiting, headache, tachycardia, hypotension, hypoglycemia, hypocalcemia, intravascular hemolysis, lymphocytosis, proteinuria, hematuria, fatal overdose
Trichloroethane, trichloroethylene, methylchloroform	Decreased myocardial contractility, arrhythmias, cardiac arrest and failure, myocarditis, renal failure, paresthesias, tinnitus, ataxia, headache, narcosis, CNS damage, sudden death
Carbon tetrachloride, ethylene dichloride	Nausea; vomiting; confusion; unconsciousness; coma; respiratory slowing; color blindness; blurred vision; memory loss; paresthesias; tremors; dermatitis; CNS edema, congestion, and hemorrhage; edema and inflammation of the lungs, kidneys, spleen, and pancreas; fatty degeneration of liver; cardiac arrhythmias; sudden death
Methylene chloride	Liver and kidney abnormalities, fatal overdose
Methyl alcohol	Abdominal discomfort, dizziness, fatigue, headache, nausea, vertigo, CNS depression, coma, vomiting, acidosis, mydriasis, retinal edema and ganglion cell destruction, philophobia, mydriasis, areflexia, hemorrhagic infiltration of basal ganglia, decreased vision and blindness, fatal overdose
Isopropyl alcohol	Irritation of eyes and mucous membranes, nausea, vomiting, abdominal pain, hematemesis, narcosis, coma, areflexia, depressed respiration, oliguria, diuresis, fatal overdose
Butyl alcohol	Coma, areflexia, depressed respiration, oliguria and diuresis, fatal overdose, irritation of eyes and mucous membranes, CNS depression, kidney and liver damage, fatal overdose

CNS, central nervous system; G-6–PD, glucose-6–phosphate dehydrogenase.
Source: Data from Feldman (1), Ford (3), LaDou (4), and So (5).

to be below levels designated in regulations as acceptable for workers (Table 23.4) (37).

Imaging Studies

Electromyogram (EMG) and nerve conduction study (NCS) abnormalities have been demonstrated in individuals and groups exposed to VOCs. Evidence of a mixed sensory/motor neuropathy has been found in many of these patients, while some studies have even demonstrated dose-response data correlating exposure dose to physiological abnormalities (36).

TABLE 23.4. Levels of exposure believed to be acceptable for workers.

Compound	Measured in:	Compounds and levels believed safe
Acetone	Urine	Acetone, formic acid: 100 mg/L
Benzene	Urine	Total phenol: 50 mg/g at end of shift
Benzene	Expired air	Benzene: preshift 0.08 ppm; at end of shift 0.12 ppm
Carbon disulfide	Urine	2-TTCA (2–thiothiazolidine 4-carboxylic acid): 5 mg/g
Ethylene oxide	Urine, blood, expired air	None
N-hexane	Urine	2,5-hexanediol: 5 mg/g at end of shift
Hydrogen sulfide	Urine, blood, expired air	None
Methane	Urine, blood, expired air	None
Methyl mercaptan	Urine, blood, expired air	None
Methanol	Urine	Formic acid: 80 mg/g at start of work week; Methanol: 15 mg/g at end of shift
Methyl-*n*-butyl ketone	Urine, blood, expired air	None
Methylene chloride	Urine, blood, expired air	None
Organochlorine	Urine, blood, expired air	None
Organophosphates	Urine, blood, expired air	None
Perchlorethylene (PER)	Blood	PER: 1 mg/L
Perchlorethylene	Expired air	PER: 10 ppm before last shift of week
Styrene	Urine	End of shift: mandelic acid (MA): 800 mg/g, phenylglyoxylic acid (PGA): 240 mg/g Before shift: MA 300 mg/g, or PGA 100 mg/g
Styrene	Blood	Styrene: at start of shift 0.02 mg/L; end of shift 0.55 mg/L
Toluene	Urine, blood, expired air	Hippuric acid in urine, toluene in blood and expired air: none
1,1,1-Trichlorethane (methyl chloroform)	Urine	Trichloroacetic acid (TCA) at end of workweek: 10 mg/L Total trichloroethanol at end of shift and at end of workweek: 30 mg/L
1,1,1-Trichlorethane (methyl chloroform)	Blood	Total trichloroethanol: 1 mg/L
1,1,1-Trichlorethane (methyl chloroform)	Expired air	Methyl chloroform prior to last shift of workweek: 40 ppm
Trichloroethylene (TCE)	Urine	TCE or TCA: 100 mg/g at end of workweek TCA plus TCE: 300 mg/g at end of workweek
Trichloroethylene	Blood	TCE: 4 mg/L at end of workweek
Vinyl chloride	Urine, blood, expired air	None
Xylene	Urine	Methylhippuric acid: 1.5 g/g at end of shift

Source: Data from American Conference of Governmental Industrial Hygienists (39).

A study performed on industrial workers in Scandinavia assessed 87 patients with diagnoses of chronic solvent intoxication after occupational exposure. Sixty-two percent had abnormal EMG/NCS results on the first evaluation and 74% on the second evaluation 3 to 9 years later. Fibrillations were noted in 54% on initial examination and 61% on reexamination. The same authors found a high percentage of slow motor and sensory conduction velocities and/or prolonged motor distal latencies in car painters versus none in nonexposed controls (38).

Computed tomography (CT) scan, MRI, positron emission tomography (PET), and single photon emission computed tomography (SPECT) have been utilized to evaluate the mechanism and extent of VOC neurotoxicity in specific cases but have shown no consistent or unique pattern of pathological change. Cerebral, cerebellar, and olivopontocerebellar atrophy are commonly reported, with most frequent abnormalities noted in the temporal lobes and frontal lobes, with associated changes in the basal ganglia and the thalamus (38).

Electroencephalographic abnormalities also have been demonstrated in many populations exposed to organic solvents. In one study, acute effects of exposure to less than 400 ppm of xylene were assessed in healthy volunteers. Such exposure increased the dominant alpha frequency and percentage during the early phase of exposure and counteracted the effect of exercise. These effects were deemed minor and not deleterious. This (or any other) study did not address the more germane issue of longer-term exposure (38).

In acute intoxication cases, the most important presentations include lethargy and depressed sensorium, while coma is relatively uncommon. Other systems (gastrointestinal, skin, respiratory) are often affected and present with easy-to-interpret changes (pneumonitis, skin erythema, vomiting) (38).

Management

Management of acute cases is supportive since no specific antidotes to VOCs are available. Indicated medications for altered mental status of unclear etiology and for suspected opioid co-ingestion include dextrose, thiamine, and naloxone and for bronchospasm selective beta-2-agonists (albuterol).

In cases of chronic exposure all reasonable means of reduction or complete removal of the toxic agent are warranted, and a consultation with poison control or an industrial hygienist may be helpful. The use of personal protective equipment and training in its use are often neglected, especially in the field and by temporary workers (see Chapters 5 and 6). In severe cases, the patient should be reevaluated with thorough neurophysiological and, if applicable, neuropsychological testing on a repeated basis with average frequency of one EMG and NCS study every 9 to 12 months until sufficient progress or stabilization is noted (39).

Neurotoxicity of Organochlorine Compounds

Pesticides such as dichlorodiphenyltrichloroethane (DDT), endrin, dieldrin, aldrin, endosulfan, chlordane, heptachlor, lindane, and chlordecone have been in use since the late 1940s and are readily available, in most countries, to be used alone or in combination with other pesticides as sprays, powders, pellets, and dusts (see Chapter 13). These are lipophilic compounds and many of them have been demonstrated to form depots in tissues with high lipid content, especially the brain. This specific chemistry of organoclorines makes serum level measurements uninformative, as severe toxicity has been documented in patients with low serum levels as a result of chronic exposure and sequestration of the toxin in the organism. Most of these compounds (cyclodienes, hexachlorocyclohexanes, and toxaphene organochlorines) inhibit the γ-aminobutyric acid (GABA) receptors and prevent chloride influx in the CNS, resulting in a typical "GABA-ergic" clinical picture of agitation, confusion, and seizures (40–42).

Organochlorines are divided into highly toxic (aldrin, dieldrin, endrin [banned in the United States], and endosulfan) and moderately toxic (chlordane, DDT [banned in the United States], heptachlor, kepone, lindane, mirex, and toxaphene). There are no nontoxic organochlorine-based pesticides, and cumulative exposure to even moderately toxic agents may lead to severe disability (42).

In acute exposure, the onset of symptoms is abrupt and caused by CNS stimulation and lowering of the seizure threshold. Patients often develop nausea and vomiting, followed by confusion, tremors, coma, seizures, and respiratory depression. Fatality may occur within 4 to 8 hours and is primarily due to respiratory failure or seizures. Cerebral edema may occur and is viewed as a negative prognostic sign. Emergency treatment with cholestyramine has been associated with better prognosis and somewhat higher efficacy than the commonly used activated charcoal (these agents can be used concurrently). Induced diuresis, hemodialysis, and hemosorption with activated charcoal have not been shown to be effective in enhancing the elimination of the toxin (40,41).

Patients with long-term occupational exposure to organochlorine pesticides may develop a variety of nonspecific complaints including headaches, nausea, fatigue, muscle twitching, and visual disturbances. There is no reliable statistical data associating exposure to organochlorines with any specific type or location of cancer. Some of the less obvious signs of cumulative toxicity of these chemicals include paresthesias of the face, auditory or visual hallucinations, and perceptual disturbances, although the latter are more reliably associated with acute toxicity (41–44).

Management

Treatment is supportive, although in cases of significant exposure, seizure control may be necessary. Seizures induced by organochlorine pesticides

respond well to benzodiazepines. The prognosis is variable based on amount and type of exposure (42).

Neurotoxicity of Organophosphate and Carbamate Compounds

Organophosphate compounds such as diazinon, disulfoton, azinphos-methyl, chlorpyrifos, and fonofos are used widely in agriculture. Some have been phased out in the United States but remain in active use in other countries. Other agents with similar action include toxic nerve gases that have gained significant publicity as potential chemical warfare and terrorism agents (Sarin). Carbamate compounds also have been developed as pesticides and are associated with less toxic effects in humans. Currently, agricultural exposure is the most common epidemiological site of organophosphate poisoning, and any worker in the industry can be affected, including manufacturers, field workers, truckers who transport pesticides or produce, and crop dusters (45).

Pathophysiology

Carbamate and carbamate-based pesticides exhibit their toxic action via inhibition of acetylcholinesterase, an enzyme found in nicotinic and muscarinic receptors in nerve, muscle, gray matter of the brain, and red blood cells. Inhibition of this enzyme leads to central, parasympathetic, and sympathetic neurotoxicity (45).

Most organophosphates (especially the nerve gases) induce irreversible phosphorylation of the serine hydroxyl moiety at the binding site of the enzyme, thus reducing the esterase activity. This block may be reversed by the administration of the commonly used specific antidote pralidoxime (2-PAM), but with passage of time the natural cellular proteinases are activated and the majority of poisoned enzyme is taken inside the cell (thus rendering it inaccessible to the action of 2-PAM) and proteolytically destroyed within 24 hours. Although the rate of synthesis of acetylcholinesterase in the neuron has not been measured with satisfactory precision, the much more easily measured enzyme levels in the erythrocyte increase very slowly, by less than 1% a day (46).

Acetylcholinesterase inhibition induced by carbamate-based pesticides is reversible, and the agents themselves have poor ability to penetrate the blood–brain barrier, which limits their clinical significance as neurotoxic agents (45,46).

In addition to the well-established rapid toxicity related to the cholinergic crisis, some of the organophosphates exhibit delayed neurotoxicity, which is due to their ability to induce axonal pathology and resulting polyneuropathy. This area of research is controversial, as is the association of preventive use

of antidotes during the first Gulf War. In several well-established cases of organophosphorous ester–induced delayed neuropathy, patients have developed the condition as a result of both acute and cumulative exposure, with a significant time delay factor (more than a week) after single acute exposures and an even less certain and more expanded latent period in chronic exposure. Typically, the spinal cord tracts and distal axons of the lower extremities are involved more than the upper extremities. Primary axonopathy is accompanied by secondary demyelination in which both sensory and motor fibers are involved. The delayed toxicity is not due to acetylcholinesterase poisoning but rather a result of phosphorylation of a receptor protein. In complicated cases of neuropathy following pesticide exposure, a sural nerve biopsy may be performed and blood samples may be analyzed for the levels of the target protein (45,46).

A unique case addressed neuropathic changes observed in a middle-aged man who had one episode of exposure to sarin during the 1995 terrorist attack in a Tokyo subway. Peripheral nerve biopsy found severe sensory and motor fiber loss and a postmortem examination revealed nearly total loss of myelinated fibers in the white matter of the spinal cord with apparent sparing of the posterior columns. Brain changes were also found to be consistent with hypoxic-ischemic encephalopathy (47).

Genetic predisposition may play a role in the development of chronic exposure–induced delayed neurotoxicity. At least two research groups found the correlation between the development of Parkinson's disease as a result of exposure to organophosphate pesticides and genetic polymorphisms of glutathione transferase, an antioxidant enzyme. As dopamine is the only known major neurotransmitter that produces an active (and toxic) free radical when metabolized by monoaminooxidase, patients with decreased cellular proxidant scavenging ability may be more susceptible to development of Parkinson's disease and dementia with Lewy bodies (44,48,49).

Elbaz and colleagues (50) performed a case-control study of Parkinson's disease in a population characterized by a high prevalence of pesticide exposure. The authors also studied the joint effect of pesticide exposure and the activity of a cytochrome CYP2D6, a protein commonly implicated in the association between pesticide neurotoxicity and the development of Parkinson's disease. The authors found that pesticides have a modest effect of increasing the incidence of Parkinson's disease in subjects who are not CYP2D6 poor metabolizers and that the effect of pesticides is increased approximately twofold in poor metabolizers. This study also found that individuals who are CYP2D6 poor metabolizers are not at increased Parkinson's disease risk in the absence of pesticide exposure (51).

Another commonly implicated protein that may be a part of the pesticide exposure link to neurodegenerative disease is alpha-synuclein, a small, highly charged protein expressed predominantly in neurons. It is the major building block of pathological inclusions that characterize many neurodegenerative disorders, including Parkinson's disease, dementia with Lewy bodies (DLB),

and neurodegeneration with brain iron accumulation type 1 (NBIA-1), which collectively are termed synucleinopathies. Several ongoing studies have established preliminary links between exposure to pesticides with abnormal levels of expression of synuclein and related proteins (52).

Alpha-synuclein is a presynaptic protein characterized by the lack of rigid well-defined structure. This protein may either stay unfolded or adopt an amyloidogenic folded conformation. It also might form several morphologically different types of aggregates, including oligomers, amorphous aggregates, and/or amyloid-like fibrils. This plasticity may explain why a single protein is believed to be involved in such a varied spectrum of neurodegenerative diseases. Preliminary evidence suggests that the ultimate structural fate of this and other amyloidogenic proteins depends on the levels of free radicals in tissue. This finding may explain the presence of the cytochrome system inhibition in the clinical history of some of the patients, as the malfunctioning cytochrome system is a known source of free radicals (53,54).

While measurement of synuclein in the brain tissue remains technically difficult, the issue of inhibition and induction of CYP2D6 is much more real and practical for all physicians. Table 23.5 summarizes current knowledge of the chemicals that induce and inhibit this cytochrome. Physicians may be well served by noting the connection between CYP2D6 status and prescribing

TABLE 23.5. Chemical compounds and cytochrome 2D6.

CYP2D6 substrates	CY2D6 inducers	CYP2D6 inhibitors
Most tricyclic antidepressants: amitriptyline, nortriptyline, clomipramine, desipramine, imipramine, doxepin	Carbamazepine	Amiodarone
Many antipsychotics: clozapine, risperidone, chlorpromazine, haloperidol, fluphenazine, thioridazine	Phenobarbital	Cimetidine
Opioids and opioid-like analgesics: codeine, hydrocodone, oxycodone, morphine, methadone meperidine, tramadol	Phenytoin	Clomipramine
Some antidepressants: fluoxetine, paroxetine, venlafaxine, trazodone	Rifampin	Desipramine
Many beta-1-blockers: bisoprolol, metoprolol, propranolol, timolol	Ritonavir	Fluoxetine
Alzheimer's disease medication: donepezil		Fluphenazine
Antiarrhythmics: flecainide, mexiletine, propafenone		Haloperidol
Stimulants: methamphetamine		Mibefradil
		Paroxetine
		Propafenone
		Quinidine
		Ritonavir
		Sertraline
		Thioridazine

Source: Data from Michalets (55).

medications that are less likely to inhibit this enzyme or to compete with other substrates, such as pesticides (55).

Diagnosis

Patients with acute poisoning present with classical symptoms of cholinergic excess. Two acronyms are used as mnemonic devices to aid in memorization of symptoms:

1. DUMBELS: diarrhea, urination, miosis, bronchospasm, emesis, lacrimation, and salivation
2. SLUDGE: salivation, lacrimation, urination, diarrhea, gastrointestinal distress, and emesis

Both mnemonics emphasize the muscarinic side of the cholinergic crisis, while no acronym has been suggested for the nicotinic side, often manifesting as fasciculations, muscle weakness, hypertension, and tachycardia. Additional muscarinic effects include reduction of sinus node and atrioventricular conduction, causing bradyarrhythmias or resultant ventricular dysrhythmias (56).

Organophosphate poisoning should be suspected in any agricultural workers who present with constricted pupils, especially if they also exhibit restlessness, emotional lability, or confusion. Other warning signs include slurred speech, ataxia, tremor, muscle weakness with cramping, fasciculations, and, less commonly, seizures. In these cases a rapid and reliable measurement of red blood cell esterase activity may be both of confirmatory diagnostic and of significant prognostic value (see Chapter 9) (56).

Emergency physicians have agreed on the classification of the degree of severity of poisoning based on easily measured red blood cell cholinesterase (see Chapter 9 for a discussion of baselines):

1. Mild poisoning: loss of 20% to 50% of baseline activity
2. Moderate poisoning: observed activity of only 10% to 20% of the expected baseline (80% to 90% loss of activity)
3. Severe poisoning: patients with less than 10% of esterase activity (or more than 90% loss) (56)

Management

Atropine was used as the sole treatment until the enzyme-specific antidote pralidoxime chloride (Protopam, 2-PAM, a relatively nontoxic substance) was developed and is still used as the sole treatment in developing countries. In the United States, the standard protocol calls for the use of pralidoxime in mild cases and coadministration of pralidoxime and atropine in moderate and severe poisonings. In cases of oral ingestion, activated charcoal in suspension may be used if the patient is seen within 30 minutes of ingestion (Table 23.6) (56)

TABLE 23.6. Medications useful in management of toxicity associated with agricultural exposure.

Drug	Adult dosage	Contraindications	Interactions	Pregnancy	Complications and adverse effects
Dimercaprol (BAL suspension in peanut oil)	0.5–3 mg/kg q4h IM for 2 d, then q.i.d. for 1 d followed by b.i.d. for 10 d. Higher doses may be needed. Maximum dose is 5 mg/kg	Documented hypersensitivity; hypersensitivity to peanuts; G-6-PD deficiency; concurrent iron supplementation therapy	Selenium, uranium, iron, or cadmium may increase toxicity	Class C—Safety for use during pregnancy has not been established	Fever, tachycardia, hypertension, headache, CNS stimulation, nausea and vomiting. Sterile abscess may develop at injection site. May induce hemolysis in G-6-PD–deficient patients
Succimer (Chemet)	PO dose 10 mg/kg q8h × 5 d; 10 mg/kg q12h × 14 d	Documented hypersensitivity	Do not administer concomitantly with edetate calcium disodium or penicillamine	Class B—Usually safe but benefits must outweigh the risks	Excreted via kidneys, adequate hydration must be maintained; patients with renal insufficiency should be treated with caution. Not the 1st choice in arsenic poisoning. Watch for nausea/vomiting, thrombocytopenia, eosinophilia, and cardiac dysrhythmias.
Penicillamine (Cuprimine, Depen)	25 mg/kg PO, q6h to maximum 1 g/d	Documented hypersensitivity	Increases effects of immunosuppressants, phenylbutazone, and antimalarials; decreases digoxin effects zinc salts, antacids, and iron may decrease effects	Class B—Usually safe but benefits must outweigh the risks	Nausea, vomiting, fever, rash, neutropenia, thrombocytopenia, eosinophilia, and Stevens-Johnson reaction

continued

TABLE 23.6. Medications useful in management of toxicity associated with agricultural exposure. (continued)

Drug	Adult dosage	Contraindications	Interactions	Pregnancy	Complications and adverse effects
Atropine (Atropair)	1 mg IV (initial or diagnostic) 2–4 mg IV q15min (therapeutic). Also, 2 mg/kg/h IV drip as needed to control secretions	Documented hypersensitivity; thyrotoxicosis, narrow-angle glaucoma, and tachycardia	Coadministration with other anticholinergics have additive effects; pharmacologic effects of atenolol and digoxin may increase; antipsychotic effects of phenothiazines may decrease; antidepressants with anticholinergic activity may increase effects of atropine	Class C—Safety for use during pregnancy has not been established	Caution in patients with (1) brain damage to prevent hyperreactive response; (2) coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension; (3) peritonitis, ulcerative colitis, hepatic disease, and reflux esophagitis; (4) prostatic hypertrophy.
Pralidoxime (2–PAM, Protopam)	1–2 g IV over 15 min initial; followed by 500 mg/h IV until improved muscle strength	Documented hypersensitivity	None reported	Class C—Safety for use during pregnancy has not been established	Relatively nontoxic compounds; not effective for poisonings caused by organophosphates without anticholinesterase activity.

Source: Data from Jeyaratnam and Maroni (56).

Aggressive and timely therapy usually leads to recovery from acute toxicity within 10 to 14 days. Delayed intervention or chronic exposure may lead to impaired recovery and possible permanent neurological sequelae. Such sequelae may lead to delayed fatalities as observed after the 1995 Tokyo terrorist attack (56).

Acute poisoning does not warrant extensive imaging or electrophysiological studies, as they may contribute little new information in a typical case. Of course, any focal deficit must be investigated as aggressively as the case warrants and local conditions would allow. Both NCS and EMG are helpful and should be repeated on a regular basis (every 9 to 12 months) in cases of pesticide-induced neuropathies and, somewhat surprisingly, also in patients who require mechanical ventilation. Singh et al. (44) examined the phrenic nerve conduction of 29 patients with organophosphate toxicity admitted to the hospital in 1997, 14 of whom required mechanical ventilation. They found that the reduction in compound muscle action potential (CMAP) correlated with the need for ventilatory assistance. By following patients with daily nerve conduction studies, the authors were able to predict successful weaning.

References

1. Feldman RG. Recognizing the chemically exposed person and approach to diagnosis. In: Feldman RG, ed. Neurotoxicology. New York: Lippincott, 1999.
2. Charcot JM. Clinical Lectures of Diseases of the Nervous System. New York: Landmark Library of Neurology and Neurosurgery, 1994.
3. Ford M. Arsenic. In: Goldfrank LR, Flomenbaum NE, et al., eds. Toxicology Emergencies. New York: McGraw Hill; 1994.
4. LaDou J. Approach to the diagnosis of the occupational illness. In: LaDou J, ed. Occupational and Environmental Medicine, 2nd ed. New York: Lange, 1997.
5. So Y. Neurotoxicology. In: LaDou J, ed. Occupational and Environmental Medicine, 2nd ed. New York: Lange, 1997.
6. Carod-Artal FJ. [Neurological syndromes linked with the intake of plants and fungi containing a toxic component (I). Neurotoxic syndromes caused by the ingestion of plants, seeds and fruits.] Rev Neurol 2003;36:860–71.
7. Vetter J. Poison hemlock (*Conium maculatum L.*) Food Chem Toxicol 2004;9:1373–82.
8. Carod Artal FJ. [Neurological syndromes associated with the ingestion of plants and fungi with a toxic component (II). Hallucinogenic fungi and plants, mycotoxins and medicinal herbs]. Rev Neurol 2003;36:951–60.
9. Van Sittert NJ, Tuinman CP. Rodenticides. Toxicology 1994;91:71–6.
10. Watson WA, Litovitz TL, Klein-Schwartz W, et al. 2003 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 2004;22:335–404.
11. Arowolo TA. Heavy metals and health. West Indian Med J 2004;53:63–5.
12. Albers JW, Kallenbach LR, Fine LJ, et al. Neurological abnormalities associated with remote occupational elemental mercury exposure. Ann Neurol 1999;25:651–9.
13. Chu CC, Huang CC, Ryu SJ, et al. Chronic inorganic mercury induced peripheral neuropathy. Acta Neurol Scand 1998;98:461–5.

14. Johnston MV, Goldstein GW. Selective vulnerability of the developing brain to lead. Curr Opin Neurol 1998;11:689–93.
15. American Academy of Pediatrics. Treatment guidelines for lead exposure in children. Pediatrics 1995;96:155–60.
16. Heyman A, Pfeiffer JB, Willett RW. Peripheral neuropathy caused by arsenical intoxication: a study of 41 cases with observations on the effects of BAL (2,3,dimercapto-propanol). N Engl J Med 1956;254:401–9.
17. Takizawa EK, Akagi H, Haraguchi K, et al. Differential diagnosis between organic and inorganic mercury poisoning in human cases: pathologic point of view. Toxicol Pathol 1999;27:664–71.
18. Urban P, Lukas E, Benicky L. Neurological and electrophysiological examination on workers exposed to mercury vapors. Neurotoxicology 1996;17:191–6.
19. Harada M. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. Crit Rev Toxicol 1995;25:1–24.
20. Tokuomi H, Okajima T, Kanai J, et al. Minamata disease. World Neurol 1961;1:536–44.
21. Miyakawa T, Murayama E, Sumiyoshi S, et al. Late changes in human sural nerves in Minamata disease and in nerves of rats with experimental organic mercury poisoning. Acta Neuropathol (Berl) 1976;35:131–8.
22. O'Carroll RE, Masterton G, Dougall N. The neuropsychiatric sequelae of mercury poisoning: the Mad Hatter's disease revisited. Br J Psychiatry 1995;167:95–8.
23. Letz R, Gerr F, Cragle D. Residual neurologic deficits 30 years after occupational exposure to elemental mercury. Neurotoxicology 2000;21:459–74.
24. Mahaffey KR. Recent advances in recognition of low-level methylmercury poisoning. Curr Opin Neurol 2000;13:699–707.
25. Grandjean P, Guldager B, Larsen IB, et al. Placebo response in environmental disease: chelation therapy of patients with symptoms attributed to amalgam fillings. J Occup Environ Med 1997;39:707–14.
26. Bender MT, Williams JM. A real plan of action on mercury. Public Health Rep 1999;114:416–20.
27. Franzblau A, Lilis R. Acute arsenic intoxication from environmental arsenic exposure. Arch Environ Health 1989;44:385–90.
28. Massey EW. Arsenic neuropathy. Neurology 1981;31:1057–8.
29. Donofrio PD, Wilbourn AJ, Albers JW. Acute arsenic intoxication presenting as Guillain-Barre-like syndrome. Muscle Nerve 1987;10:114–20.
30. Hoffman RS. Thallium toxicity and the role of Prussian blue in therapy. Toxicol Rev 2003;22:29–40.
31. Loyke HF. Effects of elements in human blood pressure control. Biol Trace Elem Res 2002;85:193–209.
32. Altmann L, Neuhann HF, Kramer U. Neurobehavioral and neurophysiological outcome of chronic low-level tetrachloroethene exposure measured in neighborhoods of dry cleaning shops. Environ Res 1995;69:83–9.
33. Altmann L, Bottger A, Wiegand H. Neurophysiological and psychophysical measurements reveal effects of acute low-level organic solvent exposure in humans. Int Arch Occup Environ Health 1990;62:493–9.
34. Lowinson J, Ruiz P. Volatile substances. Substance Abuse 1992;303–27.
35. Corsi G, Maestrelli P, Picotti G. Chronic peripheral neuropathy in workers with previous exposure to carbon disulphide. Br J Ind Med 1983;40:209–11.

36. Astrand I. Uptake of solvents in the blood and tissues of man: a review. Scand J Work Environ Health 1975;1:199–218.
37. Aaserud O, Hommeren OJ, Tvedt B. Carbon disulfide exposure and neurotoxic sequelae among viscose rayon workers. Am J Ind Med 1990;18:25–37.
38. Moen BE. Work with chemicals on deck of Norwegian chemical tankers. Int Arch Occup Environ Health 1991;62:543–7.
39. American Conference of Governmental Industrial Hygienists. Threshold limit values and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1999.
40. Rosenstock L, Keifer M, Daniell WE. Chronic central nervous system effects of acute organophosphate pesticide intoxication. The Pesticide Health Effects Study Group. Lancet 1991;338:223–7.
41. Lotti M, Becker CE, Aminoff MJ. Organophosphate polyneuropathy: pathogenesis and prevention. Neurology 1984;34:658–62.
42. Tordoir WF, van Sittert NJ. Organochlorines. Toxicology 1994;91:51–7.
43. Peter JV, Cherian AM. Organic insecticides. Anaesth Intensive Care 2000;28:11–21.
44. Singh G, Sidhu UP, Mahajan R. Phrenic nerve conduction studies in acute organophosphate poisoning. Muscle Nerve 2000;23:627–32.
45. Lessenger JE, Reese BE. The pathophysiology of acetylcholinesterase inhibiting pesticides. J Agromed 2000;7:5–19.
46. Lessenger JE, Reese BE. Rational use of cholinesterase activity testing in pesticide poisoning. J Am Board Fam Pract 1999;12:307–14.
47. Himuro K, Murayama S, Nishiyama K. Distal sensory axonopathy after sarin intoxication. Neurology 1998;51:1195–7.
48. Menegon A, Board PG, Blackburn AC, Mellick GD, Le Couteur DG. Parkinson's disease, pesticides, and glutathione transferase polymorphisms. Lancet 1998;352:1344–6. `
49. Bhatt MH, Elias MA, Mankodi AK. Acute and reversible parkinsonism due to organophosphate pesticide intoxication: five cases. Neurology 1999;52:1467–71.
50. Elbaz A, Levecque C, Clavel J, et al. CYP2D6 polymorphism, pesticide exposure, and Parkinson's disease. Ann Neurol 2004;55:430–4.
51. Deng Y, Newman B, Dunne MP, Silburn PA, Mellick GD. Further evidence that interactions between CYP2D6 and pesticide exposure increase risk for Parkinson's disease. Ann Neurol 2004;55:897–902.
52. Norris EH, Giasson BI, Lee VM. Alpha-synuclein: normal function and role in neurodegenerative diseases. Curr Top Dev Biol 2004;60:17–54.
53. Rutchik JS, Rutkove SB. Effect of temperature on motor responses in organophosphate intoxication. Muscle Nerve 1998;21:958–60.
54. Uversky VN. A protein-chameleon: conformational plasticity of alpha-synuclein, a disordered protein involved in neurodegenerative disorders. J Biomol Struct Dyn 2003;21:211–34.
55. Michalets EL. Cytochromes. Pharmacotherapy 1998;18(1):84–112.
56. Jeyaratnam J, Maroni M. Organophosphorous compounds. Toxicology 1994;91:15–27.

24

Repetitive Motion Injuries

Steven R. Kirkhorn and Guilia Earle-Richardson

Key words: repetitive stress disorders, cumulative trauma disorders, carpal tunnel syndrome, tendonitis

The terminology of repetitive motion injuries has changed over the last several years. The term now used by the United States Department of Labor and the National Institute of Occupational Safety and Health (NIOSH) to describe adverse health effects of repetitive motion to the musculoskeletal system is *musculoskeletal disorders* (MSDs). When these injuries or disorders are considered to be work related, they are identified as work-related musculoskeletal disorders (WMSDs). Other common names used interchangeably over the years have included repetitive stress injuries (RSIs), repetitive stress disorders, cumulative trauma disorders (CTDs), and overuse syndrome. Musculoskeletal disorders refer to conditions that involve nerves, tendons, muscles, and supporting structures of the body. They do not include injuries resulting from slips, trips, falls, motor vehicle crashes, or similar causes (1,2).

A definition of WMSDs by the State of Washington Bureau of Labor and Industry that captures the full spectrum is as follows:

> Non-traumatic disorders of the soft tissues of the musculoskeletal system that can be caused or aggravated by work activities such as repetitive forceful motions, awkward postures, use of vibrating tolls or equipment, or by manual handling of heavy awkward loads. Examples include carpal tunnel syndrome, tendonitis, epicondylitis, hand–arm vibration syndrome, rotator cuff syndrome, cubital tunnel syndrome, and sciatica. Work-related disorders are primarily, but not exclusively, associated with the upper extremity and back (2).

Musculoskeletal disorders may affect soft tissue (muscle, tendon, ligament, bursa, cartilage, nerve, blood vessel, disk) or bone. Generally the symptoms do not arise from one acute episode of significant trauma but are the result of continual exposure to repetitive force and microtrauma that exceeds the ability of the body to recover and adequately repair structural damage. The terms RSI, MSD, and CTD are not a specific diagnosis but include both clinical entities and symptoms of pain.

The identification and prevention of repetitive motion injuries is a priority area in agricultural medicine. Upper-extremity MSDs are a priority area of the National Occupational Research Agenda for Musculoskeletal Disorders. Additionally, the U.S. Department of Health and Human Services Healthy People 2010 project has set a goal (Goal 20-3) to reduce the rate of injury and illness cases involving days away from work due to overexertion or repetitive motion (3–5).

For the purposes of consistency, MSDs will be used to refer to repetitive motion injuries arising from occupational exposures. The focus of this chapter is on diagnosis and treatment of common MSDs affecting the upper and lower extremities, based on available evidence-based medicine, determination of work-relatedness, ergonomic issues in agriculture leading to MSDs, and prevention through engineering and work practices that are applicable to agriculture. Although the neck and back are the body parts most commonly affected by repetitive motion injuries and are mentioned in this chapter, a detailed discussion of spinal injuries and conditions were addressed in Chapter 17.

Extent of Musculoskeletal Disorders in Agriculture

According to the 2001 United States Bureau of Labor Statistics Annual Report, MSDs accounted for 522,528 (34%) of 1,537,567 nonfatal occupational injuries and illnesses involving lost time. In agriculture, forestry, and fishing, MSDs accounted for 8,733 incidents (22%) out of 40,153 nonfatal occupational injuries resulting in lost work time. Presumably, the actual numbers are higher in agriculture than reported as family farms are excluded from occupational statistics, and agricultural injuries are commonly considered to be underreported in agricultural operations, even in farms with 11 or more employees where reporting is mandatory. In 1997, the median time away from work due to overexertion injuries was 6 to 7 days. The median time off work as a result of injuries or illnesses due to repetitive motion in agriculture was 17 days (4,6).

The U.S. Department of Labor National Agricultural Workers Survey reported that 11% of workers complain of musculoskeletal pain or discomfort during their first year of work and 19% of workers with 10 or more years of farm work make such complaints. The percentage reporting joint or muscle pain was highest in those working in multiple crops (20%) and lowest in horticulture (11%). The reported rate for tendonitis in the agriculture, forestry, and fishing industry in 2001 was 1.3 per 10,000 workers compared to 1.6 per 10,000 workers in all private sector workers. The reported rate for carpal tunnel syndrome was 1.1 per 10,000 workers in agriculture, forestry, and fishing, lower than the rate of 3.0 per 10,000 for all private sector workers. Farmers are among the civilian occupations with the highest risk for hand–wrist arthritis with odds ratios (OR) of 2.71 (95% confidence interval

[CI], 1.27–5.36) by farmers, forestry, and fisheries occupation and OR of 3.6 (95% CI; 1.87–6.93) in the agricultural, forestry, and fisheries industry sector. A prevalence of 28% of hand and wrist pain and an OR of 1.72 (95% CI 1.34–2.21) was reported in a survey of New York farmers. The landscape and horticulture industry in Washington State is in the top 12 industries with the highest rates of musculoskeletal disorders in a Washington State–based review of the compensable workers' compensation cases from 1991 to 1999 (7–10).

Body Parts Affected and Common Conditions

Across all industries, the most common injuries are sprains and strains, followed by soreness and pain. The body parts most commonly affected are, in descending order, the back, neck, shoulder, wrist, knee, and multiple body systems. The mechanism most likely to result in an injury is overexertion, particularly while lifting. In a survey of migrant health centers in New York and Pennsylvania, joint and muscle strains were the most common type of injuries; they occurred most often in orchard work, and resulted from overuse, assuming an awkward position, and weight-bearing activity. Back, neck, and shoulder strains account for 39% of occupational health injuries at migrant health centers (6,11).

The California Farm Worker Survey from 1991 to 1996 reported the most prevalent types of injury events were overexertion and strenuous movement (13.5%). The body parts most commonly affected were, in descending order, the lower back, upper back, wrist, shoulder, knee, and neck. Cross-sectional studies of farmers in Ohio and Alabama have also reported sprains and strains as the most common types of injuries. Dairy farming is also associated with hand–wrist symptoms. Swedish research has identified three milking tasks (cleaning, premilking, and attaching) with high movement velocities and extreme positions (12–15).

A concern raised in a NIOSH conference regarding MSDs in children and adolescents is the impact of ergonomic hazards on the immature musculoskeletal system. Strains and sprains were one of the most common injuries in adolescents working on farms. Weeding by hand, washing and packing produce, loading and unloading produce, and tractor operation were five activities believed too strenuous for children and adults. A survey of North American fresh market vegetable growers and the children and adolescent workers reported low back (26%), foot and ankle (21%), knee (18%), and neck (16%) pain. Fresh market vegetable production requires soil preparation, planting, transplanting, weeding, hand harvesting, and product handling. Smaller operations often involve extensive and inefficient hand labor, and high levels of physical effort (see Chapter 12) (16–19).

Upper Extremity

Ergonomic risk factors for MSDs include repetitive motion, awkward posture, long duration of repetitive activity, lack of recovery time, forceful movement, vibration, uncomfortable conditions (cold, wet), and stressful work organization. Relatively few studies of sufficient quality exist to assess the work-site causative factors associated with MSDs other than back pain, hand/wrist/elbow MSDs, and knee/hip arthritis. Nonoccupational factors such as gender, age, work satisfaction, other additive occupational or recreational activities, and chronic medical conditions and lifestyle practices such as diabetes, hypothyroidism, arthritis, obesity, pregnancy, and alcohol use are potential confounding factors. There is general agreement that a combination of forces (force, repetition, posture, and vibration) is most strongly associated with carpal tunnel syndrome, tendonitis, and lateral epicondylitis, particularly high force and high repetition. There is also positive evidence for the association of force, repetition, and vibration alone or in combination with carpal tunnel syndrome. There is also positive evidence for force, repetition, and posture alone for tendonitis and force alone for lateral epicondylitis. There is insufficient evidence for posture alone as a risk factor for clinical diagnoses. Shoulder pain syndromes and shoulder tendonitis is positively associated with highly repetitive work and repeated or sustained work postures above 60 degrees flexion or abduction (16–22).

High repetition is considered to be a cycle time of less than 30 seconds or more than half of the cycle spent in an activity and greater than the recovery time. High force is considered to be 6 kg of force or greater. Frequency can also be determined by the work load index, which is the number of pieces handled per hour times the number of hours worked. Other determinants of work-relatedness include regular tasks requiring high force by the hand on the affected side, a job involving frequent, repetitive use of the same or similar movements of the affected hand or wrist, regular use of vibrating handheld tools, frequent or prolonged pressure over the wrist or base of the palm on the affected side, and regular or sustained tasks requiring awkward position (20–22).

The meat processing industry is well known as a high-risk industry for MSDs, and before implementation of a voluntary participatory ergonomics program that was instituted in the early 1990s, the prevalence of repetitive motion injuries was as much as 75 times higher than the general industry rate. Cold is also considered to play an important role in the development of MSDs. Some of the highest incidences of carpal tunnel syndrome occur in frozen food workers and butchers. A four times greater risk of carpal tunnel syndrome occurs in frozen food workers than in those performing repetitive work in normal temperatures (23,24).

Lower Extremity

The best evidence of lower extremity repetitive motion injuries applies to hip and knee osteoarthritis. A strong positive association between frequent

bending of the knee and the development of osteoarthritis of the knee has been reported. Dairy farming, which is primarily milking and tractor driving, has been shown to have odds ratios (OR) ranging from 1.39 to 2.98 for hip and knee osteoarthritis. A study of Swedish farmers reported a dose-response association between the number of cows milked (OR 4.5; 95% CI 1.9–11.0) or working more than 5 hours per day (OR 13.3; 95% CI 1.2–145.0) and the onset of hip or knee disease (25–29).

Specific Ergonomic Forces Associated with Musculoskeletal Disorders

Agricultural work varies significantly with the type of commodity and associated work practices. Certain types of work practices are strongly identified as being at greater risk for repetitive injuries, such as manual harvest of small vegetables and fruits, meat processing, and dairy farming. A 3-year, NIOSH-supported study focusing on identifying priority MSDs in California nurseries reported upper extremity and back injuries as the most commonly reported injuries. Job tasks with the highest risk of MSDs were considered to be propagation (cuttings), canning (transport to field), field work (pruning, spacing, and weeding), and shipping. Job analysis identified highly repetitive gripping, high pinch forces, contact stress, and awkward posture associated with the use of non-power hand tools and material handling, which characterize those job tasks (30).

An assessment of California vineyards by the University of California Ergonomics Research Center found a high proportion of jobs involving repetitive heavy lifting, bending, and stooping. Hand harvest risk factors included highly repetitive handgrip; exertion of high force to carry full tubs; multiple awkward positions involving the shoulders, forearms, and trunk; highly repetitive cutting and reaching; and moderate forceful exertions involving the shoulders and arms. Grapevine pruning involves a high level of muscular activity associated with hand-powered professional pruning shears and has been associated with musculoskeletal hand disorders, in particular paresthesias of the dominant hand (31,32).

In the northeastern United States, research has been conducted on ergonomic hazards for apple harvest workers. This type of hand labor exposes workers to weight-bearing hazards and awkward postures. The result is that back, neck, and shoulder strain are among the most common occupational health complaints seen at health centers within this population. A posture, activities, tools, and handling (PATH) methodology for quantifying ergonomic hazard exposure developed for industry has been adapted for orchard work. This PATH methodology is a validated work-sampling tool for quantifying ergonomic risk factors in jobs involving nonrepetitive work. In 2001 a PATH assessment of 14 apple harvest workers showed that they spent nearly two-thirds of the harvest observation period (62.9%) reaching and

picking and 78.5% of the time bearing weight. Full apple bags in this study weighed up to 42 lb (19 kg), and ladders ranged from 10 to 25 lb (4.54 to 11.34 kg). The common postures and posture-load combinations observed were the arm, shoulders, and elbows elevated with and without loads. Comparison to PATH assessments of jobs in construction and nursing show apple harvest work to be at least as hazardous (see Chapter 6) (11,33–38).

Selected Clinical Conditions

Characteristics of RMI and MSDs include the following:

1. Symptoms are related to intensity of use.
2. A condition may take years to develop and weeks to years to resolve.
3. Nonspecific symptoms predominate.
4. Specific syndromes can have nonoccupational causes.

Extrinsic risk factors of MSDs include motivation, job satisfaction, and monotony of jobs. Ergonomic factors include additive outside recreational activities, piecework, and overtime. Physiological factors of repetitive forceful work include muscle fatigue resulting in a reduced muscular activity to sustain the existing effort. If the effort exceeds 15% of maximal voluntary contraction, the muscle blood flow is reduced or cut off, leading to ischemia of tissues. This leads to biochemical changes resulting from anaerobic metabolism, accumulation of lactate and depletion of adenosine triphosphate (ATP) leading to and muscle pain and microtrauma. If there are not adequate rest cycles, the body's capacity is exceeded. Avoiding fatigue with many short rest periods during intense work can improve blood flow and counteract muscle fatigue. This can also affect other anatomic structures. One useful method of looking at upper extremity (UE) MSDs is to divide the upper extremity into the proximal UE (shoulder girdle and upper arm) and distal UE (elbow, forearm, wrist, and hand). The proximal UE affects the muscles and impingement of the rotator cuff while the distal UE exposures can affect muscle-tendon units or nerves. Categories of nerve entrapment units include tendon entrapment, peritendonitis, and epicondylitis. See Table 24.1 for categories of muscle-tendon unit conditions and Table 24.2 for specific clinical entities (39). Other upper extremity conditions that are not typically considered to be work-related are Dupuytren's contracture and ganglion cysts (39–43).

Diagnosis involves a careful occupational history, physical examination, and, infrequently, laboratory tests or imaging for MSDs, unless there is a history of trauma or unusual objective physical findings. Nerve conduction studies are critical in diagnosing nerve entrapment syndromes (40).

Treatment involves modification of the work to prevent the postural and repetitive activities that caused the problem; modification of the workplace ergonomic hazards or stressors; resting the injured part; splinting; physical

Table 24.1. Classification of muscle-tendon unit conditions.

Category	Definition	Clinical entity	Clinical findings
1. Tendon entrapment	Tendon entrapment of dorsal wrist compartment	1. DeQuervain's	1. Pain over affected compartment
2. Stenosing tenosynovitis		2. Intersection syndrome	2. Swelling, thickening 3. Crepitus
Peritendinitis	Extensor side of distal half of forearm affecting extensor tendons	Tendonitis	1. Acute inflammatory 2. Swelling, redness
Lateral/medial epicondylitis	Collagen degeneration and disorganized repair at flexor/extensor insertion at elbow	Tennis elbow and golfer's elbow	1. Localized tenderness at epicondyles 2. Pain with resisted maneuvers involving wrist

Source: Data from Rose et al. (40), Harris and Glass (41), Zuckerman et al. (42), Guidotti (43), and Fongemie et al. (44).

therapy modalities, including iontophoresis; progression to rehabilitation; and preventing deconditioning. Severe cases may require surgery (Tables 24.2 and 24.3) (39–43).

Shoulder Impingement

The rotator cuff is composed of four muscles: the supraspinatus, infraspinatus, subscapularis, and terres minor. The supraspinatus is the primary rotator cuff area involved in impingement and tears. Impingement is the primary cause of rotator cuff tendinopathy, calcification, and degenerative tears. Acromioclavicular osteoarthritis resulting in osteophyte formation often results in impingement. Repetitive overhead work, reaching, and throwing activities can begin the process of impingement beginning in the third decade. By the fifth decade, ischemia can lead to fibrosis and tendonitis and a weakened supraspinatus that is more susceptible to tears with lesser trauma (44).

Pain at night and with overhead activities is typical of shoulder impingement injuries. Clinical signs include painful arc, positive empty-can sign, lift-off sign, and Hawkins and Neer impingement signs. Radiographs may show acromioclavicular (AC) narrowing and inferior osteophyte formation. Magnetic resonance imaging (MRI) is indicated if a rotator cuff tear is suspected and may reveal impingement upon the supraspinatus tendon, supraspinatus tendinopathy, or partial or complete tear. Subacromial corticosteroid and lidocaine injection may give temporary or permanent relief. If impingement or tear is present, arthroscopy with subacromial decompression and repair is

TABLE 24.2. Common upper extremity musculoskeletal disorders (MSDs).

Disorder	Clinical features	Tests/radiographic findings	Treatment
Impingement syndrome	1. Positive impingement signs 2. Nighttime pain	1. Positive lidocaine injection test 2. AC arthropathy 3. MRI-supraspinatus tendinopathy	1. NSAIDs 2. PT 3. Subacromial injection 4. Subacromial decompression
Biceps tendonitis	1. Often anterior manifestation of impingement 2. Positive Speed's/Yrgasen's signs	1. Often unremarkable 2. Possible calcification of bicipital tendon	1. NSAIDs 2. PT 3. Steroid injections may cause tend on rupture
Acromioclavicular (AC) arthritis	1. Tender AC 2. Positive crossover	1. AC osteophyte 2. Narrowing of AC joint	1. NSAIDs 2. Judicious steroid injection 3. Resection distal clavicle in severe cases
Carpal tunnel syndrome	1. Nighttime symptoms 2. Tinel's/Phalen's signs 3. Thenar atrophy is severe	1. Positive EMG for median entrapment 2. MRI not indicated	1. Nocturnal splint 2. Steroid injection 3. Carpal tunnel release
Lateral epicondylitis	1. Lateral elbow pain 2. Pain opening doors/ holding objects	1. Occasional calcification 2. X-rays usually not indicated	1. PT/iontophoresis 2. NSAIDs/forearm strap 3. Steroid injection tendon sheath 4. Rare lateral epicondylar release
DeQuervain's tenosynovitis	1. Pain pinching 2. Positive Finkelstein's test	Not indicated	1. NSAIDs 2. Thumb spica splint 3. Steroid injection 4. Release of first dorsal compartment

EMG, electromyogram; NSAID, nonsteroidal antiinflammatory drug; PT, physical therapy.
Source: Data from Rose et al. (40), Harris and Glass (41), Zuckerman et al. (42), and Guidotti (43).

TABLE 24.3. Management strategies.

1. Work modification
   Proper working posture to keep the affected area at a neutral position
   Improve lighting
   Decrease work hours
   Decrease repetitive motion tasks
   Decrease certain hazards such as working over head or squeezing on a tool
2. Workplace hazard modification
   Proper equipment, chairs, etc.
   Proper tools
   Modify computer programs to decrease key strokes
   Mechanization
3. Resting the injured part
4. Splinting
   Night splints
   Day splints to allow the person to work
5. Antiinflammatory medications
   Nonsteroidal antiinflammatory drugs (NSAIDs)
   Cox-2 inhibitors (far more expensive than NSAIDs)
6. Injections
   Joint
   Tendon sheaths
7. Physical therapy
   Range of motion
   Iontophoresis
   Teach active exercise and conditioning programs
8. Surgery (in severe and resistant cases)

Source: Data from Rose et al. (40), Harris and Glass (41), Zuckerman et al. (42), and Guidotti (43).

diagnostic and usually the definitive treatment. Differential diagnosis includes AC arthritis, bicipital tendonitis, rotator cuff tear, labral tear, and glenohumeral arthritis (44,45).

Carpal Tunnel Syndrome

Classic carpal tunnel syndrome (CTS) is a focal nerve entrapment of the median nerve at the carpal tunnel of the wrist resulting in a complex of clinical symptoms and signs in the distal distribution of the median nerve. The criteria in the NIOSH case definition for work-related CTS are the following:

1. Symptoms suggestive of CTS (paresthesias, hypoesthesia, or pain in distribution of the median nerve)
2. Objective findings such as positive Tinel's sign, Phalen's sign, or decreased sensation in the distribution of the median nerve or abnormal electrodiagnostic testing
3. Evidence of work-relatedness (see Chapter 25)

Classic symptoms are paresthesias and pain with repetitive activity, nocturnal awakening relieved by "flicking" the wrist, and, in later stages, dropping objects, hypoesthesia in the median distribution, and thenar atrophy resulting in weakness of the abductor pollicis longus and opposition (46,47).

Tinel's and Phalen's signs and two-point discrimination lack sensitivity and specificity for the diagnosis of CTS. Electrodiagnostic testing is the gold standard but is 90% to 95% sensitive and may be false negative if performed before 4 to 6 weeks of when symptoms begin. Nonsteroidal antiinflammatory drugs (NSAIDs) are not considered to be effective, whereas nocturnal splinting, work-site modification, and steroid injection may be of satisfactory benefit. In long-standing cases with abnormal sensation and motor weakness, carpal tunnel release is the preferred initial treatment. Nonoccupational causes must be considered including metabolic conditions causing peripheral neuropathy (diabetes, hypothyroid conditions, vitamin B_{12} deficiency, chronic alcoholism), arthritis, cervical radiculopathy, and myofascial pain conditions (47).

Lateral Epicondylitis

Lateral epicondylitis is a persistent aggravating clinical entity. It is most common between 35 and 60 years of age, rarely occurs before age 20, and is seven times more common than medial epicondylitis. Causative physical factors include forceful gripping, throwing, lifting with palms up, forceful wrist extension, and repeated blunt trauma to the elbow. Poor overall conditioning may predispose to lateral epicondylitis due to fatigue of the shoulders and increased use of the wrists. The standard treatment has been use of the forearm strap, physical therapy (PT), and corticosteroid injection if inadequate response. Recent studies have indicated that steroid injections offer short-term pain relief but no greater or even poorer long-term results than PT. Surgery is reserved for severe cases, resulting in limitation of activities of daily living persisting at least 6 months and recalcitrant to nonoperative treatment. Long-term results are not encouraging, as 5% are resistant to conservative treatment, 40% observe prolonged minor discomfort, and 25% recur within 5 years (48,49).

Regulatory Issues in the United States

In 1997 California became the first, and remains the only, state in the United States with a regulation that targets ergonomic risk factors and repetitive motion injuries [Cal/OSHA GISO 5110, Repetitive Motion Injuries (RMIs)]. The regulation specifies that if two or more workers performing the same tasks had diagnosed RMIs in the same workplace within the last 12 months, a three-step ergonomics program must be implemented. A United States OSHA Ergonomics Standard was proposed and accepted but was rescinded

by the United States Senate in 2001 and cannot be considered again as an OSHA standard. Washington State had passed a similar ergonomics standard, but that was repealed by voter initiative in 2003. As of early 2005, the U.S. approach to decreasing MSDs, outside of California, is now through an industry-specific ergonomics guideline consultative voluntary program and the workers' compensation system rather than mandated regulatory programs (50–53).

Prevention and Medical Management

A key in prevention of MSDs is early recognition. Clues to early diagnosis can be found in the workplace in the following ways:

1. Review of company injury logs for cases typical of repetitive motion injuries
2. Assessment of jobs or work conditions that cause worker complaints of pain symptoms, fatigue, or paresthesias
3. Frequent references to physical aches and pains related to certain types of work assignments by workers visiting the clinic
4. Job tasks involving activities that are known to be associated with MSDs

Astute clinicians may be able to identify patterns and help bring them to the attention of employers so ergonomic preventive strategies can be developed at the work-site through safety committees, musculoskeletal symptoms surveys, and work-site evaluations for ergonomic risk factors.

Preventive strategies include the following:

1. Providing proper tools that decrease pressure points and vibration by providing adequate padding
2. Reducing activities with high repetition or increase recovery time
3. Evaluating work-sites and practices to ensure proper body positions
4. Engineering ergonomic hazards—the preferred strategy but it is often not feasible economically (54,55)

When an injury or pain disorder does occur, temporary restrictions that decrease the amount and duration of ergonomic hazards and increase the rest cycles, job rotations that alternate time spent in activities involving alternative movements and postures, and recovery time allowed each hour can be provided along with work practice modification. Shorter and more frequent breaks are more effective than less frequent but longer breaks (Table 24.3).

Further Research

Recommendations through National Occupational Research Agenda (NORA) specific to the prevention of upper extremity MSDs in agriculture include further research on the ergonomic impact and design of tools and

equipment, such as pruning shears for nursery workers and lift handles for buckets. The National Institute of Occupational Safety and Health publications such as *Easy Ergonomics: A Guide to Selecting Non-Powered Hand Tools* and *Simple Solutions: Ergonomics for Farm Workers* are valuable and free resources with specific preventive recommendations. The unique conditions of agricultural work, such as variable weather, the awkward positions required by the natural positioning of produce in the field, and the physical characteristics of living or perishable product that affect work conditions, also require further research into cost-effective engineering and work-design and remain an ongoing challenge (NORA) (55,56).

References

1. Bernard B. A critical review of epidemiologic evidence for work-related musculoskeletal disorders of the neck, upper extremity, and low back. U.S. Department of Health Human Services (DHHS) (NIOSH) 1997; publication No. 91–141. Available at http://www.cdc.gov/niosh.ergtxt5a.html.
2. State of Washington, Bureau of Labor and Industry. Work-related musculoskeletal disorders. 2002. Available at http://hoh.wa.gov/HWS/doc/OH/occ-wmd.doc.
3. Villarejo D, Baron S. The occupational health status of hired farm workers. Occup Med 1999;14(3):613–35.
4. National Occupational Research Agenda. 2001 DHHS (NIOSH) publication No. 2001–117. 2001. Available at www.cdc.gov/niosh/pdfs/2001–117.pdf.
5. Office of Disease Prevention and Health Promotion. Healthy People 2010. Washington, DC: U.S. DHHS. http://www.healthypeople.gov/document/tableof contents.htm#partb.
6. Bureau of Labor Statistics. 2003. Available at http://www.bls.gov/iif/oshwc/osh/case/ostb1154.pdf.
7. NIOSH. Worker Health Chartbook 2004. Department of Human Health Services (NIOSH) 2004; publication No. 2004–146. Available at Http://www.cdc.gov/niosh/docs/chartbook.
8. Dillon C, Petersen M, Tanaka S. Self-reported hand and wrist arthritis and occupational data from the U.S. National Health Interview Survey-Occupational Health supplement. Am J Ind Med 2002;42:318–27.
9. Gomez MI, Hwang S, Stark AD, et al. An analysis of self-reported joint pain among New York farmers. J Agric Safety Health 2003;9:143–57.
10. Washington State Department of Health. Work-related musculoskeletal disorder. 2002. Available at http://www.doh.wa.gov/HWS/doc/OH/OCC_WMD.doc.
11. Earle-Richardson G, Fulmer S, Jenkins P. Ergonomic analysis of New York apple harvest work using a posture-activities-tools-handling (PATH) work-sampling approach. J Agric Safety Health 2003;10(3):163–76.
12. Osorio A, Beckman J, Geiser C, et al. California farm survey of occupational injuries and hazards. J Agric Safety Health 1998;suppl 1:99–108.
13. Crawford JM, Wilkins JR, Mitchell GL, et al. A cross-sectional control study of work-related injuries among Ohio farmers. Am J Ind Med 1998;34(6):588–99.
14. Zhou C, Roseman JM. Agricultural injuries among a population-based sample of farm operators in Alabama. Am J Ind Med 1998;25:385–402.

15. Stal M, Pinzke S, Hansson G, et al. Highly repetitive work operations in a modern milking system: a case-study or wrist positions and movements in a rotary system. Ann Agric Environ Med 2001;10:67–72.
16. Waters TR, Wilkins JR. Conference proceedings: prevention of musculoskeletal disorders for children and adolescents working in agriculture. DHHS (NIOSH) publication No. 2004–119. Cincinnati: NIOSH, 2004.
17. Chapman LJ, Newhouse AC, Meyer RH, et al. Musculoskeletal discomfort, injuries, and tasks accomplished by children and adolescents in Wisconsin fresh market vegetable production. J Agric Safety Health 2003;9(2):91–105.
18. Gerberich SG, Gibson RW, French LR, et al. Injuries among children and youth in farm households; regional rural injury study. Injury Prevention 2001; 7(2):117–22.
19. Marlenga B, Pickett W, Berg BL. Assignment of work involving farm tractors and children on North American farms. Am J Ind Med 2001;40(1):15–22.
20. Silverstein BA, Fine LJ, Armstrong TJ. Occupational factors and carpal tunnel syndrome. Am J Ind Med 1987;11:343–58.
21. Viikari-Juntura EV, Silverstein B. Role of physical load factors in carpal tunnel syndrome. Scand J Work Environ Health 1999;25(3):163–85.
22. Latko WA, Armstrong TJ, Franzblau A, et al. Cross-sectional study of relationships between the repetitive work and prevalence of upper limb musculoskeletal disorders. Am J Ind Med 1999;36:248–59.
23. Gjessing CC, Schoenborn TF, Cohen A. Participatory ergonomic interventions in meatpacking plants. DHHS (NIOSH); publication No. 94–124. Cincinnati: NIOSH, 1994. Available at http://www.cdc.gov/niosh/94-124.html).
24. Falkiner S, Meyers S. When exactly can carpal tunnel syndrome be considered work-related? ANZ J Surg 2002;72(3):204–9.
25. Maetzel A, Makela M, Hawker G, et al. Osteoarthritis of the hip and knee and mechanical occupational exposure—a systematic overview of the evidence. J Rheumatol 1997;24:1599–607.
26. Toren A, Oberg K, Lembke B, et al. Tractor-driving hours and their relation to self-reported low back and hip symptoms. Appl Ergonomics 2002;33:136–46.
27. Thelin A, Jansson, B, Jacobsson B, et al. Coxarthrosis and farm work: a case referent study. Am J Ind Med 1997;32:497–501.
28. Gomez MI, Hwang S, Stark AD, et al. An analysis of self-reported joint pain among New York Farmers. J Agric Safety Health 2003;9:143–57.
29. Thelin A, Vingard E, Holmberg S. Osteoarthritis of the hip-joint and farm work. Am J Ind Med 2004;45:202–9.
30. Meyers JM, Miles JA, Faucett J, et al. Ergonomics in agriculture: workplace priority setting in the nursery industry. Am Ind Hyg Assoc J 1997;58:121–5.
31. Meyers JM, Miles JA, Faucett. Ergonomics risk factors for musculoskeletal disorders in wine grape vineyard work. Davis, CA: Agricultural Ergonomics Resource Center, 1998. Available at http://ag-ergo.ucdavis.edu/papers.
32. Roquelaure Y, Dano C, Dusolier G. Biomechanical strains on the hand-wrist system during grapevine pruning. Int Arch Occup Environ Health 2002;75:591–5.
33. Fulmer S, Punnett L, Slingerland D, et al. Ergonomic exposures in apple harvesting preliminary observations. Am J Ind Med 2002;suppl 2:3–9.
34. Earle-Richardson G, Jenkins PL, Slingerland DT, et al. Occupational injury and illness among migrant and seasonal farmworkers in New York State and

Pennsylvania, 1997–1999: pilot study of a new surveillance method. Am J Ind Med 2003;44(1):37–45.
35. McCurdy SA, Samuels SJ, Carroll DJ, et al. Agricultural injury in California migrant Hispanic farmworkers. Am J Ind Med 2003;44:225–35.
36. Buchholz B, Paquet V, Punnett L, et al. PATH: a work sampling-based approach to ergonomic job analysis for construction and other non-repetitive work. Appl Ergonomics 1996;27(3):177–87.
37. Paquet V, Punnett L. Ergonomic exposures to construction carpenters and carpentry laborers in tunnel construction. In: Mital A, Krueger H, Kumar, et al., eds. Advances in Occupational Ergonomics and Safety I. Amsterdam: IOS Press, 1996.
38. Paquet V, Punnett L, Buchholz B. Validity of fixed-interval observations for postural assessment in construction work. Appl Ergonomics 1996;32(3):215–24.
39. Kroemer K. Ergonomics. In: Plog BA, ed. Fundamentals of Industrial Hygiene, 5th ed. Washington, DC: National Safety Council, 2002.
40. Rose SR, Walline EK, Moore JS, et al. Ergonomics. In: McCunney RJ, ed. A Practical Approach to Occupational and Environmental Medicine, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2003.
41. Harris JS, Glass L. Occupational Medicine Guidelines: Evaluation and Management of Common Health Problems and Functional Recovery in Workers, 2nd ed. Beverly, MA: OEM Press, 2003.
42. Zuckerman JD, Miarabello SC, Newman D, et al. The painful shoulder: Part II. Intrinsic disorders and impingement syndrome. Am J Fam Pract 1991;43:497–509.
43. Guidotti T. Occupational repetitive strain injury 1992;45:582–92.
44. Fongemie AE, Buss DD, Rolnick SL. Management of shoulder impingement syndrome and rotator cuff tears. Am Fam Physician 1998;57(4):667–74.
45. Sagerman S, Truppa KL. Diagnosis and management of occupational disorders of the shoulder. In: Kasdan ML, ed. Occupational Hand and Upper Extremity Injuries and Diseases, 2nd ed. Philadelphia: Hanley and Belfus, 1998.
46. Matte TD, Baker EL, Honchar PA. The selection and definition of target work-related conditions for surveillance under SENSOR. Am J Public Health 1989;79(suppl):21.
47. Dawson DM, Hallett M, Wilboun AJ. Carpal tunnel syndrome. In: Dawson DM, Hallett M, Wilboun AJ, et al., eds. Entrapment Neuropathies, 3rd ed. Philadelphia: Lippincott-Raven, 1999.
48. Newcomer KL, Laskowski ER, Idank DM, et al. Corticosteroid injection in early treatment of lateral epiconylitis. Clin J Sport Med 2001;11(4):214–22.
49. Smidt N, van der Windt DA, Assendelft WJ, et al. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: a randomized controlled trial. Lancet 2002;359(9307):657–62.
50. Meyers JM, Miles JA, Faucett J. CAL OSHA ergonomic standards: What does it mean for vineyard employers? Practical Winery 2002. Available at http://www.practicalwindery.com/mayjune00/calosa.htm.
51. State of California Department of Industrial Relations. Subchapter 7, General Industry Safety Order. Available at http://www.dir.ca.gov/title8/5110.html.
52. Barab J. Ergonomics: Back in the ring 2002. Safety and Health. 2002. Available at http://www.nsc.org/issues/ergo/backinring.htm.
53. Smith S. Ergonomics: What's next for the state of Washington. Occupational Hazards Safety Zone, 2004. Available at http://www.occupationalhazards.com/safety_zones/35/article.php?id=11372.

54. NIOSH. Elements of ergonomics programs: A primer based on ergonomic assessments of musculoskeletal disorders. DHHS (NIOSH) 1997; publication No. 91–117. Available at http://www.cdc.gov/niosh/epstep1.html.
55. Easy ergonomics: a guide to selecting non-powered hand tools. DHHS (NIOSH) 2004; publication No. 2004–116. Available at http://www.cdc.gov/niosh/docs/2004-164/pdfs/2004-164.pdf.
56. Baron S, Estill C, Steege, et al. Simple solutions: Ergonomics for farm workers. U.S. DHHS (NIOSH) 2001; publication No. 2001–111). Available at http://www.cdc.gov/niosh/01-111pd.html.

25

Trauma in the Agricultural Setting

Gideon Letz and James E. Lessenger

Key words: mechanisms of injury, agents of injury, prehospital care, trauma care systems

By the very nature of the industry, traumatic injuries in agriculture are common and difficult to treat. In the agricultural environment, the worker is exposed to a number of hazards, well documented in other chapters of this book. The work is hard and demanding and often carried out under unfavorable and harsh weather conditions.

This chapter will document the scope of injuries in worldwide agriculture, roadblocks to timely and competent treatment, systems for medical response to traumatic injuries, and systems for returning the injured worker back to the workplace. Prevention of injuries is discussed in Chapters 4, 5, and 6.

Extent of Trauma Injuries

The numbers of agriculture related injuries and deaths vary from country to country based upon several factors, including the type of work done in that country, preventive measures, the health and nutritional status of the workers, and the medical response to injuries. Tables 25.1 and 25.2 compare agricultural injury and death rates in several countries (1–5).

In many countries, the reporting system for agricultural injuries and deaths is incomplete due to apathy, lack of funds or facilities, or political factors. Many companies and countries don't want the precise numbers known in order to hide the need for preventive measures and safety controls. In Pakistan, for example, official apathy is such that the newspapers provide a more realistic measure of injury and death than does the public health system (16).

As discussed in detail in Chapter 12, children are at greater risk for agriculture injury and death, especially by trauma. Tables 25.3 and 25.4 show the injury and death rates among children in several countries, many of which have aggressive prevention and safety programs (17–20).

TABLE 25.1. Extent of agricultural injuries.

Location	Costs	Rate
California (2002)		8.2/100 workers/year
Iowa (2002)	US$51,764/ injury	42/100 person/years
Ontario, Canada (1995 to 1996)	US$19 million/yr	
United States (1990 to 2000)		0.5 to 16.6/100 workers/year
United States (1992)	$3.14 to $13.99 billion/yr	
India (one state) (2000)	$27 million/yr	1.23/1000 workers/year
Australia (1989 to 1992)		20.6/100,000 workers/year
China (1997–1998)		33% of the workforce/year
Denmark (1998)		32% of full-time workers/year
Ohio (1995)		5/100 person/years

Source: Data from McCurdy et al. (1), Rautiainen et al. (2), Locker et al. (3), Rautianinen and Reynolds (4), Leigh et al. (6), Tiwari et al. (7), Franklin et al. (8), Xiang et al. (9), Rasmussen et al. (10), and Crawford et al. (11).

TABLE 25.2. Trauma fatalities in adult agricultural workers.

Location	Rate / 100,000 workers
United States (2000)	22
India (2000)	22
United States (1989 to 1992)	3.2
New Zealand (1989 to 1992)	4.9
Australia (1989 to 1992)	3.8
United States (1992 to 1996)	2.1
Canada (1991 to 1995)	1.6
Alaska commercial fishing (1991–1992)	200

Source: Data Rautianinen and Reynolds (4), Mag and Nag (12), Feyer et al. (13), Adekoya and Myers (14), and Pickett et al. (15).

TABLE 25.3. Extent of agricultural injuries in youth.

Location	Rate
Kentucky (1994 to 1995)	2.8/100
California (1998)	3.8/100
Minnesota (2000)	1,683/100,000
United States (1990 to 1993)	1717/100,000 farm residents

Source: Data Browning et al. (17), McCurdy and Carroll (18), Gerberich et al. (19), and Rivara (20).

TABLE 25.4. Extent of agriculture trauma fatalities in U.S. youth.

Time period	Rate /100,000 persons in age groups
1979 to 1981	9.3/100,000
1990 to 1993	8/100,000

Source: Data from Goldcamp et al. (21) and Lilley et al. (22).

Mechanisms, Agents, Types of Trauma

The mechanisms of trauma, or the way that the person is injured, vary from country to country based upon the type of crops grown and the methods used to grow them. For example, in California falling ladders are a risk to people harvesting oranges, yet in the Pacific Islands, falling coconuts are a hazard to people harvesting the product. The resulting injury may be the same in both cultures. Table 25.5 compares the major mechanisms of injury in agriculture, the typical agents where the mechanisms occur, and the typical resulting injuries.

TABLE 25.5. Mechanisms and agents of injuries, with examples of associated injuries.

Mechanism	Agent	Injury examples
Fall from a height	Farm animals	Fractures
Overexertion	Lifting boxes	Lumbar strain
Repetitive motion	Sorting fruit	Carpal tunnel syndrome
Sprains and strains	Jumping from a tractor	Sprained ankle
Lacerations	Pruning knives	Lacerated hand
Scalp avulsions	Long hair caught in machinery	Partial or complete scalp laceration
Engulfment	Falling into grain elevators or manure pits	Asphyxiation
Rollovers	Tractors and self propelled machines	Head injuries Spinal injuries Multiple trauma
Collisions	Vehicles	Head injuries Spinal injuries Multiple trauma
Blasts	Explosion of pressurized tanks	Multiple trauma Amputations
Burns	Combustibles such as gasoline	Burns
Shrapnel	Exploding fuel tanks	Lacerations Multiple organ trauma
War	Combat “collateral” injuries Unexploded ordnance Land mines	Amputations Multiple trauma Lacerations Burns
Falling objects	Trees Coconuts Ladders	Head and spinal trauma
Penetration	Animal horns Tree branches	Pneumothorax Abdominal trauma Eye injuries
Auger injuries	Augers for transporting grain or crushing wine grapes	Amputations of hands

Source: Data from Centers for Disease Control (23), Pros and Vrtiskova (24), Karaman et al. (25), Alexe et al. (26), Kirkhorn and Schenker (27), and Stiernstrom et al. (28).

Mechanized countries may have more injuries from limb entrapments in machines, while countries dependent upon animals will have more injuries from animals, such as stomping and kicking injuries or injuries from falls. The nature and extent of injuries are complicated by the pre-injury health and age of the worker, pregnancy, the potential for secondary gain through litigation, and whether personal protective equipment was used (see Chapter 6) (23–28).

Roadblocks to Treatment

With exceptions, such as ornamental horticulture, most agricultural enterprises are carried out in rural areas, far from doctors' offices, clinics, trauma hospitals, and rehabilitation facilities. Many countries, such as Bangladesh, Pakistan, Afghanistan, and countries in equatorial Africa or Central America, have minimal medical care and may not have facilities to effectively treat farm trauma except in the large cities. Many countries lack any prehospital care at all and the populace may have poor training in first aid (29).

Along with the lack of facilities, many parts of the world lack trained medical personnel and surgeons to effectively treat trauma. Especially important is the "golden hour" in trauma patients, the hour when effective treatment of shock and rapid control of bleeding is so important to the preservation of life and limb (29).

Even in the so-called "wealthy" countries, sheer distances may complicate treatment. For example, in Tulare County, California, it may take an ambulance traveling at high speeds over an hour to reach some remote places. The terrain, lack of effective roads and transportation, and swollen rivers or marshes create roadblocks to obtaining effective medical help. Weather conditions, such as blizzards, ice storms, and floods provide effective barriers to medical transportation.

War presents a major challenge to people in agriculture. Combat places farmworkers in harm's way and at risk for war-related trauma. Blockage of roads, minefields, crowded hospitals, and overworked ambulances result from combat, making it difficult to evacuate and treat farm injuries. In the aftermath of war, unexploded ordnance and landmines maim hundreds, if not thousands, of people on farms each year (30–33).

Many of the roadblocks come down to lack of money and, more important, commitment. The two must go hand in hand because without one, the other will be useless. With a commitment to effective trauma care, professionals can organize a system of evacuation and treatment geared to the local terrain and weather barriers. Professionals can also lobby for money to implement such a program.

Systems for Medical Response

Pre-Hospital Options

First aid

Many organizations, including the Red Cross, Red Crescent, and Scouts, teach basic and advanced first aid courses. Because of the long distances to medical services, some states train farm families in advanced first aid techniques.

First aid courses concentrate on control of bleeding, control of the airway, covering the wound, splinting, preventing shock, and evacuation techniques.

Ireland equips rural physicians with portable trauma kits to provide advanced trauma life support. The Donegal Pre-hospital Emergency Care Project equipped general practioners with the kits and found a significant improvement in pre-hospital survival (34).

Emergency Medical Systems

Volunteer or professional emergency medical systems (EMS) follow one of five models: hospital based, municipal, private, volunteer, and complex. These organizations vary in training, equipment, and their ability to reach the injured person. More advanced units utilize highly trained personnel and sophisticated treatment protocols and equipment. Also important is advanced training in machinery extraction, tractor rollovers, and enclosed space rescue (35–37).

There are three basic treatment philosophies in operating EMS systems:

1. Scoop and swoop: This system utilizes minimal or no stabilization of the injured person at the scene of the accident, evacuating the person to a hospital as quickly as possible.
2. Treat and swoop: These systems engage in advanced treatment at the injury site, including intravenous fluids, advanced airway control, antishock suits, and chest tubes. Some systems utilize physicians to perform advanced procedures on injured people in the field.
3. A combination of the two. Most systems use a combination of the two EMS systems depending upon the level of training of the response personnel and the complexity of equipment they are provided with (38,39).

Helicopters and "flying squads" have provided a new dimension to EMS services. Not only can they rapidly evacuate injured persons over difficult terrain but they can utilize aircraft to transport injured persons to specialty hospitals in other areas, even on other continents (40).

Physicians' Offices and Clinics

In many parts of the world, and especially in rural areas, physicians' offices are the first stop for agricultural trauma patients. They provide the advantages of availability, less crowding, and less expense than hospital emergency departments. They also may have less bureaucratic burden of regulation and paperwork. Some physicians' offices and clinics are equipped to manage major trauma and life support, but most treat minor injuries such as lacerations, minor burns, and fractures.

Emergency Departments and Hospitals

Around the world, there is a vast range of availability, training, and equipment among hospitals and emergency departments. Using protocols and training in Basic Trauma Life Support and Advanced Trauma Life Support, the management of agriculture trauma has improved in many countries. Rapid intubation, fluid resuscitation, control of hypothermia, and control of bleeding are the hallmarks of trauma support in emergency departments. Precise and rapid diagnosis using radiographs is possible in most countries, but ultrasound machines, CT scanners, and MRI units are not available in many countries. In many locations, physicians must rely on their clinical judgment to diagnose and treat trauma patients (41,42).

Advanced surgical techniques in limb re-implantation, head injury surgery, spinal salvage, and microvascular surgery have improved the salvage rates for limbs, spinal, and head injuries. Any advanced surgical program requires advanced training for surgeons, nurses, and other personnel, adequate equipment and supplies, and proper facilities.

Coordination

Training physicians who work in emergency departments in the techniques of Advance Trauma Life Support is not enough. A training program in Jamaica did not improve life and limb salvage because it was not integrated into the prehospital and surgical treatment programs. Integration of pre-hospital, clinical, emergency department, and surgical programs into one seamless system is the goal of any trauma system. Major items such as protocols and training can be standardized by a coordinating organization such as a municipality or hospital. Ironically, sometimes the little things are what really matter, such as compatibility of EKG machine lead attachments with machines in the ambulance, emergency department and operating room. The need to place and replace EKG leads or IV equipment from one component to the other wastes money and time that can be better spent in patient treatment (41,42,43).

Returning the Injured to the Workplace

Impairment is the physical inability to perform a certain function, such as the loss of an arm or vision in one eye. Disability is the social restriction upon the injured person brought by a specific impairment. An example of a disability would be the inability of a person to harvest fruit with the loss of vision in both eyes or the inability of a person to continue to sort fruit after the loss of an arm (44,45).

Rapid Return to Work

Most agriculture trauma is minor, and injured workers can and should be sent back to work in some capacity as soon as possible. A rapid return to work takes advantage of the "healthy worker effect," i.e., people get better faster if they are returned to work (44–47).

Not all employees can be immediately returned to work at full duty; yet there is some work they can do. Many injured employees can be placed on modified duty so they can be returned to work to take advantage of the healthy worker effect and at the same time earn a living. Many employers have modified duty programs for injured workers and it is important for the employer and physician to work in concert to develop a return to work program (46–48).

Rehabilitation Services

Major trauma often requires major rehabilitation to return the employee to work. Rehabilitation services include:

1. Reconstructive surgery
2. Provision of prostheses
3. Training
4. Special equipment for return-to-work, such as specially equipped vehicles
5. Assistance with activities of daily living, especially important in-head and spinal cord injuries
6. Provision of personal assist devices such as wheelchairs, canes, and crutches
7. Vocational counseling services
8. Psychological counseling services

Coordination of services is just as important in rehabilitation and return to duty as coordination of the trauma treatment. Typically, one physician is responsible for the certification of necessity for the services and the provision of the various components. However, a collegial, committee approach allows

input from the various specialty professions involved in the rehabilitative process (49,50).

References

1. McCurdy SA, Farrar JA, Beaumont JJ, Samuels SJ, Green RS, Scott LC, Schenker MB. Nonfatal occupational injury among California farm operators. J Agric Saf Health. 2004;10:103–19.
2. Rautiainen RH, Lange JL, Hodne CJ, Schneiders S, Donham KJ. Injuries in the Iowa Certified Safe Farm Study. J Agric Saf Health. 2004;10:51–63.
3. Locker AR, Dorland JL, Hartling L, Pickett W. Economic burden of agricultural machinery injuries in Ontario, 1985 to 1996. J Rural Health. 2003;19:285–91.
4. Rautianinen RH, Reynolds SJ. Mortality and morbidity in agriculture in the United States. J Agric Saf Health. 2002;8:259–76.
5. McCurdy SA, Samuels SJ, Carroll DJ, Beaumont JJ, Morrin LA. Injury risks in children of California migrant Hispanic farm worker families. Am J Ind Med. 2002;42:124–33.
6. Leigh JP, McCurdy SA, Schenker MB. Costs of occuptional injuries in agriculture. Public Health Rep. 2001;116:235–48.
7. Tiwari PS, Gite LP, Dubey AK, Kot LS. Agricultural injuries in Central India: Nature, magnitude, and economic impact. J Agric Saf Health. 2002;8:95–111.
8. Franklin RC, Mitchell RJ, Driscoll TR, Fragar LJ. Agricultural work-related fatalities in Australia, 1989–1992. J Agric Saf Health. 2001;7:213–27.
9. Xiang H, Wang Z, Stallones L, Keefe TJ, Huang X, Fu X. Agricultural work-related injuries among farmers in Hubei, Peoples Republic of China. Am J Public Health. 2000;90:1269–76.
10. Rasmussen K, Carstensen O, Lauritsen JM. Incidence of unintentional injuries in farming based on one year of weekly registration in Danish farms. Am J Ind Med. 2000;38:82–9.
11. Crawford JM, Wilkins JR 3rd, Mitchell GL, Moeschberger JL, Bean TL, Jones LA. A cross-sectional case control study of work-related injuries among Ohio farmers. Am J Ind Med. 1998;34:588–99.
12. Mag PK, Nag A. Drudgery, accidents and injuries in Indian agriculture. Ind Health. 2004;42:149–62.
13. Feyer AM, Williamson AM, Stout N, Driscoll T, Usher H, Langley JD. Comparison of work-related fatal injuries in the United States, Australia, and New Zealand: Method and overall findings. Inj Prev 2001:7:22–8.
14. Adekoya N, Myers JR. Fatal harmful substances or environmental exposures in agriculture, 1992 to 1996. J Occup Environ Med. 1999;41:699–705.
15. Pickett W, Hartling L, Dimich-Ward H, Guernsey JR, Hagel L, Voaklander DC, Brison RJ. Surveillance of hospitalized farm injuries in Canada. Inj Prev. 2001;7:123–8.
16. Ghaffar A, Hyder AA, Bishai D. Newspaper reports as a source for injury data in developing countries. Health Policy Plan. 2001;16:322–5.
17. Browning SR, Westneat SC, Donnelly C, Reed D. Agricultural tasks and injuries among Kentucky farm children: Results of the Farm Family Health and Hazard Surveillance Project. South Med J. 2003:96:1203–12.

18. McCurdy SA, Carroll DJ. Agricultural injury. Am J Ind Med. 2000;38:463–80.
19. Gerberich SG, Gibson RW, French LR, Renier CM, Lee TY, Carr WP, Shutske J. Injuries among children and youth in farm households: Regional Rural Injury Study-I. Inj Prev. 2001;7:117–22.
20. Rivara FP. Fatal and non-fatal farm injuries to children and adolescents in the United States, 1990–3. Inj Prev. 1997;3:190–4.
21. Goldcamp M, Hendricks KJ, Myers JR. Farm fatalities to youth 1995–2000: A comparison by age groups. J Safety Res. 2004;35:151–7.
22. Lilley R, Feyer AM, Langley J, Wren J. The New Zealand child work-related fatal injury study:1985–1998. N S Med J. 2004;117:U891.
23. Center for Disease Control and Prevention. Suffocations in grain bins—Minnesota, 1992–1995. MMWR Morb Mortal Wekly Rep. 1996;45:837–41.
24. Pros Z, Vrtiskova J. Scal replantation—a case report. Acta Chir Plast. 1994;36:107–10.
25. Karaman K, Gverovic-Antunica A, Rogosic V. Lakos-Krzelj V, Rozga A, Radocaj-Perko S. Epidemiology of adult eye injuries in Split-Damatian county. Croat Med J. 2004;45:304–9.
26. Alexe DM, Petriodou E, Desspypris N, Skenderis N, Trichopoulos D. Characteristics of farm injuries in Greece. J Agric Saf Health. 2003;9:233–40.
27. Kirkhorn SR, Schenker MB. Current health effects of agricultural work: Respiratory disease, cancer, reproductive effects, musculoskeletal injuries, and pesticide-related illnesses. J Agric Saf health. 2002;8:999–214.
28. Stiernstrom EL, Holmberg S, Thelin A, Svardsudd K. Reported health status among farmers and nonfarmers in nine rural districts. J Occup Environ Med. 1998;40:917–24.
29. Sibai AM, Shaar NS, El Yassir S. Impairments, disabilities and needs assessment among non-fatal war injuries in South Lebanon, Grapes of Wrath, 1996. J Epidemiol Community Health. 2000;54:35–9.
30. Bhutta SA. Children of war: The real casualties of the Afghan conflict. BMJ. 2002;324:349–52.
31. Anderson N, da Sousa CP, Paredes S. Social cost of land mines in four countries: Afghanistan, Bosnia, Cambodia, and Mozambique. BMJ. 1995;311:718–21.
32. Kinra S, Black ME. Landmine related injuries in children of Bosnia and Herzegovina 1991–2000: Comparisons with adults. J Epidemiol Community Health. 2003;57:264–5.
33. Center for Disease Control. Injuries associated with landmines and unexploded ordnance—Afghanistan, 1997–2002. JAMA. 2003;290:1846–7.
34. O'Rourke G, Hanley K, Dowling J, Murphy A, Bury G. The use of basic life support kits in general practice. Ir Med J. 1999;92:399–400.
35. Arreola-Risa C, Mock CN, Lojero-Wheatly L, de la Cruz O, Garcia C, Canavanti-Ayub F, Jurkovich GJ. Low-cost improvements in prehospital trauma care in a Latin American city. J Trauma. 2000;48:119–24.
36. VanRooyen MJ. Development of prehospital emergency medical services: Strategies for system assessment and planning. Pac Health Dialog. 2002;9:86–92.
37. Stueland DT, McCarty JE, Stamas P Jr, Gunderson PD. Evaluation of agricultural rescue course by providers. Prehospital Disaster Med. 1996;11:234–8.
38. Stueland D, McCarty J, Stamas P Jr. Prehospital care of agricultural injuries. Prehospital Disaster Med. 1993;8:193–7.

39. Applebaum D. The impact of a physician-staffed mobile intensive care unit. Am J Emerg Med. 1985;3:15–8.
40. Cope AR, Dove AF, Kulendrarajah T, McLauchlan CA. Are accident flying squads also worthwhile for medical emergencies? J R Soc Med 1991;84:144–6.
41. Fleisher M, Lindstrom D. Evaluating the implementation of health policy: Prehospital care in Pennsylvania. Eval Program Plann. 1997;10:43–51.
42. Ariyahayagam DC, Naraynsingh V, Maraj I. The impact of the ATLS course on traffic accident mortality in Trinidad and Tobago. West Indian Med J. 1992;41:72–4.
43. Boyington T, Williams D. Pre-hospital care—current concepts. Accid Emerg Nurs. 1995;3:45–7.
44. Karwat ID. Major medical and social needs of disabled rural inhabitants. Ann Agric Environ Med 1998;5:117–26.
45. Chau N, Gauchard GC, Siegfried C, Benamghar L, Dangelzer JL, Francais M, Jacquin R, Sourdot A, Perrin PP, Mur JM. Relationships of job, age, and life conditions with the causes and severity of occupational injuries in construction workers. Int Arch Occup Environ Health. 2004;77:60–66.
46. Ehrlich GE. Back pain. J Rheumatol Suppl. 2003;67:26–31.
47. Anke AG, Fugl-Meyer AR. Life satisfaction several years after severe multiple traumas—a restrospective investigation. Clin Rehabil. 2003;17:431–42.
48. Lea RD, Etheredge GD, Freeman JN, Lloyd Wax B. Familial disability patterns in individuals with chronic work-related spine injury/illness. Spine. 2003;28:2292–7.
49. Hagglund KJ, Clark MJ, Mokelke EK, Stout BJ. The current state of personal assistance services: Implications for policy and future research. NeuroRehabilitation. 2003;19:115–20.
50. Young AE, Murphy GC. Spinal cord injury rehabilitation outcomes: A comparison of agricultural and non-agricultural workers. Aust J Rural health. 1998;6:175–80.

26

Diseases from Plants

Capri-Mara Fillmore and Bruce J. Lanser

Plant-borne diseases affecting agricultural workers result from properties of the plant, its pollen, or organic dusts and molds associated with plants. This chapter will discuss asthma, rhinitis, mycotoxicosis, bysinosis, dermatitis, and green tobacco sickness.

Asthma and Rhinitis

Allergic respiratory diseases include allergic rhinitis, asthma, bronchitis, hypersensitivity pneumonitis, bronchopulmonary aspergillosis, and anaphylaxis. The more serious effects of organic dusts are fully described in Chapter 19.

Plants Causing Asthma and/or Rhinitis

Often the same identified type of stimuli may cause rhinitis in one person and asthma in another. Pollens and organic dusts including endotoxins, bacteria, glucans, insect parts, grain mites, mold or mycotoxins from fungi, and aerosolized and respirable dust from the plant product or pure plant material are the sources of virtually all plant-borne causes of rhinitis and asthma. Several years ago it was questioned as to whether grain dust asthma really existed, but this was primarily attributed to the fact that the composition of grain dust is so complex that identification of a specific antigen is difficult despite clear positive responses to dust inhalation challenge and skin testing. Grain dust has been found to significantly increase symptoms of cough, sputum, wheezing, and shortness of breath. However, these problems were found to be more severe in smokers (1,2,3).

Various types of pollens are well known to be associated with allergies and asthma. Agricultural practices, particularly harvesting and moving long-term storage grains, increase the dissemination of these various types of particles and pollens and the incidence of these allergic reactions. The pollen of members of the *Ambrosia* genus of the Compositae family, such as ragweed, are

perhaps the best known cause of allergic rhinitis. Several agricultural plant species have crossreactive proteins with group I, IV, and IX allergens, and thus it is highly likely that a worker would be allergic to all of them. The cross reactive crops are barley, corn, rye, triticale, oats, canola, and sunflower pollens. These allergies, along with ragweed, are often given the nonspecific name of "hay fever" (4,5).

Dust exposure in coffee processing facilities has also been linked to rhinitis and asthma-like symptoms. The castor bean is known to be a strongly sensitizing allergen and cross-reactive with coffee beans. Green coffee beans are particularly linked to causing allergic symptoms in coffee workers (25.8%) as compared to roasted coffee beans (2.7%). Symptoms are reported following long-term continuous coffee dust exposure but are reported to subside upon leaving the processing facilities. Incidence among coffee processors is believed to be between 10% and 30%, and is highly dependent upon amount of years worked in the industry, however one small study saw symptoms in 92% of workers (6,7).

Pathophysiology and Genetics

Plant-borne asthma and respiratory tract allergies are by definition caused by inhalation of the allergen. However, some allergens such as pollens can cause rhinitis after exposure through the conjunctiva of the eye; severe rhinitis can lead to conjunctivitis. Rhinoconjunctivitis is a common indicator of an allergy that is usually IgE-mediated, involving irritation and inflammation of the mucosa, with increased interleukens identified in nasal discharge. Ragweed (and all hayfever) allergies are activated by Type I hypersensitivity reactions. Asthma symptoms that are due to plant-borne disease are also IgE-mediated and identified by the *sine qua non* symptoms wheezing and shortness of breath typical of any type of asthma. Both plant-borne asthma and allergic rhinitis are stimulated by organic dusts, pollen, or plant particles (8).

For both allergies and asthma there is a significant hereditary component, with a stronger affect on homozygotic than heterozygotic twins. Genetic variations in two cytokines implicated in respiratory tract hyper-responsiveness (those genes encoding IL-4 and IL-13) have been implicated as one of several polymorphisms that may increase the risk (9,10,11).

Epidemiology

A study comparing respiratory symptoms of European (n = 7188) and Californian (N = 1939) farmers over the last year found 12.7% of the Europeans and 23.9% of the Californians suffered from rhinitis in the last year. In the past year, 2.8% of the European farmers and 4.7% of the Californian farmers suffered from asthma. Table 26.1 summarizes which crop was more associated with which disease (not all crops had sufficient numbers for

TABLE 26.1. Type of farming as a risk factor for respiratory symptoms. Adjusted odds ratios and 95% confidence intervals, adjusted for age, sex, smoking status, other crop exposures, using non-exposed farmers as the reference group.

Crop farmed	Rhinitis	Asthma
Grain	1.13 (1.00–1.29)	N/A
Vegetables	0.77 (0.61–0.97)	0.52 (0.32–0.83)
Tomatoes	0.77 (0.57–1.04)	N/A
Root crops	N/A	1.28 (0.94–1.75)
Fruits/berries	1.30 (1.10–1.54)	N/A
Nuts	1.23 (1.00–1.51)	N/A
Flowers	1.29 (0.98–1.70)	1.71 (1.06–2,77)
Cotton	1.77 (1.08–2.89)	N/A

Data from: Monso E, Schenker M, Radon K, et al. (12).

evaluation). Cotton farming was more highly associated with rhinitis than any other crop, though nut, fruit/berry, and grain crops were associated with a statistically significant increase in risk, and flowers were almost statistically significant in their association. Asthma was most statistically associated with flower crops, although grain crops were not evaluated, a mild association was found between root crops and asthma. The table even suggests that vegetable farming is associated with significantly less rhinitis and asthma. Though not included in Table 26.1, oilseed rape flour or oil is often associated with occupational asthma. Although latex allergies have been well-documented in hospital workers, natural rubber plantation workers have at least 4 times the exposure to natural rubber latex aeroallergens as hospital workers according to one study (Table 26.1) (12,13,14).

Prevention and Management

The preferred treatment for workers with occupational asthma would be to remove them from the exposure causing asthma, but this may not necessarily be reasonable for economic reasons. Depending on a farmer's assets or the ability and willingness of a company to invest in their workers, respirators are likely to decrease asthma and allergies from any plant-borne antigens. Simple commercial or industrial dust masks can also be used as an inexpensive alternative to respirators, however they are not highly effective. Several studies have noted that growing up on a farm is associated with a decreased risk of asthma and allergies related to plant-borne diseases, particularly when exposed to farm stables and unpasteurized milk (15,16).

Occupational asthma is generally well controlled with the beta-adrenergics and steroid inhalants common to treatment of all types of asthma. In cases of acute exacerbation unresponsive to increases of inhaled medication, oral steroids (for example starting at 40 to 60 mg per day of prednisone) with decreasing dosage over 6 to 10 days is typically used. Rhinitis symptoms are

generally easier to control with minimal medications and are associated with fewer side effects than asthma (15,16).

Mycotoxicosis

Mycotoxicosis is any disease that results from a fungus. Generally attributed to fungi are hypersensitivity reactions, infections (mycoses), and mycotoxicoses. Though fungus is not usually considered a plant, in most cases the toxic exposure to fungi are from fungi growing on plants, nuts, or grains. More than 300 secondary metabolites from filamentous fungi (molds) have been classified as mycotoxins to date; the most common genera are *Aspergillus, Penicillium*, and *Fusarium* (17,18,19).

Hypersensitivity Reactions

Thermopoilic actinomycetes, Cryptostroma, Graphium, Penicillium, Aspergillus, Mucor, and *Pullularia* are all fungal genera that produce spores capable of causing agricultural occupational hypersensitivity pneumonitis as well as the less severe allergic reactions. The most common cause of mycotoxin hypersensitivity pneumonitis is probably *T. actinomycetes,* which grows readily in decaying vegetation, such as hay or silage (especially when vegetation appears moldy). Hypersensitivity pneumonitis is described in detail in Chapter 19 (17–20).

Mycoses Infections

Mycoses infections are rare in agricultural workers and rarely caused by work exposures. *Candidiasis, Pneumocysts*, and *Cryptococcus* are among the most common, however they are generally only found among immunocompromised persons who are generally too ill to be working in agriculture (17–20).

Pulmonary Mycotoxicosis

Mycotoxicosis is generally in the pulmonary form. In contrast with hypersensitivity pneumonitis, no lung sounds are associated with pulmonary mycotoxicosis but they are sometimes heard in organic dust toxic syndrome. Although several causes of organic dust toxic syndrome probably exist, the literature frequently suggests the syndrome to be the same as pulmonary mycotoxicosis. A review of 20 cases of apparent farmer's lung disease found 6 cases clearly to be farmer's lung and 14 more likely to have a mycotoxin origin. Not all organic dust toxic syndromes have been proven to be of mycotoxin etiology, but it is very difficult to prove this. Two of the farmers in a case series of 38 U.S. farmers with toxic pulmonary reactions had genera

Fusarium and *Penicillium* in culture of their lung biopsies. *A. fumigatous* and *A. nidulans* were cultured from bronchoalveolar lavage fluids in farmers handling moldy silage. The trend has been for increasing frequency of mycotoxicosis symptoms in the farming populations, and the cause has been suggested to be due to the much larger silos currently used in agriculture (20,21,22).

Other Health Effects of Mycotoxins

Little is known about the prolonged human effects of exposure to mycotoxins. One reason so little research has been done on its association with chronic disease is the difficulty and expense. Airborne exposure levels at coffee, cocoa bean, and spice processing plants resulted in increased blood levels of ochratoxin A, a secondary metabolite of *Aspergillis* and *Penicillium* (also common in grains and vine fruit), which has been found carcinogenic, genotoxic, teratogenic, immunotoxic and nephrotoxic in animals. The nephrotoxin affect has been shown in agricultural workers and rural residents in several Eastern European countries, and the rare urothelial tumor is 50 to 100 times more likely to occur in these countries (23–26).

Linseed and peanuts are associated with *A. flavus* and its aflatoxin B1, which is associated with lung cancers among some workers and liver cancer in others. Pregnant women working with grain production have a twofold increased risk of preterm births or late abortions compared to non-grain farmers, particularly during humid climate conditions (27–30).

Byssinosis

Exposure to cotton dust causes acute and chronic respiratory illness. Byssinosis is the acute chest tightness and/or shortness of breath that initially occurs on the first day of work following a weekend. Those affected are workers who prepare fibers for spinning. It eventually progresses to affect workers on all working days and ultimately causes a permanent decrease in ventilatory capacity. The same symptoms are associated with the processing of flax, hemp, and sisal for textiles. Early stage periodicity is the best way to distinguish it from asthma and other obstructive airway diseases (31,32,33).

Etiology and Prevention

The etiology is no longer believed to be cotton dust, but dust contaminated with endotoxin. The endotoxin is the outer membrane lipopolysaccharide of gram-negative bacteria, specifically lipid. The endotoxin can be liberated from several genera of gram-negative bacteria and is heat-stable (31).

Prevention measures have included decreasing dust and reducing trash in the working environment, which has reduced some of the prevalence. One study found the spraying of cotton with bactericidal water solutions of benzododecinium bromide succeeded in decreasing the amount of endotoxin, but impact on decreasing the prevalence of byssinosis has yet to be studied (33).

Phytodermatitis

Skin diseases represent the largest group of occupational diseases affecting agricultural workers, who are at the greatest risk for occupational skin disease in the United States, accounting for roughly two thirds of cases. Inedible plant products represent the largest group of causative agents for occupational skin disease among agricultural workers. Identifying and treating skin diseases in agricultural workers presents a difficult situation for the health care provider as the diseases often present similarly; secondary infections or triggers may be present; the causative agents differ in appearance and toxicity greatly on a regional and seasonal basis; and extensive exposure histories may be necessary to determine a likely causative agent (34,35).

While numerous plants can cause skin disease following various routes of contact, from the common household chrysanthemum to wild feverfew, only the most relevant families are presented here. Phytodermatitis can generally be classified by the four groups discussed below: allergic contact dermatitis, irritant contact dermatitis, urticaria, and phytophotodermatitis. For a summary of the various plants and plant families associated with each skin disorder, see Table 26.2 (34–38).

Allergic Contact Dermatitis

Clinical Presentation

Acute allergic contact dermatitis (AACD) usually will develop within 12 to 24 hours of contact with a plant containing a particular allergen to which an individual is sensitive, but can take as long as 72 hours to develop. The patient nearly always presents with an itchy rash that is visible on exposed skin surfaces as a papulovesicular eruption in patches, lines, or scratch marks. The rash can include erythema, vesiculation, weeping, pruritis, and vesicles coalesced into bulae. While it is commonly believed that the allergen can be spread from person to person, or scratched out of the lesion, this is not the case, as the allergen fixes in the skin within a few minutes. Before the allergen is set in the skin, it is possible, however, to spread the allergen away from the initial site, leading to streak or scratch marks. A secondary

TABLE 26.2. Selected plants associated with phytodermatitits.

Allergic contact dermatitis	Irritant contact dermatitis
African poison ivy (*Smodingium argutum*)	Barberry (*Berberis*)
	Bramble (*Rubus*)
Cashew (*Anacardium occidentale*)	Buttercups (*Ranunculus*)
	Cacti
Chrysanthemum	Daffodil (*Narcissus*), tulip, and hyacinth (*Hyacinthus*) bulbs
Dandelion (*Taraxacum*)	
Garlic and onion (*Allium*)	
Ginkgo tree (*Ginkgo biloba*)	Hot peppers (*Capsicum*)
Hot peppers (*Capsicum*)	Lady's slipper (*Cypripedium*)
Japanese lacquer tree (*Toxicodendron verniciflua*)	Photodermatitis
	Celery (*Apium*)
Liverworts (*Frullania*)	Citrus
Mango (*Mangifera indica*)	Fig (*Ficus carica*)
Marigold (*Tagetes*)	Gas plant (*Dictamnus*)
Marking nut tree (*Semecarpus anacardium*)	Parsley (*Petroselinum*)
	Parsnip (*Pastinaca*)
Poison ivy (*Toxicodendron radicans*, *T. rydberrgii*)	Queen Anne's Lace (*Daucus carota*)
Poison oak (*T. diversilobum*, *T. toxicarium*)	Rue (*Ruta graveolens*)
	Urticaria
Poison sumac (*T. vernix*)	Castor bean (*Ricinus communis*)
Ragweed (*Ambrosia*)	
Wild feverfew, congress grass, or carrot weed (*Parthenium hysterophorus*)	Chrysanthemum
	Citrus
	Garlic (*Allium*)
Wormwood (*Artemisia*)	Kiwi fruit
	Stinging nettle (*Urtica dioica*)
	Strawberry

Data from: Juckett G (39).

infection can result from scratching, and an individual without plant contact can develop AACD from allergen present on clothing or equipment. If exposure occurs through clothing or on most body surfaces, the lesions can produce diffuse edema. This form of dermatitis typically will clear within 10 days but can last up to several weeks. Unlike photodermatitis, AACD rarely leaves behind any scars or changes in pigmentation. With repeated exposure to the same allergen, the AACD can become chronic. If it does remain acute, symptoms will usually worsen with each subsequent exposure. However, as one reaches older adulthood, sensitivity appears to decrease (35–40).

The short onset of symptoms associated with AACD lends to an easier diagnosis of the trigger than with chronic allergic contact dermatitis, which is characterized by similar skin lesions that are persistent and not itchy. There also tends to be more redness associated with chronic dermatitis, however the causative plant triggers are no different (36,41).

Plants Causing Dermatitis

By far the most common causes of dermatitis in agricultural workers are members of the the Anacardiaceae family of the *Toxicodendron* genus: poison ivy, poison oak, and sumac poison collectively, followed by pesticides. The phytochemical substance common to the three related plants, not members of the ivy, oak, or sumac families, is a light, nearly colorless oily substance, urushiol. These plants have very fragile leaves, which allows for the oily urushiol to escape from the resin canals onto the surface of the leaves following minor contact. The difference among the substances in these three plants is in the number of carbons and saturation of the side chains, owing to varying levels of potency (35,38,42).

Poison ivy, *T. radicans and T. rydbergii,* is related to the cross-reacting species of cashew (*Anacardium occidentale*), which causes dermatitis as a result of a brown oily substance in the cashew nut shell; and ginkgo (*Ginkgo biloba, Grevillea*), which contains ginkgolic acid (similar to urushiol). Poison oak, *T. diversilobum* and *T. toxicarium*, is related to the Indian marking nut (*Semecarpus anacardium*), which contains a black juice used to mark clothing; and Japanese lacquer (*Rhus verniciflua*), which contains a thick substance used to lacquer furniture and other items. Poison sumac, *T. vernix*, most commonly affects peat farmers and is related to the mango (*Mangidera indica*), which causes dermatitis when the fruit is eaten with the skin intact. The entire genus *Toxicodendron* is related to African poison ivy (*Smodingium argutum*), which is native to South Africa as a tree or shrub and is generally very similar to the American poison ivy. There is great debate over the classification of these three plants. Many want them to be considered from the genus *Rhus*, with *Toxicodenron* as a subgenus. This is in large part a result of the great variety among these plants. Therefore, many will refer to "Rhus dermatitis" when discussing poison ivy, oak, or sumac exposure, but this is no longer considered correct (34).

Although pollen from Compositae family, *Ambrosia* genus, like ragweed is well known to induce rhinitis, skin contact is required for dermatitis (with the exception of feverfew which can cause dermatitis by pollen or plant material). The common members of this family causing dermatitis include: short, low, or common ragweed and Roman wormwood (*A. artmisiaefolia*) (the most ubiquitous, and a high sensitizer), western ragweed (*A. coronopifolia*), great, tall, or high ragweed (*A. aptera*), lance-leaved ragweed (*A. bidentata*), false ragweed (*A. acanthicarpa*), or Hooker's gaertneria (*Franseria acanthicarpa*). Dermatitis caused by ragweed can be seen throughout the growing season (spring through fall). It causes a widespread sensitivity reaction on exposed skin surfaces, mimicking photodermatitis. The allergen can be contacted directly from the plant, fomites, or airborne (most common). Other plants within this highly allergenic family include lichens (symbiotic algae and fungi) that are usually found growing flat on rocks or trees in moist areas such as the Pacific Northwest; the lady slipper (*Cypripedium* and *Paphiopedilum*), an

orchid; tulips (*Tulipa*), which cause "tulip finger" (hyperkeratosis and fissuring in the fingertips) among frequent handlers of the bulbs. A plant that is allergenically similar to the Compositae family and cosmetically similar to the lichens but a member of the Jubulaceae family is the liverwort (*Frulania*) which incites an allergic response to sesquiterpene lactones (34,38,41,43).

Pathophysiology

The reaction to the allergen in the skin is of a type IV hypersensitivity nature. The immune system reacts to the allergen with lymphocytic T cells, causing a cell-mediated response. After contact with the skin, urushiol (from poison ivy, oak, or sumac) causes a delayed hypersensitivity reaction that humans do not have at birth. Persons exposed to urushiol before the age of five are not as likely to develop a sensitivity to it as is someone first exposed between five years of age and adulthood. Even if exposed during this time period, roughly 10% of the population cannot develop sensitivity to urushiol, and others will not if the level of exposure is not great enough (36,41,42).

Epidemiology and Geography

Among the general population, it is estimated that roughly 70% are sensitive to urushiol. It is challenging to estimate the incidence rates of poison ivy, oak, and sumac exposure among agricultural workers in the United States because so many farms are exempt from mandatory reporting to the Bureau of Labor Statistics (37,44).

Generally, poison ivy can be found as crawling vines east of the Rocky Mountains near bodies of water in the east and Midwest, and more spread-out from water in the south. Somewhat similarly, poison sumac can be found in boggy areas. Poison oak is generally found west of the Rocky Mountains as a vine, shrub, or small tree. None of these three plants grow well above 4000 feet of elevation, and are not found in desert areas. They are native to the Americas and very rarely found in Europe. Poison oak is restricted to North America, while poison ivy and poison sumac can be found in North and South America, and poison ivy is also found in East Asia. Within the Americas, the three plants are seldom found in Texas, Arizona, central Mexico, northern Canada, or Alaska and are unknown in the Hawaiian islands. The plants themselves vary greatly in appearance depending upon geographic region (34,37,38).

Ragweed, the most important allergenic plant in the *Ambrosia* genus and Compositae family, is found naturally in North America but also in Australia, Europe (occasionally), and India. Feverfew or carrotweed (Parthenium hysterophorus) is native to the southern United States but is called the "scourge of India" as it caused an epidemic of AACD in India. Liverwort (*Frulania*) thrives in humid climates, including the Pacific Northwest, tropics, and subtropics (34,38,41,43).

Prevention

To add to the challenge of preventing exposure, the old adage, "Leaves of three, let it be. Berries white, poisonous sight" does not always hold true, as the virulent weeds can grow with leaves in groups of five, seven, or even nine, however, this does serve as a useful general guide. The most important first step in educating about avoiding poison ivy, poison oak, or poison sumac is determining how each plant grows in a particular area (vine or shrub, specifics of the leaves etc.). The plant's appearance during each season must also be determined, as dermatitis can be caused during all seasons, despite being considered a summer problem. Poison ivy can be found in varying sizes during the seasons, and can be any shade of green, red, yellow, or brown. Burning poison ivy, poison oak, or poison sumac can also cause allergic contact dermatitis. While few cases have been reported, urushiol can be present in the air near burning plants and can be significant enough to cause an itchy rash (40,45).

Protective clothing is the most effective prevention if workers are unable to avoid the plant altogether. It is important to take care when removing clothing and cleaning equipment, as the urushiol can remain on the surface.

Management

If exposure does occur, the oil should be washed off as soon as possible (within 10 minutes), and any clothing that could have contacted the plant should be removed and washed. Treating contact dermatitis depends largely on the severity of the exposure. Often the dermatitis is mild enough to be treated with an ice pack for pain relief or cool oatmeal baths if the exposure is more widespread. If the dermatitis is more severe, but localized, aluminum acetate compresses can be used (1:40 dilution) or topical steroids, and systemic antihistamines can be used to control severe itching. Milder treatments should be used on sensitive areas (face and genitals). If the dermatitis is severe, oral corticosteroids, such as prednisone, can be used in decreasing dosage over six days, starting between 40 and 60 mg, however as the severity increases, so too should the duration of treatment. With very severe cases, the dosage should be tapered over at least 10 to 14 days to prevent relapse (34,36).

Complications and Sequelae

If relapse does occur, particularly with the Anacardiaceae family, the dermatitis can progress to erythema multiforme. While few incidences have been reported, several cases are documented in the medical literature that show classic presentation of erythema multiforme within one week of allergic contact dermatitis caused by poison ivy that was treated with prednisone. All cases were observed as prednisone was being tapered. Likely erythema multiforme eruptions may be suppressed in most cases by a slow tapering of prednisone. Re-exposure to poison ivy could also trigger the erythema multiforme during treatment with prednisone. Other sequelae include the secondary skin

infections likely (beta-hemolytic streptococcus) from scratching a rash. Once a person reacts for the first time, subsequent exposures are, of course, likely to result in more severe cases of dermatitis (36,46).

Irritant Contact Dermatitis

Plant substances that cause direct irritation to human skin nearly instantaneously, without a body-mediated reaction, are inducers of irritant contact dermatitis (ICD). These reactions can range in severity based upon season, a plant's age, weather, area and thickness of skin exposed, and geographic location. ICD can be caused by either a chemical substance released by the plant or by some physical feature that causes mechanical injury. The best example of the latter are cacti, while poinsettias are the most frequently seen example of the former. Cactus needles and other mechanically injurious plants are frequently associated with secondary infections, such as aseptic foreign body granulomas and chronic septic arthritis. Poinsettias (*Euphorbia splendens*) and related primarily tropical plants contain a milky white sap that can cause erythema and bullae. Another common irritant is calcium oxalate, which pierces the skin with small, needle-like crystals. ICD caused by calcium oxalate crystals has been noted in Mexico among workers in tequila distilleries and farmers on *Agave tequilana* plantations. The disease that results is known locally as "*Mal de agaveros"* (agave worker's sickness) and begins within 1 hour of contact with the agave plant (37–47).

Urticariogenic Plants

Urticariogenic plants are similar to cacti in that they cause mechanical injury, but they also involve a pharmacologically active toxin and are often tropical as opposed to desert plants. Nearly all plants in this group belong to the family Urticaceae, and the most prolific plants are nettles (*Urtica*). They contain minute stinging hairs that can inject a fluid containing histamine, acetylcholine, and serotonin into the skin, causing an immediate inflammatory response characterized by a burning sensation followed by itching. Stings tend to be self-limiting and thus do not usually require treatment (39,41).

Not all urticariogenic plants contain stinging hairs; for example, various urticariogenic fruits, such as kiwi and strawberries, do not. However, kiwi-induced urticaria has been noted as a significant occupational hazard in New Zealand, where the kiwi fruit is a major cash crop (48).

Phytophotodermatitis

Two clinical presentations exist for phytophotodermatitis (PPD or simply photodermatatis), however berloque dermatitis is only associated with psoralens in perfumes, so dermatitis bullosa striata pratensis will be

considered here. There are four plant families associated with bullosa striata pratensis. Members of the Umbelliferae family are the most common causes of PPD and include wild parsnip (*Pastinaca sativa*), cow parsnip (*Heracleum maximum*), and wild carrot (*Daucus carota*). Bergamot orange, lime, and the gas plant are members of the Rutaceae family, which is the second most common cause of PPD in the United States. Although rare in the United States, the remaining two families are more prevalent elsewhere in the world. Figs and other *Ficus* species are members of the Moraceae family, and the *Psoralea* species are members of the Leguminosae family (41).

The active agents in these plants that cause PPD, are various furocoumarins (psoralens), which are natural photosensitive substances that are activated by ultraviolet light. Psoralens are contained in a plant's sap, which can come in contact with a person's skin with varying degrees of difficulty. The substance remains inactive on the skin until exposed to sunlight. Following sun exposure, an uncomfortable rash develops. It closely resembles the rash associated with poison ivy dermatitis, however it occurs only in areas exposed to the sun. The rash is characterized by burning and painful sensations, vesiculation, and erythema. Unlike poison ivy rashes, PPD rashes do not resolve as quickly. The rash can develop shortly following plant and sun exposure but may last from 1 to 2 weeks, leaving behind streaky hyperpigmentations on the skin that can remain for several months. Treatment of PPD is similar to AACD in that all that can be achieved is the relief of symptoms. As with all other forms of dermatitis, a person should promptly wash any surfaces that are presumed to have been exposed to any plant products that could be potentially harmful (49).

Green Tobacco Sickness

Symptoms

Green tobacco sickness has been reported in the medical literature among tobacco harvesters in Kentucky, Florida, Tennessee, North Carolina, India, Malaysia, and Japan. Prior to 1970, green tobacco sickness had not been described within the medical community, but was apparently well-known among tobacco farmers. Green tobacco sickness, which has also been called "green symptom" or "tobacco cropper's sickness," is a self-limiting occupational illness. The diseased patient presents with generalized weakness, nausea and vomiting, headache, diarrhea, pallor, dizziness, and prostration. It has also been associated with occasional fluctuations in blood pressure or heart rate. Generally, the symptoms mimic those associated with nicotine intoxication in novice smokers. These acute symptoms most frequently appear during working hours (within a few hours of exposure) and as a result may be confused with heat exhaustion but may begin in the evening, with almost no cases being reported the following day. While these symptoms can

create great discomfort and require time away from work, green tobacco sickness has not been associated with any long-term sequelae or mortality. However, no studies have been done to determine if there are any long-term effects, such as cardiovascular or other diseases, resulting from frequent bouts of green tobacco sickness. Additionally, while the duration of symptoms is relatively short, only 12 to 24 hours, green tobacco sickness does recur frequently, especially when working conditions remain similar (50–58).

Etiology

Green tobacco sickness has generally been seen only among tobacco pickers, not stringers or workers involved in any later stage of processing. Tobacco pickers often begin work early in the morning, when leaves are fresh with dew. The leaves are broken from the plant and retained under the picker's arm or in hand – the method of holding varies by geographic location and type of tobacco plant being harvested. Periodically, the picked leaves are collected by wagons or trucks that follow behind the pickers and are taken to a barn where stringers, wearing protective plastic aprons and gloves, clip leaves to poles to hang for curing. It is believed that few stringers get green tobacco sickness because of the protective clothing but also because the leaves have already begun to dry once the stringers have contact with them (50,52,55).

The etiology is not entirely understood, however it is believed that nicotine (*Nicotiana tabacum*) is absorbed through the skin from the tobacco leaves. When the leaves are separated from the tobacco plant, a gummy substance is emitted. This substance easily covers a cropper's hands and clothing as the leaves are held close to the body. Additionally, nicotine is soluble in water, which can easily be absorbed by the skin. For this reason, incidence of green tobacco sickness is more prevalent in the morning when leaves are wet with dew or during rainy periods and extremely humid weather. One study that examined nicotine content of dew and croppers' clothing found that dew on the workers contained anywhere from 33 to 84 μg and clothing contained between 58 and 98 μg of nicotine. This study also estimated that in any given morning, a tobacco picker is exposed to the nicotine content of more than 30 cigarettes, via nicotine in dew. Further studies have shown a rise in urinary cotinine (a marker of nicotine absorption) among non-smoking croppers, further suggesting dermal absorption of nicotine as the etiology of green tobacco sickness (50,51,54,55,58).

Incidence of green tobacco sickness also varies by the type of tobacco being harvested. Burley tobacco, the primary crop in Kentucky and Tennessee, contains 13% more nicotine than does flue-cured tobacco (the primary crop in the remainder of the Southern United States). Despite the higher nicotine content in burley tobacco, the nature of flue-cured tobacco harvesting appears to pose a greater risk of green tobacco sickness for harvesters.

Nevertheless, case reports and most studies fail to mention the type of tobacco involved (50,59).

Epidemiology

It is believed that incidence rates for green tobacco sickness are low because it may be misdiagnosed, previous estimates do not reflect the changing nature of the workforce (more Latino migrant workers), and because of a lack of education among the public (farmers specifically) and medical community. In addition, croppers are not likely to be seen by a medical professional as a result of the recurrent nature of the illness and the fact that symptoms appear and resolve without notice over a short time period. Despite these challenges, estimates of incidence rates in Kentucky and North Carolina during a particular growing season are roughly 10 cases per 1,000 tobacco farmers. As a result of the relationship between the type of tobacco, weather conditions, and green tobacco sickness, cases are nearly always found in clusters. Studies examining green tobacco sickness cases on particular farms have found between 24% and 89% of harvesters becoming ill. While the incidence rates vary greatly, young age has consistently been found to increase the risk for green tobacco sickness. In one study, workers under the ago 30 were 3 times more likely to have green tobacco sickness. Additionally, as the length of time employed in the tobacco industry increases, disease risk decreases, especially after 5 years of employment. In terms of race, early studies have all shown significantly higher incidences among white workers, despite the higher prevalence of African Americans working in tobacco fields. These studies relied on emergency room cases, and it is believed that fewer African Americans sought treatment (50,52,56,59,60).

The point of greatest contention in the literature is whether smoking provides a protective effect for tobacco farmers. In some studies it appeared to do so, however the results are highly disputed and not always reproduced. Smoking is certainly not recommended as a form of disease prevention. If any protective effect is obtained from smoking, it appears that green tobacco sickness would still occur once the nicotine level in the body rose above the person's "normal" nicotine threshold (51,52).

Prevention and Management

Frequently used forms of protective clothing (e.g., long-sleeved shirts), appear to provide little benefit. It is believed that waterproof protective clothing would provide significant protection from green tobacco sickness, but such equipment is not practical for use during the warm and humid tobacco harvesting months in the Southern United States. Such equipment could lead to heat exhaustion, and is not favored by tobacco workers. It has been suggested that harvesters not pick the tobacco leaves in the early morning when the

leaves are still wet, or after a heavy rainfall, however this solution must be weighed against the economic cost (50,52,55,59).

Prophylactic drug use has also been proposed but not fully evaluated for effectiveness. Once a tobacco farmer has suffered from green tobacco syndrome and is fully recovered, 50 mg of dimenhydrinate or 25 mg of diphenhydramine could be taken before breakfast and lunch to prevent the onset of symptoms when conditions are such that exposure is likely, but there has been no controlled clinical trial of the effectiveness of this preventive treatment. Theoretically these drugs could also be used immediately after exposure. Due to the self-limiting nature of most cases of green tobacco sickness, treatment may not be necessary. To prevent symptoms or reduce their severity, it is recommended that a worker, if exposed, increase fluid intake and rest. If symptoms are severe and vomiting is prolonged, a physician could administer intravenous hydration, anti-emetics, and 25 mg dyphenhydramine im. In cases where bradycardia or tachycardia is involved, treatment with atropine may be required, however it should be used only in patients with hemodynamic compromise. Green tobacco sickness must be differentially diagnosed from pesticide poisoning. Although symptoms may be similar in some cases, treatment differs significantly (60,61).

References

1. von Mutius E. Influences in allergy: epidemiology and the environment. J Allergy Clin Immunol 2004;113:373–9.
2. Chan-Yeung M, Enarson DA. Prospective changes in lung function in grain elevator workers in large terminals in Vancouver. In: Dosman JA, Cockroft DW, editors. Principles of Health and Safety in Agriculture. Boca Raton: CRC Press, 1989:131–4.
3. Broder I. Overview of adverse pulmonary effects of grain dust. In: Dosman JA, Cockroft DW, editors. Principles of Health and Safety in Agriculture. Boca Raton: CRC Press, 1989:97–103.
4. Chakraborty P, Gupta-Bhattacharya S, Chowdhury I, et al. Differences in concentrations of allergenic pollens and spores at different heights on an agricultural farm in West Bengal, India. Ann Agric Environ Med 2001;8:123–30.
5. Astwood JD, Mohapatra SS, Ni H, et al. Pollen allergen homologues in barley and other crop species. Clin Exp Allergy 1995;25:66–72.
6. Larese F, Fiorito A, Casasola F, et al. Sensitization to green coffee beans and work-related allergic symptoms in coffee workers. Am J Ind Med 1998;34:623–7.
7. Uragoda CG. Acute symptoms in coffee workers. J Trop Med Hyg 1988;91:169–72.
8. Kirkhorn SR, Garry VF. Agricultural lung diseases. Environ Health Perspect 2000;108 Suppl 4:705–12.
9. Sherman CB, Tosteson TD, Tager IB, et al. Early childhood predictors of asthma. Am J Epidemiol 1990;132:83–95.
10. Duffy DL, Martin NG, Battistutta D, et al. Genetics of asthma and hay fever in Australian twins. Am Rev Respir Dis 1990;142:1351–8.

11. Howard TD, Koppelman GH, Xu J, et al. Gene-gene interaction in asthma: IL4RA and IL13 in Dutch population with asthma. Am J Hum Genet 2002;70:230–6.
12. Monso E, Schenker M, Radon K, et al. Region-related risk factors for respiratory symptoms in European and Californian farmers. Eur Respir J 2003;21:323–31.
13. Alvarez MJ, Estrada JL, Gozalo F, et al. Oilseed rape flour: another allergen causing occupational asthma among farmers. Allergy 2001;56:185–8.
14. Sri-akajunt N, Sadhra S, Jones M, et al. Natural rubber latex aeroallergen exposure in rubber plantation workers and glove manufacturers in Thailand and health care workers in a UK hospital. Ann Occup Hyg 2000;44:79–88.
15. Braun-Fahrlander C, Gassner M, Grize L, et al. No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. Eur Respir J 2004;23:407–13.
16. Riedler J, Braun-Fahrlander C, Eder W, et al. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. Lancet 2001;358:1129–33.
17. Abramson D. Mycotoxins in Grains. In: Dosman JA, Cockroft DW, editors. Principles of Health and Safety in Agriculture. Boca Raton: CRC Press, 1989:125–30.
18. Bunger J, Westphal G, Angelika M, et al. Cytotoxicity of occupationally and environmentally relevant mycotoxins. Toxicology 2004;202:199–211.
19. Bhatnagar D, Yu J, Ehrlich KC. Toxins of filamentous fungi. Chem Immunol 2002;81:167–206.
20. May JJ, Stallones L, Darrow D, et al. Organic dust toxicity (pulmonary mycotoxicosis) associated with silo unloading. Thorax 1986;41:919–23.
21. Perry LP, Iwata M, Tazelaar HD, et al. Pulmonary mycotoxicosis: a clinicopathologic study of three cases. Mod Pathol 1998;11:432–6.
22. Lecours R, Laviolette M, Cormier Y. Bronchoalveolar lavage in pulmonary mycotoxicosis (organic dust toxic syndrome). Thorax 1986;41:924–6.
23. Iavicoli I, Brera C, Carelli G, et al. External and interal dose in subjects occupationally exposed to ochratoxin A. Int Arch Occup Environ Health 2002;75:381–6.
24. Sage L, Garon D, Seigle-Murandi F. Fungal microflora and ochratoxin a risk in French vineyards. J Agric Food Chem 2004;52:5764–8.
25. Soyoz M, Ozcelik N, Kilinc I, et al. The effects of ochratoxin A on lipid peroxidation and antioxidant enzymes: a protective role of melatonin. Cell Biol Toxicol 2004;20:213–9.
26. Peraica M, Radic B, Lucic A, et al. Toxic Effects of Micotoxins in Humans. Bull WHO 1999;77:754–66.
27. Hayes RB, van Nieuwenhuize JP, Raatgever JW, et al. Afatoxin exposures in the industrial setting: an epidemiologic study of mortality. Food Chem Toxicol 1984;22:39–43.
28. Olsen JH, Dragsted L, Autrup H. Cancer risk and occupational exposure to aflatoxins in Denmark. Br J Cancer 1988;58:392–6.
29. Kristensen P, Irgens LM, Andersen A, et al. Gestation age, birth weight, and perinatal death among births to Norwegian farmers, 1967–1991. Am J Epidemiol 1997;146:329–8.
30. Kristensen P, Andersen A, Irgens LM, et al. Hormone-dependent cancer and adverse reproductive outcomes in farmers' families – effects of climatic conditions favoring fungal growth in grain. Scand J Work Environ Health 2000;26:331–7.

31. Christiani DC, Wegman DH, Eisen EA, et al. Cotton dust and gram-negative bacterial endotoxin correlations in two cotton textile mills. Am J Ind Med 1993;23:333–42.
32. Bouhuys A, Zuskin E. Byssinosis: occupational lung disease in textile workers. In: Frazier CA, editor. Occupational Asthma. New York: van Nostrand Reinhold, 1980:33–52.
33. Hend IM, Milnera M, Milnera SM. Bactericidal treatment of raw cotton as the method of byssinosis prevention AIHA J 2003;64:X88–94.
34. Lovell CR. Plants and the Skin. London: Oxford, 1993.
35. Mathias CG. Epidemiology of occupational skin disease in agriculture. In: Dosman JA, Cockcroft DW, editors. Principles of Health and Safety in Agriculture. Boca Raton: CRC Press, 1989:285–7.
36. Wooldridge WE. Acute allergic contact dermatitis: how to manage severe cases. Postgrad Med 1990;87(4):221–4.
37. Weed Science Society of America. Poison-ivy/poison-oak/poison-sumac – the virulent weeds [cited 13 October 2004]. Available from http://www.wssa.net/photo& info/larrymitich_info/ poisonivy.htm.
38. Marks Jr. JG, Elsner P, DeLeo V. Contact & Occupational Dermatology, third edition. St. Louis: Mosby, 2002.
39. Juckett G. Plant dermatitis: possible culprits go far beyond poison ivy. Postgrad Med 1996;100(3):159–63,167–71.
40. Zafren K. Poison Oak Dermatitis. Wilderness Environ Med 2001;12(1):39–40.
41. Stoner JG, Rasmussen JE. Plant dermatitis. J Am Acad Dermatol 1983;9(1):1–15.
42. Epstein WL. Occupational poison ivy and oak dermatitis. Dermatol Clin 1994;12(3):511–6.
43. Benezra C, Ducombs G, Sell Y, et al. Plant Contact Dermatitis. Burlington: BC Decker, 1985.
44. Earle-Richardson G, Jenkins PL, Slingerland DT, et al. Occupational injury and illness among migrant and seasonal farmworkers in New York State and Pennsylvania, 1997–1999: pilot study of a new surveillance method. Am J Ind Med 2003;44:37–45.
45. Parkinson. Images in Clinical Medicine. The Many Faces of Poison Ivy. N Engl J Med 2002;347:35.
46. Cohen LM, Cohen JL. Erythema multiforme associated with contact dermatitis to poison ivy: three cases and a review of the literature. Cutis 1998;62:139–142.
47. Salinas MC, Ogura T, Soffchi L. Irritant contact dermatitis caused by needle-like calcium oxalate crystals, raphides, in *Agave tequilana* among workers in tequila distilleries and agave plantations. Contact Dermatitis 2001;44:94–6.
48. Lovell CR. Phytodermatitis. Clin Dermatol 1997;15:607–13.
49. Adams SP. Dermacase: Phytophotodermatitis. Can Fam Physician 1998;44:503,509.
50. McBride JS, Altman DG, Klein M, et al. Green tobacco sickness. Tob Control 1998;7:294–8.
51. Onuki M, Yokoyama K, Kimura K, et al. Assesment of urinary cotinine as a marker of nicotine absorption from tobacco leaves: a study on tobacco farmers in Malaysia. J Occup Health 2003;45:140–5.
52. Gehlbach SH, Williams WA, Perry, LD, et al. Green tobacco sickness: an illness of tobacco harvesters. JAMA 1974;229:1880–3.

53. Weizenecker R, Deal WB. Tobacco cropper's sickness. Fla Med Assoc J 1970;57:13–4.
54. Ghosh SK, Parikh JR, Gokani VN, et al. Studies on occupational health problems during agricultural operation of Indian tobacco workers. J Occup Med 1979; 21:45–7.
55. Hipke ME. Green tobacco sickness. South Med J 1993;86:989–92.
56. Centers for Disease Control and Prevention. Green tobacco sickness in tobacco harvesters – Kentucky, 1992. MMWR Morb Mortal Wkly Rep 1993;42:237–40.
57. Edmonson WD, Smith BD. Green tobacco sickness (radycardia in a young farmer). J Tenn Med Assoc 1996;89:85–6.
58. Gehlbach SH, Williams WA, Freeman JI, et al. Nicotine absorption by workers harvesting green tobacco. Lancet 1975;1:478–80.
59. Quandt SA, Arcury TA, Preisser JS, et al. Migrant farmworkers and green tobacco sickness: new issues for an understudied disease. Am J Ind Med 2000;32:307–15.
60. Arcury TA, Quandt SA, Preisser JS, et al. The incidence of green tobacco sickness among Latino farmworkers. J Occup Environ Med 2001;43:601–9.
61. Ives TJ. Use of dimenhydrinate in the treatment of green tobacco sickness. Drug Intell Clin Pharm 1983;17:548–9.

27

Diseases from Animals, Poultry, and Fish

James E. Lessenger

Key words: zoonoses, mammals, reptiles, poultry, livestock, fish, aqua farming

Poultry, animals, and fish raised and slaughtered for human consumption comprise a large and varied group of mammals, birds, reptiles, amphibians and fish. They may be raised in the wild or in small backyard farm plots for a family's own consumption. More commonly they are raised in small and medium farms and, in some countries, feedlots or ponds that are many hectares in size.

In the same way that contaminated food can infect those who consume the meat (see Chapter 2), agricultural workers can become ill from the animal or poultry that they raise. Many of the illnesses are the same, but some are intrinsic to the farm and not found in the contaminated product (1).

The emergence of new zoonotic diseases and the resurgence of old ones like tuberculosis and cholera, reflect changes in human ecology:

1. Rural-to-urban migration resulting in high-density peri-urban slums
2. Increasing long-distance mobility and trade
3. Social disruption of war and conflict
4. Changes in personal behavior
5. Human-induced global changes, including widespread forest clearance and climate changes (2).

Animals and birds are also raised and sold as pets. Rats, mice, parakeets, snakes, prairie dogs, iguanas, and other animals not normally consumed by humans are raised in kennels and kept in homes.

Means of Transmission

Workers in production agriculture may come in contact with animals and animal products in the course of their job tasks. Table 27.1 lists the circumstances of contact where disease can be transmitted from animals to humans.

TABLE 27.1. Means of transmission from animals to humans.

Animal bites
Animal secretions
Saliva
Semen
Vaginal secretions
Skin contact
Veterinary care
Procedures such as castration, dehorning
Pushing, pulling animals
Feeding the young
Carcass handling
Slaughter
Necroscopy
Eggs
Milk
Handling freshly cooked or uncooked meat or poultry products
Eating or drinking uncooked or unpasteurized products before or during processing
Manure
Urine
Feces
Veterinary treatment

Source: Data from Jemmi et al. (1), Spencer et al. (3), Dutkiewicz (4), Guan and Holley (5), and Weber and Rutala (6).

A key problem is the lack of foot protection so that the unprotected feet of workers come in contact with feces of the animals. The fecal-hand route of transmission is also critical. Perhaps the most insidious and difficult to control is the consumption of raw poultry and meat products by workers in farms and processing plants. Many people in agriculture are living on subsistence or below-subsistence wages and consume products off the processing lines. Many of these products are not fully processed and may contact pathogens that have not been killed through cooking or irradiation (see Chapter 2) (Table 27.1) (3,4).

The improper handling of manure is a major source of disease, including the use of manure on food crops, the discharge of manure into community water sources, and the spread of manure onto areas where children play. In Canada, an outbreak of *Escherichia coli* O157:H7 was traced to organic growers who contaminated their produce with cow manure containing *E. coli*. Also in Canada, an outbreak of *Citrobacter freundii* infections was associated with parsley originating from an organic garden in which pig manure was used. Other documented infections of humans from manure-contaminated foods includes *Listeria monocytogenes* in cabbage contaminated by sheep waste, *Cryptosporidium* spread by municipal water contaminated by cattle, *Salmonella hartford* in food prepared by contaminated water from a shallow well polluted with poultry manure, and *Pleisomonas shigelloides* infection associated with well-water contaminated by poultry manure (5).

Agricultural Workers at Risk

Workers, visitors, inspectors, veterinarians, and people who live on or adjacent to farms, ranches, feedlots, processing plants, and other agricultural endeavors are at risk for contracting diseases from animals, poultry, or fish. One needs only to follow the animals from the farm to the feedlots, slaughter house, processing and sorting lines, and packaging plants to appreciate the large number of people who are at risk due to contact with animals and animal products. Physicians and other health care professionals are also at risk as they visit farms and plants for inspections or orientations (6).

Prevention

Methods of preventing the transmission of infectious material from animals and poultry to agricultural workers mirror in many ways the safety techniques for protection from chemicals, trauma and other hazards (see Chapter 6). The methods are summarized in Table 27.2.

Key to the prevention of the transmission of animal disease to humans is the proper processing of food products. This includes proper cook times and temperatures, adequate refrigeration, and appropriate transportation, processing, and stocking in stores.

Personal protective equipment includes hats or head coverings and protective coats or uniforms that can be laundered and left at the plant or farm. Boots should also be cleaned and left at the farm or plant. Especially in poultry operations, protective particulate masks may be necessary. In some

TABLE 27.2. Methods for preventing the infection of agriculture workers from poultry or animals.

Proper food processing
Personal protective equipment (Chapter 6)
Masks, hats, coveralls, gloves
Protective physical barriers
Policies and procedures
Veterinary herd monitoring
Rapid culling
Public health monitoring for disease trends and epidemics
Medical monitoring
Immunizations (Chapter 25)
Education and training (Chapter 5)
Development of technologies to prevent transmission
Hygiene
Hand washing
Government regulations and monitoring (Chapter 4)
Supervision

Source: Data from Davies and Wray (7), Fone and Barker (8), Meslin (9), Gardner (10), and Richardson et al. (11).

situations, especially when handling urine or feces, protective gloves are important (see Chapter 6).

Protective physical barriers in farm, ranch, or plant design allow for the raising or processing of food products without actual contact of humans with the animals or products. Built-in barriers, changing rooms, boot baths, and hand-free handling techniques allow for the safe and efficient handling of food.

In British chicken hatcheries, an aggressive combination of egg sanitization and handling methods was successful in decreasing zoonotic infections and diseases spread through flocks. Procedures included:

1. Design changes in incubators
2. Whole building ventilation systems
3. Control of dust, fluff, and aerosol production
4. Disinfection of surfaces and equipment
5. Improved handling of wastes (7).

Policies and procedures to limit or prevent physical contact with animals, feces, or urine prevent transmission. Rules prohibiting the consumption of food products on farms and ranches or on production lines are especially important. Not only can the production food product be infectious to workers, but food brought in by workers can become contaminated, which mandates eating areas for workers away from the livestock (7).

Aggressive veterinary monitoring of livestock can detect early evidence of disease outbreaks in herds. Similarly, public health monitoring of disease in humans can detect and appropriately treat epidemics of food-borne disease in humans and trace the source to the food-processing breakdown that caused the disease. Hazard analysis of critical control points (HACCP) is crucial to the prevention of infections in herds. Low cost, ease of performance, and rapidity of results are the key criteria for the tests, and are sometimes more important than the performance characteristics of sensitivity, specificity, and reproducibility. Field test kits are available for bacterial, protozoa, antibiotic residue, and other parameters of animal health (8,9,10).

Medical monitoring can detect early disease and prevent its spread to other employees, the food product, and family members. Pre-placement medical monitoring can identify people who are susceptible to infection, for example people with diabetes or immune diseases. In parts of the world where bovine tuberculosis is common, TB skin test monitoring can detect early infections and allow early treatment (8,9).

Immunizations are expensive, unavailable in many parts of the world, and only recommended for areas of high infectivity or occupations of high risk such as veterinarians. Three critical immunizations are tetanus, rabies, and influenza (see Chapter 25). Vaccines against salmonella, shigella, and other pathogens are in development or testing.

Training and education in proper handling techniques are important. Proper ways of herding, handling, and caring for animals and poultry can prevent infection and the transmission of infectious material. See Chapter 5 for details of education and training.

Research and the development of new techniques to prevent transmission are critical. For example, airborne dust has been discovered to be a carrier of pathogens in broiler breeder pullets (chicken pens). The use of an electrostatic space charge system has decreased the particle concentration and, in the process, decreased the potential of disease transmission to other chickens and to poultry workers (11).

Hygiene, both in the person and in the workplace, is essential in preventing the transmission of disease. For example, in many German piggeries workers must shower and change clothing when they enter and leave the buildings. This technique prevents the infection of the pigs with outside pathogens, the transfer of pathogens from one piggery to another, and the transfer of pathogens to the home environment. Especially important are the cleaning of machinery and the timely cleaning of animal and poultry urine and feces. Not only can urine and feces be infectious but they can attract insects that can spread pathogens. As in medicine, the most important hygiene procedure is aggressive hand washing for all persons handling food products.

In Louisiana, for example, alligator farmers must wear rubber boots and waders to protect themselves from pathogens (but not from bites, which can go right through the protective ensembles). Each day, the pens must be flushed and hosed off to remove the wastes that could harbor pathogens dangerous to the alligator colonies and workers.

Governmental regulations and oversight are important in providing standardization and systemization of methods and procedures to reduce the risk of infection to agricultural workers. Good regulations and oversight are evidence-based and consistent with sound agricultural methods (see Chapter 4).

It is not enough to have rules, regulations, equipment and techniques to prevent the spread of pathogens from animals and poultry to workers. Fair and consistent supervision by knowledgeable managers is critical to see that the proper equipment and supplies are used and that handling and hygiene rules and regulations are carried out.

Mammalian-Borne Diseases

Game are mammals killed or captured in the field for human consumption or for their hides, including elk, boars, bison, and deer. Production animals include cattle, pigs, goats, sheep, horses, dogs, deer, and other animals grown in small to large farms and ranches for human consumption. Typically the animals are slaughtered and dressed in various cuts made from the different parts of the animal. In addition, many animals are raised and kept as pets.

Viral Diseases

Rabies

Rabies is a common viral infection in children who live in rural areas and in people who handle un-immunized mammalian animals. The prophylaxis for rabies is discussed in Chapter 31. With the exception of four cases where the disease was treated with intensive therapy, the disease is considered universally fatal. Therefore, immunizations and prophylaxis are critical.

Monkeypox in prairie dogs

During May and June 2003, the first cluster of human monkeypox cases in the United States was reported. Most patients with this febrile, vesicular rash illness presumably acquired the infection from prairie dogs. Monkeypox virus was demonstrated by using polymerase chain reaction in two prairie dogs in which pathologic studies showed necrotizing bronchopneumonia, conjunctivitis, and tongue ulceration. Immunohistochemical assays for orthopoxviruses demonstrated abundant viral antigens in surface epithelial cells of lesions in conjunctiva and tongue, with lesser amounts in adjacent macrophages, fibroblasts, and connective tissues. Viral antigens in the lung were abundant in bronchial epithelial cells, macrophages, and fibroblasts. Virus isolation and electron microscopy demonstrated active viral replication in lungs and tongue. Both respiratory and direct mucocutaneous exposures are potentially important routes of transmission of monkeypox virus among rodents and to humans. Prairie dogs can be studied for insights into transmission, pathogenesis, and vaccine and treatment trials, because they are susceptible to severe monkeypox infection (12).

Prion disease

Chronic wasting disease (CWD) in North American deer and elk has been associated with Creutzfeldt-Jakob disease (CJD) in 3 hunters who killed, prepared, and ate their own game. An absolute association was not established, but further monitoring is ongoing (see Chapter 29). Creutzfeldt-Jakob disease does not appear to be a problem with workers who raise cattle or dairy cows (13).

Bacterial Diseases

Champylobacter

Chlamydophila abortus is a well recognized pathogen causing abortions in cattle and goats. A recent report from Germany cites a case where a pregnant woman became infected from farm animals and aborted. This rare zoonotic infection underlines the insidious and widespread problem of zoonotic infections on farms (14,15).

Campylobacter jejuni and *C. coli* have recently become recognized as common bacterial causes of diarrhea. Infection can occur at any age. Sources of infection are typically mammalian and avian hosts. The usual incubation period of campylobacter enteritis is 2 to 5 days. Fever, diarrhea and abdominal pain are the most common clinical features. The stools frequently contain mucus and, a few days after the onset of symptoms, frank blood. Significant vomiting and dehydration are uncommon. A rapid presumptive laboratory diagnosis may be made during the acute phase of the illness by direct phase-contrast microscopy of stools. Isolation of the organism from stools requires culture in a selective medium containing antibiotics and incubation under reduced oxygen tension at 42°C. The organism persists in the stools of untreated patients for up to 7 weeks following the onset of symptoms. Erythromycin may produce a rapid clinical and bacteriologic cure and should be used to treat moderately to severely ill patients as well as patients with compromised host defenses (14).

Salmonella

Salmonellosis is one of the most important public health disease problems, affecting more people and animals than any other single disease in agriculture. In Canada, for example, there were 7,138 cases of food-borne salmonellosis in humans during 2003. The native habitat of members of the genus Salmonella is the intestinal tract of warm-blooded and many cold-blooded vertebrates. In humans, the incubation period is 6 to 48 hours and produces headache, malaise, nausea, fever, vomiting, abdominal pain, and diarrhea (with and without blood). Salmonella is also capable of invading the intestinal mucosa, entering the blood stream, and causing septicemia, shock, and death. The diagnosis is made through the clinical presentation and confirmation with blood and stool cultures and serology. Treatment is first started empirically pending culture results and then adjusted if necessary. Multi-drug resistant *S. typhimurium* bacteria have been documented to be present in milk after pasteurization (16,17).

Listeriosis

Listeria monocytogenes is a zoonotic food-born pathogen that is responsible for 28% of food-related deaths in the United States annually and that is a major cause of food recalls worldwide. Agricultural exposure is through drinking unpasteurized milk or direct contact with the animal or manure. The disease pattern is similar to salmonella (18).

Tuberculosis

Tuberculosis (TB) continues to be a worldwide infectious problem for humans. While human-to-human infection is of greatest concern, one infected dairy herd can infect hundreds, if not thousands, of people.

Potentially, tuberculosis can infect any mammal, although production cattle, especially dairy cattle, are at greatest risk. Complicating efforts to combat the disease is the fact that deer, badgers, elk and other wild species have been found to harbor the mycobacterium. In England, badgers were found to be spreading the infection to herds of cattle. Also, in England and Ireland, herds of sheep were found to be infected. In New Zealand, wild brush tail possums (*Trichosurus vulpecula*) were discovered to be the main source of infection in livestock, including deer herds. In Tanzania, tuberculosis-infected herds were found more often in small, pastoral farms that have little veterinary monitoring, as opposed to the large, commercial enterprises (19–22).

In a Los Angeles zoo, TB was found in two Asian elephants, three Rocky Mountain goats, and one black rhinoceros. An investigation found no active cases of tuberculosis in humans; however, tuberculin skin-test conversions in humans were associated with training the elephants and attending an elephant necropsy (23).

Human-to-animal transmission of TB has been documented. In an exotic animal farm in Illinois, three elephants died of Mycobacterium tuberculosis and a fourth tested culture-positive. Twenty-two handlers were screened for TB; eleven had positive reactions to intradermal injection with purified protein derivative. One had a smear-negative, culture-positive active TB. DNA comparisons by IS6110 and TBN12 typing showed that the isolates from the four elephants and the handler with active TB were the same strain, thus documenting that the infection of the elephants came from the handler (24).

Mycobacterium (tuberculosis) can infect agricultural workers in a number of ways:

1. Human-to-human contact with co-workers through the inhalation of respiratory droplets
2. Drinking contaminated, unpasteurized milk
3. Direct contact with infected animals
4. Direct contact with the secretions of infected animals such as respiratory droplets, milk, manure, urine, semen, and vaginal secretions
5. Direct contact or inhalations of respiratory droplets during necropsy, slaughter, or processing of meat or dairy products (20–24).

The clinical presentation is that of weight-loss, night sweats, a chronic cough, and hemoptysis. Asymptomatic workers are typically discovered through public health surveys. Diagnosis is through the purified protein derivative (PPD) skin test, smears of respiratory secretions demonstrating acid-fast bodies, cultures of respiratory secretions and other body fluids, radiographs demonstrating caseating granulomas, and other typical findings. Treatment is by multidrug therapy, complicated by regional drug resistance patterns (20–24).

Protozoal Disease

Giardia infections have been associated with contaminated sewage and water in agricultural environments, producing gastroenteritis. In the Sierra foothills of California, cattle drink water contaminated by infected beavers. Beaver- and cattle-contaminated water is then consumed by unsuspecting tourists who develop crampy abdominal pain, fevers, and a profuse bloody diarrhea. The *Giardia* infections are easily treated with metronidazole (5).

Avian-Borne Diseases

Fowl are birds that grow in the wild. Nearly every bird found in the wild can be prepared for human consumption. Poultry are birds grown in farm environments for human consumption. Common poultry include: chickens, turkeys, ducks, pigeons, game hens, geese, doves, and peacocks.

Viral Diseases

Avian Influenza

Avian influenza A (H5N1) first infected humans in 1997, in Hong Kong. The virus was transmitted directly from birds to humans. Eighteen people were admitted to hospitals, and 6 died. In 2003, 2 cases of avian influenza A (H5N1) infection occurred among members of a Hong Kong family, 3 of whom had traveled to mainland China. One person died. How or where these 2 people became infected was not determined.

Influenza A has the potential to cross species and has been implicated in the 3 flu pandemics in the 20th century (1918, 1957 and 1968). Pandemics occur when 3 conditions are met:

1. The emergence of influenza A virus with a hemagglutinin subtype is completely different from that of strains circulating in humans for many preceding years.
2. There is a high proportion of susceptible people in the community (i.e., a population with low antibody titers to the new strain).
3. Efficient person-to-person transmissibility of the new virus is possible with accompanying human disease (25-27).

The reported signs and symptoms of avian influenza in humans include:

1. Typical flu-like symptoms such as fever, cough, sore throat, and muscle aches

2. Eye infections
3. Pneumonia
4. Acute respiratory distress syndrome (ARDS)
5. Multiple organ failure
6. Lymphopenia
7. Elevated liver enzyme levels
8. Abnormal clotting profiles.

Physicians are advised to isolate the patient, initiate droplet precautions, and contact their local medical officer for further discussions if an epidemiological link is suspected.

The World Health Organization (WHO) is moving to rapidly produce a new influenza vaccine capable of protecting people against the H5N1 strain of avian influenza A. Preliminary genetic tests conducted in CDC laboratories in Atlanta, London, and Hong Kong suggest that the H5N1 strain is resistant to amantadine and rimantadine but is believed to be susceptible to neuraminidase inhibitors.

The WHO has recommended urgent, rapid culling of infected and exposed bird populations to eliminate the reservoir of the H5N1 strain. In addition, WHO has discouraged the practice of marketing live poultry directly to consumers in areas currently experiencing outbreaks of avian influenza A (H5N1). Some countries have introduced trade restrictions to protect animal health. However, available data do not suggest that processed poultry products (i.e., refrigerated or frozen carcasses and products derived from them) or eggs from affected areas pose a public health risk. The virus is killed by cooking (25–27).

Newcastle Disease

Newcastle disease is caused by virulent strains of APMV. Death rates among naive bird populations can exceed 50%. The virus responsible for Newcastle disease has been known to cause conjunctivitis and upper respiratory infections in humans since the 1940s. The disease is self-limiting and does not have any permanent consequences (28).

West Nile Virus

In 2002, Wisconsin public health officials were notified of two cases of febrile illness in workers at a commercial turkey breeder farm. A high prevalence of West Nile virus antibody was found among workers and turkeys. An associated high incidence of febrile illness among farm workers also was observed. Possible non-mosquito transmission among birds and subsequent infection of humans was postulated, but the mode of transmission was unknown (29).

Bacterial Diseases

Avian tuberculosis was diagnosed in two mature rheas on different ratite farms over a 2-year period. Both birds died after weight loss and development of granulomas in the lungs of one bird and bilaterally in the cubcutis cranial to the shoulder in the other. Smears and cultures of the granulomas were positive for acid-fast bacilli and tuberculosis (30).

Psittacosis

Chlamydophila (Chlamydia) psittaci, *C. trachomatis,* and *C. pneumoniae* can be passed from birds of all species to humans. Wild pigeons and pheasants have been demonstrated to be a source. Wild birds in captivity, pets (usually cockatiels, parakeets, parrots, and macaws), and production animals can infect workers, and there are reports of customs and health inspection workers becoming infected. Infection is through contact with feces, urine, and oral secretions (31).

Mild infection produces a tracheobronchitis with flu-like symptoms of cough, congestion, myalgias, fatigue, and fever. In severe infections, untreated workers, and immunocompromised workers, pneumonia, sepsis, shock, and death can occur. Radiographs reveal a lobar infiltrate (31).

Diagnosis is by detection of the 16s rRNA gene of *C. Psittasi* in sputum with a PCR analysis, and a typical radiographic appearance and culture. Tetracyclines and erythromycin are effective for treatment. Prevention is through close monitoring and culling flocks and pet birds and personal protection equipment (32).

Campylobacter Jejuni

Raising poultry at home is common in low-income countries. Studies demonstrate that proximity to free-range domestic poultry increases children's risk of infection with diarrhea-causing organisms such as *Campylobacter jejuni*. Corralling might reduce the risk, but research on the socioeconomic acceptability of corralling is lacking. Many people report that home-grown poultry and eggs taste better and are more nutritious. They enjoy living around animals and want to teach their children about raising animals. To prevent theft, some residents shut their birds in provisional enclosures at night but allege that birds are healthier, happier, and produce better meat and eggs when let loose by day. Many rural peoples view bird feces in the house and yard as dirty, but few see a connection to illness. Residents consider chicks and ducklings more innocuous than adult birds and are more likely to allow them inside the house and permit children to play with them. Additional food and water costs with corralling are a significant obstacle for some. Adequate space and corral hygiene must also be addressed to make this intervention

viable. Developing a secure, acceptable, and affordable corral remains a challenge for rural populations (33,34).

Salmonellosis

Although approximately 95% of disease caused by non-typhoidal salmonella is transmitted by food-borne vehicles, four documented salmonella outbreaks in the 1990s have been traced to contact with young poultry. No environmental studies of source hatcheries were completed. A case-control study was performed by comparing culture-confirmed *Salmonella infantis* in Michigan residents, identified between May and July 1999, with two age- and neighborhood-matched controls. Eighty environmental and bird tissue samples were collected from an implicated hatchery; all salmonella isolates underwent pulsed-field gel electrophoresis (PFGE) analysis. The study included 19 case-patients sharing the same PFGE subtype and 37 matched controls. Within 5 days before illness onset, 74% of case-patients resided in households raising young poultry compared with 16% of controls (matched OR 19.5; 95% CI 2.9, 378.1). Eight hatchery samples yielded *S. infantis* with PFGE subtypes matching the patients' isolates. This investigation identified birds from a single hatchery as the source of human illness and confirmed the link by matching PFGE patterns from humans, birds and the hatchery environment. Subsequent public health interventions reduced, but did not eliminate, transmission of poultry-associated salmonellosis. Five additional PFGE-linked cases were identified in spring 2000, necessitating quarantine of the hatchery for depopulation, cleaning and disinfection (35).

Fish-Borne Diseases

Fish farming, or aquaculture, for fish and shellfish is becoming more common and more internationalized with every passing year. In the United States, more than half the seafood consumption is imported, much of it from fish farming. The world's seafood trade is very complex, and if is often difficult or impossible to determine where the seafood is raised or harvested. For example, the United States imports salmon from Switzerland and Panama though neither country is known for large salmon fisheries (36).

In general, farmed fish is as safe and nutritious as wild-caught species, but there are public health hazards associated with ignorance, abuse, and neglect of aquaculture technology. Numerous small fish ponds increase the shoreline of ponds causing higher densities of mosquito larvae and cercaria, which can increase the incidence and prevalence of lymphatic filariasis and schistosomiasis. Especially dangerous is the use of human waste draining to fertilize or create ponds. Technology abuse includes the misuse of therapeutic drugs, chemicals, fertilizers and natural fish habitat areas. Technology neglect includes the failure to pay attention to mosquito habitats and the concomitant increase in malaria, as well as the propagation of other organisms (36).

Human exposure can be through direct skin contact with fish or the consumption of contaminated fish or shellfish products or contaminated water. The main pathogens acquired topically from fish (through spine puncture or open wounds) are *Aeromonas hydrophila*, *Edwardsiella tarda*, *Erysipelothrix rhusiopathiae*, *Mycobacterium marinum*, *Streptococcus iniae, Vibrio vulnificus,* and *Vibrio damsela. S. iniae* has recently emerged as a public health hazard associated with aquaculture, and *M. marinum* often infects home aquarium hobbyists. Common zoonoses contracted through the consumption of contaminated products or water include salmonella, leptospirosis, yersiniosis, and tuberculosis (37).

Salmonella

Salmonellae species have been found associated with all of the poikilothermic vertebrate species studied, as well as the mollusks and crustaceans (38).

Leptospirosis

Leptospirosis does occur in the poikilothermic vertebrates, as evidenced by positive serological reactions and by the isolation of pathogenic leptospiral serovars. The finding of leptospirosis species in fish, mollosks and other aquatic species are of special importance in view of the increased worldwide interest in aquaculture farming. Since 1975, 24 of the 101 (23.7%) reported human cases of leptospirosis in Hawaii have been associated with aquaculture industries (taro farms, prawn farms and watercress farms) (39).

Yersiniosis

Species of *Yersinia* are a particular problem in fish and in people involved in fish farming. Workers who wade in fish ponds or drink drainage water are especially at risk. *Yersinia enterocolitica* has been demonstrated to be a causative agent in acute diarrhea illness in humans after workers become infected through the feces-hand-oral route (19).

Tuberculosis

Tuberculosis has also been reported in freshwater and marine fish species (piscine tuberculosis), especially in those grown on fish farms. *Mycobacterium marinum* and *M. celonae* have been demonstrated in fish farms (30).

Reptile-Borne Diseases

Turtles, lizards, snakes, green iguanas (Iguana iguana), alligators, and crocodiles are grown from eggs in farms for their hides and meat. Some species are also grown for sale as pets.

Salmonella infections in persons who had contact with reptiles usually cause gastroenteritis but can result in invasive illness, including septicemia and meningitis, especially in infants and immunocompromised persons. For decades, reptiles have been known to be a source for salmonellosis; however, numerous reptile owners remain unaware that reptile contact places them and other household members, including children, at greater risk for infection. (40)

Captive reptiles (such as iguanas) are routinely identified as reservoirs of Salmonella and the number of reports about reptile-associated salmonellosis is increasing. In Germany and Austria, salmonella was detected in 54.1% of fecal reptile samples cultured. The percentage of salmonella-positive samples was significantly lower in turtles as compared with lizards and snakes, as salmonella was only detected in one sample from a single turtle out of 38 turtles investigated. In all, 42 different salmonella serovars were found. All isolated salmonella belonged to the species *enterica*, predominantly to the subspecies I (n = 46) and IIIb (n = 30) but also to subspecies II (n = 3), IIIa (n = 6), and IV (n = 2). All isolates were sensitive to the antimicrobials examined. A significantly higher percentage of salmonella-positive reptiles was detected in the group of owners who purchased reptiles in comparison with pure breeders. The high percentage of salmonella in reptiles in the study confirms the risk for the transmission of the infection to humans (41).

Amphibian-Borne Diseases

Amphibians include frogs, toads, newts, and salamanders that are caught in the wild or grown on farms for use as food or as pets. Frogs are caught in the wild and grown in farms for their meat, primarily frog legs. Eating inadequately cooked frog legs can lead to an infection of *Alaria americana*, a trematode. Increasing evidence suggests that amphibians can pose risks for salmonellosis in humans (42).

References

1. Jemmi T, Danuser J, Griot C. Zoonoses as a risk when associating with livestock or animal products. Schweiz Arch Tierheilkd 2000;142:665–71.
2. Weiss RA, McMichael AJ. Social and environmental risk factors in the emergence of infectious diseases. Nat Med 2004;10:(12Suppl):s70–6.
3. Spencer JL, Guan J. Public health implications related to spread of pathogens in manure from livestock and poultry operations. Methods Mol Bio 2004; 268:503–15.
4. Dutkiewicz J. Occupational bio hazards: Current issues. Med Pr 2004;55:31–40.
5. Guan TY, Holley RA. Pathogen survival in swine manure environments and transmission of human enteric illness: A review. J Environ Qual 2003;32:383–92.
6. Weber DJ, Rutala WA. Zoonotic infections. Occup Med 1999;14:247–84.
7. Davies RH, Wray C. An approach to reduction of Salmonella infection in broiler chicken flocks through intensive sampling and identification of cross-contamination hazards in commercial hatcheries. Int J Food Microbiol 1994;24:147–60.

8. Fone DL, Barker RM. MAFF statuatory incident reports in surveillance, prevention, and control of human *Salmonella typhimurium* infection. Commun Dis Rep CDR Rev. 1996;6:R76–8.
9. Meslin FX. Surveillance and control of emerging zoonoses. World Health State Q 1992;45:200–7.
10. Gardner IA. Testing to fulfill HACCP (Hazard Analysis Critical Control Points) requirements: Principles and examples. J Dairy Sci 1997;80:3453–7.
11. Richardson LJ, Mitchell BW, Wilson JL, Hofacre CL. Effect of an electrostatic space charge system on airborne dust and subsequent potential transmission of microorganisms to broiler breeder pullets by airborne dust. Avian Dis 2003;47(1):128–33.
12. Guarner J, Johnson BJ, Paddock CD, Shieh WJ, Goldsmith CS, Reynolds MG, Damon IK, Regnery RL, Zaki SR; Veterinary Monkeypox Virus Working Group. Monkeypox transmission and pathogenesis in prairie dogs. Emerg Infect Dis 2004;10(3):426–31.
13. Hoey J. Wild game feasts and fatal degenerative neurological illness. CMAJ 2003;169(5):443.
14. Pospischil A, Thoma R, Hilbe M, Grest P, Zimmermann D, Gebbers JO. [Abortion in humans caused by Chlamydophila abortus (Chlamydia psittaci serovar 1)] Schweiz Arch Tierheilkd 2002;144(9):463–6.
15. Meijer A, Brandenburg A, de Vries J, Beentjes J, Roholl P, Dercksen D. Chlamydophila abortus infection in a pregnant woman associated with indirect contact with infected goats. Eur J Clin Microbiol Infect Dis 2004;23:487–90
16. Woodward DL, Khakhria R, Johnson WM. Human salmonellosis associated with exotic pets. J Clin Microbio 1997;35:2786–90.
17. Olsen SJ, Ying M, Davis MF, Deasy M, Holland B, Iampietro L, et al. Multidrug-resistant *Salmonella typhimurium* infection from milk contaminated after pasteurization. Emerg Infect Dis 2004;10:932–5.
18. Borucki MK, Reynolds J, Gay CC, McElwain KL, Kimi SH, Knowles DP, Hu J. Dairy farm reservoir of Listeria monocytogenes sporadic and epidemic strains. J Food Prot 2004;67:2496–9.
19. Bailey GD, Vanselow BA, Hornitzky MA, Hum SI, Eamens GJ, Gill PA, et al. A study of the foodborne pathogens: Campylobacter, Listeria and Yersinia, in faeces from slaughter-age cattle and sheep in Australia. Commun Dis Intell 2003;27:249–57.
20. White PC, Benhin JK. Factors influencing the incidence and scale of bovine tuberculosis in cattle in southwest England. Prev Vet Med 2004;63:1–7.
21. Griffin JF, Chinn DN, Rodgers CR. Diagnostic strategies and outcomes on three New Zealand deer farms with severe outbreaks of bovine tuberculosis. Tuberculosis (Edinb) 2004;84:293–302.
22. Shirima GM, Kazwala RR, Kambarage DM. Prevalence of bovine tuberculosis in cattle in different farming systems in the eastern zone of Tanzania. Prev Vet Med 2003;57:167–72.
23. Oh P, Granich R, Scott J, Sun B, Joseph M, Stringfield C, et al. Human exposure following Mycobacterium tuberculosis infection of multiple animal species in a metropolitan zoo. Emerg Infect Dis 2002;8:1290–3.
24. Michalak K, Austin C, Diesel S, Bacon MJ, Zimmerman P, Maslow JN. Mycobacterium tuberculosis infection as a zoonotic disease: Transmission between humans and elephants. Emerg Infect Dis 1998;4:283–7.

25. Capua I, Alexander DJ. Avian influenza: recent developments. Avian Pathol 2004;33(4):393–404.
26. Capua I, Alexander DJ. Human health implications of avian influenza viruses and paramyxoviruses. Eur J Clin Microbiol Infect Dis 2004;23(1):1–6.
27. Weir E, Wong T, Gemmill I. Avian influenza outbreak: update. CMAJ 2004;170(5):785–6.
28. Pedersen JC, Senne DA, Woolcock PR, Kinde H, King DJ, Wise MG, et al. Phylogenetic relationships among virulent Newcastle disease virus isolates from the 2002–2003 outbreak in California and other recent outbreaks in North America. J Clin Microbiol 2004;42:2329–34.
29. Center for Disease Control and Prevention. West Nile virus infection among turkey breeder farm workers: Wisconsin, 2002. Morb Mortal Wkly Rep 2003;52:1017–9.
30. Sanford SE, Rehmtulla AJ, Josephson GK. Tuberculosis in farmed rheas (Rhea americana). Avin Dis 1994;38:193–6.
31. Elliott JH. Psittacosis. A flu like syndrome. Aust Fam Physician. 2001;30(8):739–41.
32. Heddema ER, Kraan MC, Buys-Bergen HE, Smith HE, Wertheim-van Dillen PM. A woman with a lobar infiltrate due to psittacosis detected by polymerase chain reaction. Scand J Infect Dis 2003;35(6–7):422–4.
33. Butzler JP. Campylobacter, from obscurity to celebrity. Clin Microbiol Infect 2004;10:868–76.
34. Karmali MA, Fleming PC. Campylobacter enteritis. Can Med Assoc J 1979;120(12):1525–32.
35. Wilkins MJ, Bidol SA, Boulton ML, Stobierski MG, Massey JP, Robinson-Dunn B. Human salmonellosis associated with young poultry from a contaminated hatchery in Michigan and the resulting public health interventions, 1999 and 2000. Epidemiol Infect 2002;129(1):19–27.
36. Garrett ES, dos Santos CL, Jahncke ML. Public, animal, and environmental health implications of aquaculture. Emerg Infect Dis 1997;3:453–7.
37. Lehane L, Rawlin GT. Topically acquired bacterial zoonoses from fish: a review. Med J Aust. 2000 Sep;173(5):256–9.
38. Minette HP. Epidemiologic aspects of salmonellosis in reptiles, amphibians, mollusks and crustaceans–a review. Int J Zoonoses. 1984;11(1):95–104.
39. Minette HP. Leptospirosis in poikilothermic vertebrates. A review. Int J Zoonoses. 1983;10(2):111–21.
40. Centers for Disease Control and Prevention (CDC). Reptile-associated salmonellosis—selected states, 1998–2002. MMWR Morb Mortal Wkly Rep 2003 Dec 12;52(49):1206–9.
41. Geue L, Loschner U. Salmonella enterica in reptiles of German and Austrian origin. Vet Microbiol 2002;84(1–2):79–91.
42. Fernandes BJ, Cooper JD, Cullen JB, Freeman RS, Ritchie AC, Scott AA, Stuart PF. Systemic infection with Alaria americana (Trematoda). Can Med Assoc J 1976;115(11):1111–4.

28

Diseases from Soil

Royce H. Johnson, Augustine D. Muñoz,
and Alan Scott Ragland

Key words: blastomycosis, chromomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, mycetoma, mycoses, scedosporium infection, sporotrichosis

Agricultural occupations are associated with a variety of soil-borne pathogens and diseases. Pathogen specific environmental conditions such as humidity, compost, animal manure, and decaying wood often produce geographically localized epidemiology. Soil-borne infections from occupational or vocational exposure usually occur through inoculation of the organism into the skin or by inhalation of the organism. Pathogens discussed in this chapter include bacterial and fungal agents directly or indirectly related to agricultural work in the soil itself (Table 28.1) (1,2).

Histoplasmosis

Histoplasmosis is the most prevalent of the systemic mycoses; cases are reported on every continent except Antarctica. Temperate zones between latitudes 40˚N and 30˚S provide the 35 to 50 inches of rainfall, 67% to 87% humidity, and temperature range of 22˚C to 29˚C needed for the mycelial phase of the fungus to grow. Temperature and humidity may affect infection rate and severity of clinical manifestations. The fungus prefers acidic soil conditions with high nitrogen content. This is thought to account for the association of histoplasmosis with avian and bat guano. Infections of a broad array of mammals have been reported, but the avian species appear to escape disease because of their higher body temperatures (1,2,3).

Infection with *Histoplasma capsulatum* begins with inhalation of microconidia. The vast majority of those infected will have no immediate symptoms. Symptoms of the acute pulmonary phase include fever of 42˚C, headache, arthralgia, myalgias, a nonpleuric substernal chest pain from mediastinal and hilar lymph node enlargement, erythema nodosum or

TABLE 28.1. Systemic fungi.

Organism	Microscopic description of yeast (infectious) form
Histoplasma capsulatum	Polar budding with thin neck between mother and daughter cells (3-4 microns) μm
Blastomyces dermatitidis	Thick refractile wall; multinucleated with single, broad - based bud (8-15 microns)
Coccidioides immitis *Coccidioides posadaii*	Spherule with many endospores
Sporothrix schenckii	Oval or cigar-shaped yeast with budding

Source: Data from Kaplan (1) and MacKinnon (2).

erythema multiformi, pericarditis, and a patchy pneumonitis on chest x-ray. They begin 7 to 21 days after exposure. Symptoms usually resolve within 10 days. Evidence of past infection includes pulmonary calcifications with a Ghon-like complex on chest x-ray and liver or splenic calcifications (3).

Approximately 5% of immunocompetent patients with histoplasmosis will develop progressive disseminated histoplasmosis (PDH). The incidence in immunocompromised patients such as HIV, transplant recipients, or the elderly is higher. PDH can develop after reactivation of dormant disease or reinfection with a large inoculum. PDH produces a wide range of disease that is categorized by clinical presentation into acute, subacute, or chronic (2,3).

Acute PDH is mostly seen in infants or immunocompromised patients. Patients develop abrupt onset of fever and malaise, weight loss, diarrhea, cough, hepatomegaly, lymphadenopathy and pancytopenia. Fatality is nearly universal without treatment. Subacute PDH has a more prolonged presentation with less fever and less striking laboratory abnormalities. The prolonged course of subacute PDH produces more distinctive clinical features such as ulcers in the large and small bowel with diarrhea, cramping, or perforation, endocarditis, intracranial masses, or chronic meningitis. Involvement of the adrenal gland occurs in 80% of subacute PDH patients, but symptoms of adrenal insufficiency are uncommon. Chronic PDH has a more prolonged presentation with milder symptoms. Malaise and lethargy are the most common complaints with oropharyngeal ulcers being the most common physical finding. There is notable absence of major organ involvement as seen in subacute PDH (1,2,3).

In addition to PDH, histoplasmosis has several clinical entities associated with chronic inflammation. Involvement of the lymph nodes can produce a mediastinal fibrosis that encroaches on vital structures. A fibrous mass called a histoplasmoma may develop from chronic inflammation, usually in the lung. Anterior uveitis or panophthalmitis may develop. More commonly seen is the ocular histoplasmosis syndrome that is characterized as a posterior uveitis/chorioditis that may result in neovascularization, scarring, and macular hemorrhage. Cavitary pulmonary histoplasmosis is characterized by fever,

productive cough, dyspnea, weight loss, night sweats, hemoptysis, and upper lobe cavitations on the chest x-ray (1,2,3).

In addition to *Histoplasma capsulatum*, African soil also supports *Histoplasma duboisii*. The clinical presentation of this species is usually restricted to skin and bone, although progressive disseminated disease has been reported. Skin lesions are usually ulcers, nodules, or plaques resembling psoriasis or subcutaneous nodules without inflammation (cold abscess). The skull, ribs, or other bones develop oteolytic lesions with associated sinus tract or cystic bone formation (3).

The definitive diagnosis of histoplasmosis comes from culturing the organism from the patient or by visualization on a tissue specimen with silver stain (Figure 28.1). Antigen testing for histoplasmosis is most useful for rapid diagnosis and may be used to monitor therapy and relapse. Anti-histoplasma antibodies develop 2 to 6 weeks after infection. Interpretation of this antibody testing has limitations that must be considered, such as cross reactivity with blastomycosis and coccidioidomycosis. Development of commercial PCR testing will allow rapid and specific diagnosis. Skin testing is useful for epidemiologic studies but has little diagnostic value (3).

Patients with acute pulmonary and cavitary histoplasmosis may resolve without treatment. Patients with severe symptoms, mediastinal fibrosis, subacute or chronic PDH should be treated with itraconazole, ketoconazole or amphotericin B. Patients with acute PDH, meningitis, or endocarditis can be treated with amphotericin B. The fibrous histoplasmoma do not require treatment unless there is anatomical encroachment at which time they should be surgically removed (3).

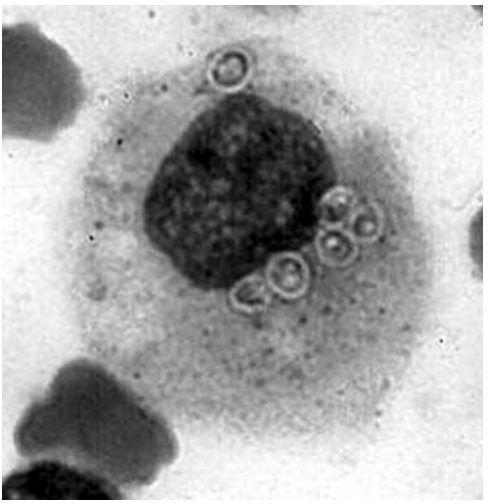


FIGURE 28.1. Intracellular *histoplasmosis capsulatum:* macrophage on peripheral blood smear. *Photo courtesy of Dr. Alan Scott Ragland.*

Blastomycosis

Blastomycosis is a systemic mycosis, principally found in North America but also reported in the river valleys of Africa, India, and the Middle East. Sporadic cases and a small number of epidemics suggest this mycosis is endemic to the Mississippi and St. Lawrence River valley basins. *Blastomyces dermatitidis* may be isolated from soil rich in decaying organic matter and has been associated with the woodland areas along waterways. Sporadic cases are most closely associated with outdoor occupations, but analysis of epidemics does not demonstrate differences in sex, age, race, or occupation (1,4,5).

Blastomyces dermatitidis almost always enters the body through the lungs although direct inoculation of the skin is possible. Approximately 30 to 45 days after exposure half of the patients infected will develop the myalgias, arthralgia, chills, fevers, and dry cough associated with the acute pulmonary phase. From the lung the mycosis may spread hemotogenously to any organ of the body with preference for skin (40% to 89%), the prostate (10% to 30%) and the bones and joints (10% to 30%) (4,5).

Chronic pulmonary disease may manifest with a productive cough or hemoptysis, weight loss, and pleuritic chest pain. Chest x-rays may demonstrate lobar pneumonis, cavitation, mass lesions, fibronodular changes, or miliary patterns. Large pleural effusions are rare (4,5).

Disseminated skin lesions occur in three forms, and a single patient may have all manifestations. The more common lesion is a gray to violet verruciform plaque, with central scarring and hypopigmentation possible. An exudate may reveal diagnostic yeast. The second form of the skin lesion begins as a pustule and spreads as a superficial ulcer characterized by raised borders and central granulated tissue that bleeds easily with minor trauma. Subcutaneous nodules may appear that represent microabscesses and may also yield diagnostic yeast. Skin disease that results from direct inoculation demonstrates only regional adenitis (2,4,5).

While any bone may become infected, the long bones, vertebrae, and ribs are the most common sites involved. Bony lesions are well-circumscribed osteolytic lesions with contiguous soft tissue spread or draining sinus tracts. Vertebral involvement may manifest as a paravertebral abscess mimicking tuberculosis (2,4,5).

Blastomycosis of the genitourinary tract generally involves the prostate and epididymis, resulting in symptoms of prostatitis and pyuria. Diagnostic yeast may often be recovered from the urine after prostate massage. Treatments for blastomycosis may not effectively penetrate the prostate, which can serve as a nidus for reoccurrence (2,4,5).

Blastomycosis has been reported in the liver, spleen, gastrointestinal tract, thyroid gland, pericardium, and adrenal glands. The central nervous system is seldom directly involved unless the host is immunocompromised, such as in HIV infection.

Identification of the distinctive yeast phase from tissue using KOH prep or silver stain is diagnostic of blastomycosis. DNA probe assay can provide specific and rapid identification of cultures (6).

An immunocompetent host with mild or moderate disease can be treated with ketoconazole or itraconazole. Immune impaired hosts and those with severe disease should be treated with amphotericin B (5).

Coccidioidomycosis

Coccidioides immitis and *Coccidioides posadasii* are systemic fungi residing in the soils of the Western Hemisphere between the latitudes of 40˚N and 40˚S. The fungi prefer alkaline soil in arid climates with rainfall between 5 to 20 inches and hot summers and winters with few freezes. *Coccidioides* can be isolated from the soil after the winter rains as propagating fungi, but infections usually occur during the hot summer months through October. In the United States, coccidioidomycosis is endemic to Arizona, New Mexico, the southern California desert regions, and southwestern Texas. Evidence of past infection in residents of endemic areas ranges from 60% to 90% (1,2).

Reports associate coccidioidomycosis with agriculture or other dust generating occupations. Cotton farmers, sheepherders, irrigators and many other agricultural workers are at occupational risk. Up to 40% of nonendemic agricultural workers may become infected with coccidioidomycosis after employment in endemic areas. Despite these associations, occupational risk of coccidioidomycosis in endemic areas must be assessed in relation to community risk and non-occupational exposure (7).

Infection begins with inhalation of the arthroconidia into the lung. Inside the lung arthroconidia develop into the diagnostic spherule containing numerous endospores that spread the infection within the body. About 40% of persons infected will have symptoms severe enough to seek medical attention. Cough, fever, arthralgias, rash, chest pain, shortness of breath, fatigue, and weight loss develop 7 to 21 days after exposure. A fine papular rash, erythema nodosum or erythema multiforme may develop early and does not represent disseminated disease. The combination of fever and arthralgias has been termed “desert rheumatism” (1).

In meningitis, laboratory studies may reveal an eosinophilia of the serum or cerebral spinal fluid. In pneumonia, chest x-ray may reveal a unilateral infiltrate, adenopathy, and effusion. About 8% of adults with coccidioidomycosis will develop cavitary lung lesions. Half of these lung cavities will resolve within two years, but superinfection, bleeding, rupture or mycetomas are potential complications. Uncommonly, coccidioidal pneumonia causes diffuse infiltrates and fulminate respiratory failure. Most cases of coccidioidal pneumonia resolve within several weeks to several months, but 4.6% of infected persons have disease that disseminates outside the lung (8,9).

The most common sites for dissemination of coccidioidomycosis outside the lung are the skin, bone, joints, and the central nervous system. Disseminated skin lesions vary from a papule with verrucose or keratotic features to ulcers or fluctuant abscesses. The knee is the most common site of synovitis. Vertebral body osteomyelitis may produce paraspinal abscesses and associated symptoms. Meningitis is the most serious presentation of disseminated coccidioidomycosis with the complication of hydrocephalus, vasculitis, or infarcts. Death is certain if untreated (8,9).

The diagnosis is first made by establishing exposure to an endemic area. An extensive exposure is not required, so a detailed travel history of the last two years is needed. Coccidioides species grow easily in the laboratory, so isolation from tissue or visualization of endosporulating spherules on microscopic exam is diagnostic. IgM antibodies that develop briefly in the early phases of infection suggest acute infection. Complement fixing antibody titers are considered diagnostic if performed in a capable laboratory (8,9).

Most patients, including meningitis patients, can be treated with fluconazole though some will require high doses and prolonged therapy. Patients with rapidly progressive or broadly disseminated disease should be treated with amphotericin B (9).

Sporotrichosis

Sporothrix schenckii is a dimorphic fungus. At temperatures lower than the human body temperature the fungus exists in a hyphal form, while at body temperature it exists as a yeast form. In the body, the organism reproduces by budding and forms cigar-shaped yeast cells which can rarely be round or oval. This organism has worldwide distribution in temperate to tropical climates and is endemic to a remote area in Peru. The organism can be found in sphagnum moss, decaying wood, other vegetation, hay, and soil. Infected animals or animals contaminated with infected soil can pass the organism to humans by scratching, biting, or casual contact (10).

The clinical presentation is that of a lymphocutaneous infection presenting as an ulcer after inoculation of the fungus, a respiratory infection that presents as tuberculosis after inhalation of the conida, or an osteoarticular infection that occurs after deeper inoculation or by hematogenous spread. One or multiple joints may be involved. Meningitis can also occur in people who are immunocompromised, such as those with lymphoma or AIDS. Similarly, disseminated disease occurs rarely in patients with AIDS. Diagnosis is confirmed by culture of the organism from aspirated material, tissue biopsy, sputum or body fluid (10).

Treatment will vary depending on the illness. Lymphocutaneous disease can be treated with itraconazole or fluconazole as a second line treatment. Treatment for mild respiratory or osteoarticular infection can start with itraconazole. Duration of treatment should be one year or longer. Severe

pulmonary disease, meningitis or disseminated disease should be treated with amphotericin B, followed by itraconazole suppressive therapy (11,12).

Cryptococcosis

Cryptococcosis is a systemic infection caused by the fungus *Cryptococcus neoformans*. Other names for this infection include European blastomycosis and torulosis. It is a basidiomycetous encapsulated yeast, with two variations: *neoformans* and *gattii*. *Neoformans* can be found in soil worldwide that has been frequented by birds, especially pigeons and chickens. Infections are most associated with immunocompromised patients. *Gattii* is not associated with bird guano but has been grown from river red gum trees, forest red gum trees and in tropical and subtropical areas of Hawaii, Brazil, Australia, Southeast Asia, Central Africa. In contrast to *Neoformans*, *gattii* is mostly associated with the immunocompetent host (13).

Illness is caused by inhalation of the organism. The most common presentation for immunocompetent hosts is either an asymptomatic pulmonary infection or as cough, fever, sputum production, and pleuritic chest pain. The central nervous system has a high predilection for involvement, especially in immunocompromised patients and should be suspected whenever there is an infection detected at any organ site. Diagnosis is confirmed by isolation of the yeast form of the organism from the host or by twofold increase of the cryptococcal antigen (13,14).

Treatment depends on the immune status of the host and the anatomic site of the disease. Medications include amphotericin B, flucytosine, fluconazole and itraconazole. These agents are used alone or in combination depending on the clinical setting (12,14).

Scedosporium Infection

Scedosporium is a widely distributed mold. It exists as two species: S. *apiospermum* (asexual anamorph of *Pseudallescheria boydii*) and *S*. prolificans (*S. inflatum*). The organism is isolated from soil, potting mix, compost, and animal manure. Infection is by inhalation of spores or by direct inoculation into skin. The range of illness includes colonization, local skin infection, deep infection or disseminated disease. Normal and immunocompromised hosts can be infected. Infections have been reported from the United States, Canada, Germany, France, the Netherlands, and Spain (with a high incidence in northern Spain) (1,15).

The clinical presentation is that of a respiratory infection such as pneumonia that may progress to a fungus ball and allergic bronchopulmonary mycosis with colonization. The skin, bones, joints, and eye can be involved as sites of localized infections. Disseminated disease with sepsis, fungemia, and

multiorgan failure can occur. The diagnosis is confirmed by isolation of *Scedospermum* from tissue, fluids or exudates (1,15).

Treatment for *S. apiospermum* is with voriconazole or itraconazole used with terbinafine. The organism is variably susceptible to amphotericin B and resistant to fluconazole and flucytosine. The treatment for *S. prolificans* is problematic because it shows resistance to all agents. Voriconazole is the most active against *S. prolificans* (12,16).

Chromomycosis

Chromomycosis is a chronic fungal infection that is caused by a large number of fungal genera that share a similar clinical and gross mycologic appearance. Included among these are *Fonsecaea* and, more recently, *Exophiala*. The causative organisms are among the most common fungi found in soil and decaying organic matter. Cutaneous injury to the lower extremities is the principle mode of entry but any traumatized skin may become infected. The initial injury is often of minor extent and may be forgotten long before clinical presentation. The majority of cases are agriculture related (2,15).

The fungus produces a slowly progressive infectious process that may first be noted as a papule or nodule and progresses to a warty lesion that may eventually appear as exuberant "cauliflower" lesions. Fistulae are uncommon as is bony invasion or visceral disease (1,2,15).

The diagnosis is suspected on the basis of clinical appearance and epidemiology. Pathology yields a pyogranuloma as seen with some endemic fungi. Characteristic "sclerotic bodies" with characteristic hyphal elements may be identified on microscopy. Appropriate material for fungal culture may yield characteristic pigmented colonies with oval hyphae. An experienced mycologist can speciate the organism by its microscopic appearance. Differential diagnosis includes mycobacterial disease, endemic fungi, tertiary syphilis, yaws, leishmaniases, and carcinoma (2,15).

Treatment varies with the extent of the disease. Early disease may be treated successfully with surgery or liquid nitrogen. A variety of anti-fungals have been used. Therapy with ketoconazole, itraconazole with or without 5-flurocytosine have received significant attention. Thermal therapy may be useful, particularly as an adjunct. Newer azoles or echinocandins may prove to have efficacy (2,12,15).

Mycetoma

Mycetoma is a descriptive term to describe a number of bacterial and fungal infections with a similar clinical appearance. The etiologic agents are typically saprophytic organisms found in soil or plant debris that gain entry to skin and subcutaneous tissue through minor trauma. The original

description in the Madura region of India and the most common clinical involvement of the foot are the origins of the common clinical name, "Madura foot." The same process may occur in the hand and, less commonly, other locations on the body. The infection has broad geographic distribution with an increased incidence in tropical and subtropical areas (2).

The clinical presentation is that of a slowly progressive, fistulizing swelling of a localized area. Pain is variable and often less than one might anticipate from visual inspection. As the disease progresses, bony destruction occurs. Characteristic granules may be seen to exit from the fistulae and are of a variety of colors depending on the organisms (17).

Mycetomas are caused by a variety of bacteria and fungi. Bacteria include, predominantly, members of the genus *Actinomadura* and *Nocardia* and are referred to as actinomycetomas. Frequent fungal pathogens include the genera of *Madurella* and *Scedosporium* (1,17,18,19).

The diagnosis is based on the clinical appearance and the presence of granules in the fistulae. The diagnosis may be supported by the radiographic appearance of bony destruction. A definitive diagnosis requires the microbiologic isolation of the offending organisms, which are best obtained from surgical biopsy. The differential diagnosis includes botryomycosis, tuberculosis, coccidioidomycosis, and other chronic invasive infections (17,18).

Medical treatment is dependent on the isolation of the pathogen and an understanding of its sensitivity. Surgery has a limited or no role in treatment, outside of assisting in diagnosis (18,19).

References

1. Kaplan W. Epidemiology of the principal systemic mycoses of man and lower animals and the ecology of their etiologic agents. JAVMA 1973;163:1043–7.
2. MacKinnon JE. Regional peculiarities of some deep mycoses. Mycopathologia et Mycologia applicata 1972;46:249–65.
3. Wheat LJ. Current diagnosis of histoplasmosis. Trends in Microbiology 2003;11:488–94.
4. Klein BS, Vergeront JM, Disalvo AF, et al. Two outbreaks of blastomycosis along rivers in Wisconsin. Am Rev Respir Dis 1987;136:1333–8.
5. Pfister AK, Hamaty D. A survey of North American blastomycosis in West Virginia. The West Virginia Medical Journal 1966;62:434–5.
6. Scalarone GM, Legendre AM, Clark KA, Pusater, K. Evaluation of a commercial DNA probe assay for the identification of clinical isolates of *Blastomyces dermatitidis* from dogs. Journal of Medical and Veterinary Mycology 1992;30:43–9.
7. Johnson WM. Occupational factors in coccidioidomycosis. J. Occ Med 1981;23:367–74.
8. Ragland S, Arsura E, Ismail Y, Johnson R. Eosinophilic pleocytosis in coccidioidal meningitis. Am J Med 1993;95:254–7.
9. Johnson RH, Caldwell JW, Welch G, Einstein HE. The great coccidioidomycosis epidemic: Clinical features. In: Einstein H, Cantanzaro A, eds. Proceedings of the 5th International Conference on Coccidioidomycosis, August 1994. Washington D.C.: National Foundation for Infectious Diseases, 1996.

10. Rex JH, Okuysen PC. *Sporothrix schenckii*. In: Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases 5th ed. Philadelphia:Churchill Livingstone, 2000.
11. Kaufman CA, Hajjeh R, Chapman SW. IDSA practice guidelines for the management of patients with sporotrichosis. Clinical Infectious Diseases 2000;30:684–93.
12. Gilbert DN, Moellenring RC, Eliopoulos GM, Sande MA, eds. The Sanford Guide to Antimicrobial Therapy 34th ed. Hyde Park:Antimicrobial Therapy Inc., 2004.
13. Cox GM, Perfect JR. Microbiology and epidemiology of cryptococcal infections. [*Epub* prior to publication, www.uptodate.com].
14. Diamond RD. *Cryptococcus neoformans*. In: Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases 5th ed. Philadelphia:Churchill Livingstone, 2000:2707–18.
15. Hospenthal DR, Bennett JE. Miscellaneous fungi and prototheca. In: Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases 5th ed. Philadelphia:Churchill Livingstone,2000:2772–4.
16. Spelman D, Morrissey C. Miscellaneous and emerging fungal infections. Epub prior to publication, *www.uptodate.com*.
17. Mitchell G, Wells GM, Goodman JS. Sporotrichoid *nocardia brasiliensis* infection. Am Rev Respir Dis. 1975; 12:721–3.
18. Causey WA, Sieger B. Systemic Nocardiosis caused by n*ocardia brasiliensis*. Am Rev Respir Dis. 1974;109:134–7.
19. Ahmed A, Adelmann D, Fahal A, et al. Environmental occurrence of *Madurella mycetomatis*, the major agent of human eumycetomas in Sudan. JCM 2002;40:1031–6.

29

Emerging Zoonotic Agents of Concern in Agriculture

Ricky Lee Langley and Carl John Williams

Key words: zoonoses, hepatitis E, hendra, manangle, lyme disease, erhichia, transmissible spongiform encephalopathy (TSE), hantavirus

Throughout the world, we are seeing unprecedented changes in our economic, social, and ecological systems that are having adverse impacts on plants, animals, and humans. These changes are leading to the resurgence of old diseases and the emergence of new ones. The landscape and diversity of animals in many regions are changing due to overgrazing and deforestation. Increasing pollution of water bodies by nitrogen-rich waste-water, fertilizers, and soil runoff and loss of wetlands and mangroves due to development and aquaculture, diking, and drilling is promoting growth of marine and freshwater algal blooms. These algal blooms may be toxic to animals and humans. Monitoring the patterns of temperature, wind, precipitation, and biodiversity has enormous implications for surveillance of disease vectors and reservoirs (1).

Human communicable diseases can be classified according to the source of infection as:

1. Anthroponoses: source is an infected human
2. Zoonoses: source is an infected animal
3. Sapronoses: source is an abiotic substrate (nonliving environment) (2)

A characteristic of most zoonoses and sapronoses is that once transmitted to a human, the epidemic chain is usually broken. However, a limited number of zoonoses are sometimes communicable from one person to another. Zoonotic diseases can be classified as either synanthropic zoonoses with an urban or domestic cycle in which the sources of infection are domestic animals or exoanthropic zoonoses with a sylvatic (feral and wild) cycle in nature. However, some zoonotic diseases can circulate in both urban and natural cycles (2).

There are greater than 200 known zoonotic diseases in the world and more are being found as people move into or change environments that were

previously uninhabited by humans, thus exposing them to new vectors. Zoonotic agents have a major economic impact on agriculture, especially in third world countries. In many areas, vaccines are not available to prevent diseases in domestic animals, thus the infected animal suffers and humans may either starve if there are large die-offs or may contract a zoonotic illness. In many cases where a zoonotic disease is found, whole herds are slaughtered to prevent the spread of disease outside the affected area. Mass slaughter has had a major economic impact on farmers in both developed and undeveloped nations. For example, thousands of cows in Great Britain were destroyed due to "mad cow disease." In Southeast Asia, millions of chickens have been slaughtered to prevent the spread of avian influenza. In Singapore and Malaysia, thousands of pigs have been killed to prevent the spread of Nipah virus (2).

This chapter covers a few of the emerging zoonotic diseases in developed nations, especially the United States. We have chosen hepatitis E, Hendra virus, Nipah virus, Menangle virus, hantavirus, Lyme disease, ehrlichiosis, and transmissible spongioform encephalopathies as emerging zoonotic agents to present in detail.

Hepatitis E

History

Hepatitis E, formerly known as enterically transmitted non-A, non-B hepatitis, is a viral infection with clinical and epidemiological features of acute hepatitis. It is a principal cause of acute hepatitis in many developing nations and has been increasingly seen in industrialized countries. It is endemic in third world countries that have poor sanitary practices. Most cases in developed countries have been traced to travel to endemic areas; however, sporadic cases do occur in patients with no history of travel, suggesting possible reservoirs in developed countries (3).

Agent

Hepatitis E is a small (32 to 33 nm), nonenveloped, positive sense, single-stranded RNA virus with icosahedral symmetry. It has a 7.2kb genome that is capped and polyadenylated. There are 4 currently recognized genotypes and 1 serotype (4).

Clinical Signs and Symptoms

Signs and symptoms resemble other types of viral hepatitis. Abdominal pain, anorexia, dark urine, fever, hepatomegaly, jaundice, malaise, nausea, and vomiting are seen. Less common manifestations include arthralgias, diar-

rhea, pruritis, and urticaria. Fulminant hepatitis may develop, especially in pregnant women. The overall mortality ranges from 1% to 3% but may be as high as 25% (higher in some studies) during pregnancy. Death of the fetus, abortion, premature delivery, or death of a live-born soon after birth are common complications of hepatitis E infection during pregnancy. Vertical transmission has been reported to occur in 33% to 100% of cases (5–9).

Reservoirs and Occurrence

Humans and animals with subclinical hepatitis E infection may serve as reservoirs. Antibodies against or hepatitis E RNA has been detected in cows, sheep, pigs, deer, monkeys, rats, and even a cat. Nucleotide sequence studies show high if not 100% identity between human and animal hepatitis E RNA (10–12).

Mode of Transmission

Hepatitis E is excreted in the feces and is transmitted by the fecal-oral route. Transmission is usually by ingestion of contaminated drinking water. Rare cases of person-to-person transmission have been recorded. There is a possibility that transmission by blood transfusion may occur. In the United States where no outbreaks of hepatitis E have been reported, a low prevalence of antibodies to hepatitis E (<2%) in healthy populations is found (5,13).

Some, but not all, studies in sewage workers have shown a higher prevalence of antibodies to hepatitis E when compared to a control population. Studies in swine farmers and swine veterinarians have also shown antibodies to hepatitis E in 10.9% and 23% respectively. There are reports of cases of hepatitis E developing after ingestion of raw deer or wild boar meat, again suggesting a zoonotic infection (14–19).

Incubation Period and Communicability

The incubation period averages 40 days with a range of 15 to 60 days. The period of infectivity is not known but the virus can be found in the stool 14 days after illness onset. There is no known chronic form of the disease (5).

Methods of Control and Management

Education on sanitary disposal of feces and handwashing after defecation and before handling food is paramount. While there is no specific treatment for hepatitis E, a vaccine is under development. Where animal or human manure is used for fertilization of crops, potential contamination of produce or shellfish (from runoff) with viral agents is of concern. This may be a means of introducing hepatitis E into new areas of the world by increasing globalization of food markets. Proper washing and cooking of food should be practiced (4,5).

Hendra Virus

History

In the Brisbane suburb of Hendra, authorities in Queensland, Australia, were advised of acute respiratory disease in horses at a stable in September 1994. By the end of September, 13 horses had died. The sick horses were anorexic, depressed, usually febrile, had an elevated respiratory rate, and became ataxic. Head pressing was occasionally noted and a frothy nasal discharge occurred before death. Two humans working with the horses also developed respiratory illness with fever and myalgia. One man died, and the other remained ill for 6 weeks (20).

Agent

Hendra virus, formerly known as equine morbillivirus, is a member of a new genus, Henipaviruses, within the family Paramyxoviridae. It is a single-stranded, enveloped RNA virus. It varies in size from 38 to 600 nm and is covered with 10 nm and 18 nm surface projections. It contains herringbone nucleocapsids that are 18 nm wide with a 5-nm periodicity (20).

Clinical Signs and Symptoms

In humans only a few cases have been documented, and two thirds of those had a respiratory illness with severe flu-like signs and symptoms. Two out of three cases in humans resulted in death, one died from acute respiratory illness and one from an encephalitis. In horses, respiratory disease characterized by dyspnea, vascular endothelial damage, and pulmonary edema may occur. Nervous signs may also occur. Following experimentally induced infections, cats and guinea pigs have developed fatal respiratory illness (21,22).

Histopathological studies show Hendra virus induces syncytial cells in vascular tissues and is primarily vasotropic and neurotropic, generating interstitial pneumonia or encephalitis (23).

Reservoir and Occurrence

Fruit bats, especially flying foxes of the genus Pteropus, appear to be the reservoir in nature (24).

Mode of Transmission

The virus is thought to be transmitted to horses by bats and then from horses to humans. There is evidence of horse to horse transmission via nasal secretions, saliva, and/or urine. Some evidence exists that the Australian tick,

Ixodes holocyclus, may transmit Hendra virus from flying foxes to horses and other mammals (25).

Incubation Period and Communicability

Incubation period is unknown since so few cases have been reported, but it appears to be approximately 7 days in humans. The virus is not known to be communicable among humans (25).

Method of Control and Management

Early recognition of disease in horses is important to prevent spreading to other horses and humans. Reduce exposure to fruit bats. Wear personal protective equipment and use good sanitation practices when it is necessary to contact potentially infected animals. The drug ribavirin has been shown to be effective in in-vitro studies. The clinical usefulness of this drug is not known (26).

Menangle Virus

History

In August 1997, an outbreak of reproductive disease occurred in a piggery in Australia. Two humans working at the piggery were infected. The disease was associated with a flu-like illness with a rash in the workers. The virus causes embryonic mortalities, stillbirths, mummified fetuses, and congenital abnormalities in the pigs (27).

Agent

Menangle virus is a single stranded, pleomorphic, enveloped RNA virus. Surface projections 17+ nm long have been noted on the envelope. It is a new member of the genus Rubulavirus within the family Paramyxoviridae (28).

Clinical Signs and Symptoms

Fever, chills, rigors, and drenching sweats characterized patients' illness, in addition to headaches, myalgias, and photophobia. About 4 days later, a spotty, red nonpruritic rash developed on the torso. Spleen enlargement occurred in one patient. Both eventually recovered after a few weeks (29).

In pigs, mummified fetuses, stillborn piglets with arthrogryposis, craniofacial deformities such as brachygnathia, occasional fibrinous body cavity effusions, and pulmonary hypoplasia were found. Degeneration of the brain and spinal cord has been noted along with nonsuppurative myocarditis in some piglets (30).

Reservoir and Occurrence

Menangle virus appears to a virus of fruit bats (flying foxes) of the genera Pteropus. Tests on birds, cattle, sheep, cats, and a dog around the affected piggery were seronegative. In piggeries where the virus is detected, neutralizing antibodies are found in a high percentage (up to 95%) of pigs by slaughter age (30,31).

Mode of Transmission

The mode of transmission among pigs is unknown, but respiratory, fecal, or urinary excretion is postulated. The mode of spread from pigs to humans is unknown (30,31).

Incubation Period and Communicabilty

Incubation period and communicability are unknown in humans. Heavy occupational exposure appears to be needed for transmission from pigs to humans.

Method of Control and Management

Serologic testing and segregation of positive pigs used to eradicate menangle virus from one piggery. Prevention of exposure of pigs to fruit bats may possibly be beneficial (31).

NIPAH Virus

History

In 1998 and 1999 a new disease that spread among pigs, characterized by respiratory and neurologic symptoms and sometimes accompanied by sudden death of sows and boars, occurred in Malaysia and Singapore. The original name proposed for this new pig disease was porcine respiratory and neurological syndrome or "barking pig syndrome." The disease occurred in close association with an epidemic of encephalitis in pig farmers. In Malaysia, more than 265 encephalitis cases in humans occurred with a mortality rate of approximately 40%. A new paramyxovirus was found and named Nipah virus. The outbreak stopped after pigs in the affected area were destroyed. In Singapore in 1999, 11 workers in an abattoir developed an encephalitis or pneumonia resulting in one death. Importation of pigs from Malaysia was banned. The virus was found to be transmitted to other animals including dogs, cats, and horses. An outbreak in 2004 in Bangladesh has been recently reported with a 60% to 70% mortality rate.

The mode of transmission in the Bangladesh outbreak has not been determined. Because of its high mortality rate and spread to domestic animals, this agent has the potential to be considered an agent of bioterrorism (32–37).

Agent

Nipah virus is a single stranded, enveloped RNA virus. The virions are enveloped particles composed of a tangle of filamentous nucleocapsids and measure as large as 1900 nm in diameter. The nucleocapsid has the characteristic helical and herringbone structure of paramyxoviruses. The Nipah virus belongs to a new genus Henipaviruses within the family Paramyxoviridae. The Nipah virus genome is 12 nucleotides longer than the Hendra virus genome, and both have identical leader and trailer sequence lengths and hexamer-phasing positions for all their genes (38,39).

Clinical Signs and Symptoms

The disease presents as an acute encephalitis with symptoms of fever, headache, and giddiness followed by coma. Distinctive clinical features include segmental myoclonus, areflexia and hypotonia, hypertension, and tachycardia. Neurologic relapse occurred in a few patients after initial mild disease. Several of the survivors had relapsed or late-onset encephalitis. In the Singapore outbreak, 3 patients presented with atypical pneumonia, one later developed hallucinations and evidence of encephalitis. Cerebrospinal fluid was abnormal in 75% at presentation. Magnetic resonance imaging shows the presence of discrete high-signal-intensity lesions disseminated throughout the brain. The main histopathologic findings include a systemic vasculitis with extensive thrombosis and parenchymal necrosis, especially in the central nervous system (40–44).

Reservoir and Occurrence

Fruit bats, especially Pteropus sp., appear to be the natural reservoir of Nipah virus. Viruses related to Nipah and Hendra appear to be more widespread in Southeast Asia than previously thought (45,46).

Mode of Transmission

The virus appears to be transmitted from fruit bats to pigs and from pigs to humans. Respiratory secretions and urine of infected pigs have been shown to contain Nipah virus and may be vehicles of transmission. Nipah virus has been detected in respiratory secretions and urine of patients. Thus it is possible to be infected from secretions of infected patients, but epidemiologic data do not suggest human-to-human transmission is common (47).

Incubation Period and Communicability

The mean incubation period appears to be 10 days. While the virus has been detected in human urine and respiratory secretions, human to human transmission, if it occurs, appears to be rare (48).

Method of Control and Management

Limiting exposure of pigs to fruit bats is important. Culling infected pigs may help stop spread within the herd. Wear personal protective equipment including goggles. The use of ribavirin appears to reduce the mortality of encephalitis cases (49,50).

Hantavirus

History

There are currently more than 20 recognized sero/genotypes of hantaviruses. The different hantavirus types are associated with different types of diseases. Two major diseases are recognized: hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS). HFRS is primarily a disease of Europe and Asia while HPS is only recognized in the Americas. This discussion will be limited to HPS.

The initial outbreak of illness from Hantavirus in the United States. was described in 1993, however the earliest case of a serologically confirmed infection was in a person that developed an HPS-like illness in 1959. Since 1993, cases in North, Central, and South America have been recognized. The sero/genotype of the virus appears to be different by country although clinical manifestations are similar (51,52).

The first outbreak in the United States appeared in June and July 1993 in the Four Corners (Arizona, Colorado, Utah, New Mexico) region. In the United States since then, as of September 1, 2004 there have been 379 cases noted in 32 states. The overall case fatality in the United States has been 36% (52).

Agent

Hantaviruses are negative sensed, single stranded, enveloped viruses belonging to the Bunyaviridae family of viruses. There are at least 13 viruses known to cause HPS. The first virus isolated from the Four Corners area was given the name Sin Nombre virus. Other hantaviruses in the United States that have caused disease in humans include Bayou virus, Black Creek Canal virus, New York, and Monongahela virus. Most HPS in the United States is caused by Sin Nombre virus. Several other viruses are known to cause HPS in Central and South America including Andes virus, Bermejo virus, Juquitiba

virus, Laguna virus, Lechiguanas virus, Oran virus, and Choclo virus. Numerous other hantaviruses have been found in rodents on both continents but have not been shown to cause disease in humans at the present time. This may be related to the lack of contact with the rodents or possibly less virulence of the virus (53).

Clinical Signs and Symptoms

Patients initially present with a nonspecific febrile illness. In addition, fever, muscle aches, headache, chills, dizziness, non-productive cough, nausea, and vomiting are noted. In about half of the patients malaise, diarrhea, and lightheadedness are reported. Patients may report shortness of breath. Less frequent reports of arthralgias, back pain, and abdominal pain are noted. Cough and tachypnea develop around day seven. Once the cardiopulmonary phase develops, the disease progresses rapidly (53,54).

Laboratory findings include an elevated white cell count with a marked left shift of the myeloid cells. Atypical lymphocytes are frequently present. In the majority of cases, the platelet count is low. A rapid fall in the platelet count may herald the development of a pulmonary edema phase. The hematocrit may be elevated in about 50% of the cases. In severe cases of HPS, disseminated intravenous coagulation may occur, but this is rare. Proteinuria, mild elevation of liver enzymes, amylase, CPK, and creatinine has been reported. Within 24 hours of initial evaluation, hypotension and progressive evidence of pulmonary edema and hypoxia occur (53,54).

HPS has a characteristic radiologic evolution that begins with minimal changes of interstitial pulmonary edema progressing to alveolar edema with severe bilateral involvement. Pleural effusions are common (53).

HPS has been reported during pregnancy. Symptoms and signs, physical findings, and laboratory values were similar to nonpregnant patients, although fever was lower. No evidence of transplacental transmission was found (54).

Histologic evaluation of infected tissue show that viral antigens are distributed primarily within the endothelium of capillaries throughout various tissues. Histopatholgic lesions are mainly seen in the lungs and spleen. Immune complexes have been detected in the sera and may be responsible for the increased capillary permeability, vascular injury, platelet lysis, and kidney damage. Individuals with HLA-B*3501 have an increased risk of developing severe HPS, suggesting that CD8(+) T cell responses contribute to pathogenesis (55,56).

Reservoir and Occurrence

All hantaviruses known to cause HPS are carried by New World rats and mice in the family Muridae, subfamily Sigmodontinae. It appears that each virus has a specific rodent host. The deer mouse, Peromyscus maniculatus, is

the host of the Sin Nombre virus. The white footed mouse, Peromyscus leucopus, is the reservoir for New York virus. Black Creek canal virus is hosted by the cotton rat, Sigmodon hispidus, and the Bayou virus is hosted by the rice rat Oryzomys palustris. Various other sigmodontine rodents in Central and South America are hosts for hantaviruses in these regions. In the United States, studies of people in endemic areas show the prevalence of antibodies to SNV among healthy people is low (0.3%). Studies in mammalogy field workers show a prevalence of antibodies to hantaviruses of slightly higher than 1%. In South America, seroprevalence surveys show rates as high as 30% in some populations engaged in farming (56,57).

Mode of Transmission

Inhalation of the virus, which is shed in rodent urine, feces, and saliva, is felt to be the main method of disease transmission in man. Cases have been reported after a rodent bite, and researchers think that people may become infected if they touch some object that has been contaminated with rodent excretions and then touch their nose or mouth. People may possibly be infected if they eat food contaminated with rodent excretions. No evidence of person to person transmission has been documented in the United States, however in South America, the Andes virus can be spread by person to person. When exposure information was analyzed, 70% of cases of HPS were closely associated with peridomestic activities, such as cleaning, in homes that showed signs of rodent infestation (58).

In the United States, farm animals, dogs, cats, ticks and biting insects have not been shown to transmit disease to humans. However a recent study has found hantavirus-specific RNA in chiggers and an ixodid tick parasitizing wild rodents in Texas (59).

Incubation Period and Communicability

The incubation period of HPS after exposure to rodents is 9 to 33 days with a median of 14 TO 17 days. Nosocomial transmission and person to person spread have not been noted in the United States, but the Andes virus has been shown to be transmitted by these routes in South America (60).

Method of Control and Management

Methods to eliminate or minimize contact with rodents at home, in the workplace and in recreational areas are important. Seal up holes and gaps in the home and garage. Remove any food sources that rodents may access. The Centers for Disease Control and Prevention has recommendations for properly cleaning up areas infested by rodents. There is no specific treatment, cure, or vaccine for hantavirus infection. If there is a suspicion of hantavirus infection, immediate transfer to an intensive care unit is mandatory. Ribavirin

does not appear to be effective. Passive immunotherapy using plasma from patients that have recovered from HPS may be beneficial, but no studies of clinical effectiveness have been conducted (52,61,62).

Lyme Disease

History

Borrelia burgdorferi, a spirochete, is the causative agent of Lyme disease, which is a multisystem disorder. Skin lesion(s), erythema migrans (EM), followed in some patients by rheumatologic, neurologic, and cardiac abnormalities are the most common clinical manifestations (63).

The disease was first characterized almost 30 years ago when Steere and colleagues investigated an unusual cluster of illnesses resembling juvenile rheumatoid arthritis that occurred in 1975 near Lyme, Connecticut. *B. burgdorferi* was identified as the etiologic agent of Lyme disease and *Ixodes scapularis* was identified as the principal vector of the spirochete (63).

Agent

The genus *Borrelia* is in the order *Spirochetae*, which contains other genera that are pathogenic to humans and animals, such as *Leptospira* and *Treponema*. It is a spiral shaped gram negative bacteria and contains a single linear chromosome. The organism is readily killed by drying and by exposure to disinfectants. Other Borrelia species may cause illness in humans, but only B burgdorferi is recognized as a cause of Lyme borreliosis in the United States (63).

Clinical Signs and Symptoms

The clinical manifestations of Lyme disease occur in three stages, generally appearing in sequence. Stage one is a rash, erythema migrans (EM), which occurs at the site of tick attachment. Cardiac and acute neurologic, and other dermatologic signs constitute stage two, or early disseminated infection. Arthritis and chronic neurologic disease comprise stage three, or late disseminated infection (64).

Stage one is a localized infection. Following delivery of *B. burgdorgeri* from the tick to the host skin the bacteria will spread and replicate locally in the dermis and epidermis, which results in the EM rash. This lesion typically appears within one month of the tick bite. However, in many patients the rash goes unrecognized or does not occur. The rash is frequently accompanied by influenza-like symptoms. Appropriate treatment during this phase is essential to preventing subsequent stages of disease from developing (64).

Within days to weeks of the tick bite, bacterial dissemination via the cardiovascular or lymphatic system may occur. A wide range of symptoms may

result, depending on the site of deposition of the bacteria. Objective signs of acute neuroborreliosis occur in about 15% of untreated patients. Manifestations can include lymphocytic meningitis, Bell's palsy, and cerebellar ataxia. Additionally, in untreated patients, atrioventricular block may occur. (65–67)

In the third stage of disease patients may have recurrent attacks of arthritis beginning months after the initial infection. Up to 60% of untreated patients will have intermittent attacks of joint swelling and pain, particularly in large joints such as the knee. After several attacks of arthritis, some patients may experience persistent joint inflammation (67).

Diagnosis is usually based on the recognition of characteristic clinical signs, a history of exposure in an area where the disease is endemic, and an antibody response to *B. burgdorferi*. When serologic testing is indicated, CDC recommends testing initially with a sensitive first test, such as an enzyme-linked immunosorbent assay followed by testing with the more specific Western immunoblot test to corroborate equivocal or positive results obtained with the first test (68).

Serodiagnostic tests are insensitive during the first few weeks of infection. During this period, up to 30% of patients will have a positive IgM response. By convalescence (two to four weeks later), up to 80% of patients have a positive IgM response. In contrast, after one month, almost all patients will have a positive IgG response (69).

Following antibiotic therapy, antibody levels decrease gradually, but IgG and IgM titers may persist for years after therapy. Therefore, an IgM response cannot always be interpreted as a demonstration of recent infection unless clinically compatible characteristics are also present (69,70).

Reservoir and Occurrence

B. burgdorferi is maintained in nature in a cycle that involves hard ticks of the *Ixodes* genus as vectors and small mammals as reservoir hosts. *Ixodes* ticks attach to a host and take a blood meal at each stage of life (larva, nymph, adult) then drop off the host and molt in the environment. All three stages can feed on people but the nymph stage is most often implicated in transmission of disease to persons (71).

Mode of Transmission

Certain species of ticks in the genus *Ixodes* feed on field mice in their larval stage. Mice, who serve as the reservoir for *B. burgdorferi*, are asymptomatically infected and carry a high number of these spirochetes in their bloodstream. The white-footed mouse (*Peromyscus leucopus*) is a key reservoir species for B. burgdorferi in the United States. After feeding on an infected mouse, the newly infected *Ixodes* larva will harbor *B. burgdorferi* for the remainder of its life. Larval ticks develop into nymphs following this blood

meal from a mouse. Immature ticks typically require two to four days of attachment to the host to complete a blood meal. The nymph must take another blood meal prior to molting into an adult, and this feature of the tick life cycle places persons at risk. The peak feeding time for nymphs is from May through late summer, when human outdoor activity is at a peak (70,71).

Adult ticks will take a final blood meal, usually in late fall or winter, prior to laying eggs. White-tailed deer are the preferred hosts for adult ticks, but serve as poor reservoirs for *B. burgdorferi*. White-tailed deer thus serve to maintain the population of ticks, and not that of *B. burgdorferi*. *Ixodes scapularis* are not found in geographic regions where deer are absent, and tick abundance appears to be directly related to deer abundance. *B. burgdorferi* is transmitted trans-stadially from larvae to nymph to adult, so even adult tick bites pose a risk to people. Importantly, a tick must be attached to its human host for at least 24 hours for *Borrelia* transmission to occur (64,71,72,73).

Lyme disease is acquired from the bite of an infected tick. *Ixodes scapularis* is the dominant vector of *B. burgdorferi*. Although *B. burgdorferi* has been detected in other blood-feeding arthropods such as the American dog tick (*Dermacentor variabilis*), mosquitoes, fleas, and tabanid flies (deer flies, horse flies), the presence of the spirochete in these arthropods is transient, and they are unlikely to transmit the spirochete to new hosts. There is no evidence to support person-to-person transmission. Transplacental transmission has been reported, but it appears that adverse birth outcomes are rare. Transmission of *B. burgdorferi* by the transfusion of blood obtained from a spirochetemic donor has never been reported (74–78).

Incubation Period and Communicability

Incubation typically ranges from 3 days to one month for EM lesion. However, if this stage is unrecognized the patient may present with late manifestations up to months later. Lyme disease is not communicable from person to person (79,80).

Method of Control and Management

Most persons treated for Lyme disease have an excellent prognosis. However, treatment is highly variable depending upon the clinical presentation of the patient. Treatment generally consists of oral or parenteral antibiotic therapy (79,80).

Prevention of infection through the use of personal protective measures is ideal. Using DEET on exposed portions of skin and treating clothing with permethrin are effective at preventing not only tick-borne diseases, but also mosquito and other arthropod-borne diseases. Persons should also conduct tick checks after exposure to tick habitat (79,80).

Ehrlichiosis

History

Ehrlichiosis is one of a number of bacterial tickborne diseases that occur in the United States. The most common by far is Lyme disease, but others include Rocky Mountain spotted fever, tularemia and ehrlichiosis. In the United States ticks can also be responsible for transmitting parasites and viruses, which may cause illness (81).

There are numerous ehrlichial species that can infect humans and animals worldwide, five of which are known to infect humans. However, this section will focus on those species that cause clinical illness in humans in the United States. *Ehrlichia sennetsu*, the cause of sennetsu fever in the far east, is not known to exist in the United States. *Ehrlichia canis*, the cause of canine monocytic ehrlichiosis, does occur in the US, but has only rarely been documented to infect persons in other countries (81).

Ehrlichiosis is considered an emerging zoonotic pathogen based on the fact that both conditions affecting humans in the United States are newly identified and not fully characterized. Ehlichiosis was initially characterized as a condition of dogs in the 1930s. *E. canis* was identified as a pathogen causing illness in military working dogs in Vietnam in the 1960s. Human ehrlichiosis is a newly recognized disease in the United States and was first identified in 1986. The agent of human monocytic ehrlichiosis (HME), *Ehrlichia chaffeensis*, was first identified in 1991. The name is derived from Fort Chaffee Arkansas, where the Ehrlichia species was first isolated from an ill soldier. Human granulocytic ehrlichiosis (HGE) was first recognized in a series of patients from Minnesota and Wisconsin in the early 1990s (82–84).

Agent

Members of two genera can cause clinical ehrlichiosis in the United States. Ehrlichia and Anaplasma species belong to the family Anaplasmataceae. Ehrlichia and Anaplasma are gram negative, obligate intracellular bacteria that replicate in the vacuoles of eukaryotic cells. In humans, the ehrlichial infections are named based on the type of white blood cell that is infected, i.e., monocytic or granulocytic. *Anaplasma phagocytophilum*, known prior to 2001 simply as the HGE agent, is the causative organism of HGE. Also, several cases of human ehrlichiosis in Missouri have been attributed to infection with *E. ewingii*, the causative agent of granulocytic ehrlichiosis in dogs (85,86).

Clinical Signs and Symptoms

HME and HGE represent two clinically indistinguishable yet epidemiologically and etiologically distinct diseases. Infection generally results in acute,

influenza-like illness with fever, headache, malaise and frequently low white blood cell and thrombocyte counts. Nausea, vomiting, and a rash may be present in certain cases. Intracytoplasmic bacterial aggregates (morulae) may be visible in the white blood cells of some patients. Because the symptoms are relatively non-specific, a definitive diagnosis depends on development of a clinically compatible illness in conjunction with supportive laboratory results (87).

Reservoir and Occurrence

The agents of ehrlichiosis are maintained in wildlife hosts and are transmitted between animals through the bites of infected ticks. White tailed deer are important reservoirs for both *E. chaffeensis* and *E. ewingii*. Humans and domestic animals such as dogs are thought to be largely accidental hosts and are unlikely to play an important role in the natural maintenance of these pathogens (88–90).

Mode of Transmission

E. chaffeensis and *E. ewingii* are transmitted among reservoir species and to accidental hosts by the lone star tick (*amblyomma americanum*), which occurs widely throughout the southeastern and south central United States. In the northeastern and midwestern United States, *A. phagocytophilum* is maintained in white tailed deer and small rodents. Transmission to humans occurs through the bite of the black legged tick (*Ixodes scapularis*). Tick transmission is believed to be the only epidemiologically important means of acquiring infection (90–93).

Incubation Period and Communicability

The incubation period ranges from 7 to 21 days for both conditions. Neither condition is communicable from person to person (93).

Method of Control and Management

If ehrlichial infection is suspected based on clinical findings or history of tick exposure, initiation of antimicrobial treatment should not be delayed. The tetracycline class of antibiotics is the drug of choice for treating ehrlichiosis (93).

Prevention of infection through the use of personal protective measures is ideal. Using DEET on exposed portions of skin and treating clothing with permethrin are effective at preventing not only tick-borne diseases, but also mosquito and other arthropod-borne diseases. Persons should also conduct tick checks after exposure to tick habitat (93).

Transmissible Spongiform Encephalopathis

History

Transmissible spongiform encephalopathies (TSEs) constitute a rare group of neurodegenerative disorders. They are invariably fatal and affect humans and animals. TSEs in animals include transmissible mink encephalopathy, scrapie (affecting sheep and goats), bovine spongiform encephalopathy (BSE or mad cow disease), and chronic wasting disease (CWD) of deer and elk. TSEs in humans include Creutzfeld-Jakob disease (CJD), new variant CJD, fatal familial insomnia, Gertsman-Straussler-Scheinker syndrome, and kuru. Each of the TSEs is unique and apparently has a very limited host range, yet they all share characteristics that allow them to be grouped together (94).

Creutzfeld-Jakob Disease

Creutzfeld-Jakob Disease (CJD) was first described in Europe in 1920 and 1921, though it probably occurred prior to that and was not recognized. This disease occurs at a rate of about one case per million persons worldwide and generally affects only persons aged 65 years or more. It presents as a rapidly progressive dementia terminating in death roughly four to five months after symptom onset. CJD can have an incubation period of up to 20 years. Diagnosis is based on observation of clinically compatible symptoms, and a definitive diagnosis can only be determined postmortem through histopathologic examination of central nervous system biopsy specimens. As mentioned previously, most cases of CJD appear spontaneously (94,95).

In 1995 a new variant of CJD (nvCJD) was identified in the United Kingdom. Clinically, this variant was very similar to classic CJD but affected much younger persons, generally in their thirties. From 1995 through June 2002, a total of 124 human cases of vCJD were reported in the United Kingdom, 6 cases in France, and 1 case each in Ireland, Italy, and the United States. The case-patients from Ireland and the United States had each lived in the United Kingdom for more than 5 years during the UK BSE epidemic. The discovery of nvCJD following the BSE outbreak in the UK is very important because it appears that the agent causing BSE is capable of crossing the species barrier and causing illness in humans in the form of nvCJD (95,96).

Bovine Spongiform Encephalopathy

Beginning in 1986 an epidemic of bovine spongiform encephalopathy (BSE) was identified in numerous European countries, most notably in the UK. Although it has not been definitively determined, this epidemic apparently arose via feeding ruminant-derived protein contaminated with the

scrapie agent to cattle in the United Kingdom. It is suspected that rendering plant procedural changes in the 1970s resulted in the failure to inactivate the scrapie agent. Transmission by contaminated feed appears to have been the only mechanism by which cattle became infected. No evidence of horizontal spread from animal to animal has been documented in the BSE outbreak (96).

The BSE epidemic in the United Kingdom peaked in 1992 with over 3,500 new cases per month in cattle. Beginning in 1988, the United Kingdom instituted a number of control measures beginning with a ban prohibiting the feeding of ruminant-derived protein to ruminants. In 1990 this ban was extended to prohibit the feeding of specified bovine offal (brain, spinal cord, thymus, tonsil, spleen) to other ruminants, and in 1996 the mammalian meat and bone meal prohibition was instituted. The restrictions have worked to the extent that through the first half of 2004 only 233 cases have been reported to the Dept. of Environment, Food and Rural Affairs, the UK equivalent to the USDA. In calendar year 2003, 457 cases were reported (95–98).

In the United States, the feeding of rendered cattle products to other cattle has been prohibited since 1997, and the importation of cattle and cattle products from countries with BSE or considered to be at high risk for BSE has been prohibited since 1989. These measures have minimized the potential exposure of animals and humans to the BSE agent. Nonetheless, on December 23, 2003, the USDA made a preliminary diagnosis of BSE in a single nonambulatory dairy cow in Washington State. The BSE international reference laboratory in Weybridge, England, subsequently confirmed this diagnosis. This was the first time BSE has been identified in the United States (98,99).

Potential Transmission of BSE to Humans

Epidemiologic and laboratory evidence suggests that the BSE agent has been transmitted to humans via consumption of BSE-contaminated cattle products, causing nvCJD. However, the risk for acquiring vCJD from consumption of BSE-contaminated product is low, presumably because of a species barrier that provides some degree of protection against development of nvCJD. BSE is the only TSE of animals that has ever been linked with human disease. In the United Kingdom, where an estimated 1 million or more cattle probably were infected with BSE, cases of nvCJD continue to be reported; however, the number of cases of nvCJD remains small, with 147 probable and confirmed vCJD cases identified as of August 2004, including those of three persons residing in Ireland, Canada, and the United States who are believed to have been exposed to BSE in the United Kingdom. No cases of nvCJD have been identified where the patient did not have exposure within a country where BSE was occurring (96–100).

Chronic Wasting Disease

Although CWD was first identified as a syndrome in the 1960s and the etiologic agent was found to be a spongiform encephalopathy in 1978, there has been a growing public health concern about the condition recently as it has been identified in new areas. CWD was first identified in Colorado and Wyoming over 25 years ago. Since 1996 CWD has been found in Kansas, Montana, Nebraska, Oklahoma and South Dakota in captive elk herds. Additionally, it has been identified in wild deer in Nebraska, South Dakota and Wisconsin. Given the popularity of deer hunting there is concern that CWD could pose a risk to human health as BSE did in cattle over 10 years ago. To date, only three species of mammals are known to be naturally susceptible to CWD: mule deer (Odocoileus hemionus), white tailed deer (Odocoileus virginianus), and elk (Cervus elaphus). Cattle and other livestock seem to be resistant (97,100–102).

To date no association has been made between CWD and neuropathologic illness in humans. A 2003 report of fatal neurologic illness in men who participated in wild game feasts concluded that there was no association between CWD and CJD type disease, though continued surveillance for both diseases is warranted. Nonetheless, it is currently advised that animals with evidence of CWD should be excluded from human and animal food chains due to the possibility that the CWD prion could cross the species barrier (103).

Agent

In 1982 Prusiner first described the concept of the prion to characterize the agent that causes TSEs. Prions are small proteins (253 amino acids in humans) that are encoded on different chromosomes in different species. The exact function of the prion protein is unknown, but it is believed to be involved in neuronal copper metabolism and synaptic transmission. Normal cellular prion protein (PrP^{c}) is susceptible to degradation by protease. However, in certain instances PrP^{c} is converted to a protease resistant form of the protein (PrP^{res}) that accumulates in neural tissue, inevitably resulting in degenerative disorders and death (104–107).

PrP^{c} and PrP^{res} are identical in terms of their primary amino acid sequence and differ only in conformational changes. It is theorized that a post-translational, conformational change of PrP alpha-helices into beta-sheets is the pathologic mechanism causing change from PrP^{c} to PrP^{res}. Following introduction of PrP^{res} into the mammalian body, PrP^{res} promotes conversion of PrP^{c} to PrP^{res} through direct contact, resulting in a toxic accumulation of PrP^{res} in neurologic tissue (102–107).

Acquisition and Communicability

The origin of PrP^{res} in any given mammal is thus critically important. There are several ways by which it may arise. In humans, PrP^{c} may spontaneously

change into PrP^{res}, or inheritance of a defective gene that codes PrP^{c} may cause the prion protein to be abnormally shaped. Finally, acquired cases may occur when PrP^{res} from an infected mammal is introduced into a susceptible mammal through contaminated central nervous system tissue. In animals the origin of PrP^{res} is thought to be acquired only. In humans or animals, there is a dynamic pathogenic process that occurs for acquired cases. The process can be broken down into distinct phases of infection and peripheral replication, CNS neuroinvasion, and neurodegeneration (94,96).

References

1. Epstein P. Emerging Diseases and Ecosystem Instability: New Threats to Public Health. Am J Public Health 1995;85:168–172.
2. Hubalek Z. Emerging Human Infectious Diseases: Anthroponoses, Zoonoses, and Sapronoses. Emerg Inf Dis 2003;9:403–404.
3. Krawczynski K, Aggarwal R, Kamili S. Hepatitis E. Infect Dis Clin North Am 2000;14:669–87.
4. Wang L, Zhuang H. Hepatitis E: An overview and recent advances in vaccine research. World J Gastroenterol 2004;10(15):2157–62.
5. American Public Health Association. Hepatitis E. In: Control of Communicable Diseases Manual, 17th ed. Chin J, ed. 2000; 255–7.
6. Smith JL. A review of hepatitis E virus. J Food Prot 2001;64(4):572–86.
7. Singh S, Mohanty A, Joshi Y, Deka D, Mohanty S, Panda S. Mother-to-child transmission of hepatitis E virus infection. Indian J Pediatr 2003;70(1):37–9.
8. Kumar A, Beniwal M, Kar P, Sharma J, Mutthy N. Hepatitis E in pregnancy. Int J Gynaecol Obstet 2004;85(3):240–4.
9. Kumar R, Uduman S, Rana S, Kochiyil J, Usmani A , Thomas L. Sero-prevalence and mother-to-infant transmission of hepatitis E virus among pregnant women in the United Arab Emirates. Eur J Obstet Gynecol Reprod Biol 2001;100(1):9–15.
10. Wang Y, Zhang H, Xia N, Peng G, Lan H, Zhuang H, et al. Prevalence, isolation, and partial sequence analysis of hepatitis E virus from domestic animals in China. J Med Virol 2002;67(4):516–21.
11. Hirano M, Ding X, Li T, Takeda N, Kawabata H, Koizumi N, et al. Evidence for widespread infection of hepatitis E virus among wild rats in Japan. Hepatol Res 2003;27(1):1–5.
12. Hirano M, Ding X, Tran H, Li T, Yakeda N, Sata T, et al. Prevalence of antibody against hepatitis E virus in various species of non-human primates: Evidence of widespread infection in Japanese monkeys (Macaca fuscata). Jpn J Infect Dis 2003;56(1):8–11.
13. Khuroo M, Kamili S, Yattoo G. Hepatitis E virus infection may be transmitted through blood transfusions in an endemic area. J Gastroenterol Hepatol 2004;19(7):778–84.
14. Vildosola H, Colichon A, Barreda M, Piscoya J, Palacios O. Hepatitis E IgG antibodies seroprevalence in a Peruvian risk group. Rev Gastrolenterol Peru 2000;20(2);111–16.
15. Vaidya S, Tilekar B, Walimbe A, Arankalle V. Increased risk of hepatitis E in sewage workers from India. J Occup Environ Med 2003;45(11);1167–70.

16. Withers M, Correa M, Morrow M, Stebbins M, Seiwatana J, Webster W, et al. Antibody levels to hepatitis E virus in North Carolina swine workers, non-swine workers, swine, and murids. Am J Trop Med Hyg 2002;66(4):384–8.
17. Meng X, Wiseman B, Elvinger F, Guenette D, Toth T, Engle R, et al. Prevalence of antibodies to hepatitis E virus in veterinarians working with swine and in normal blood donors in the United States and other countries. J Clin Microbiol 2002;40(1):117–22.
18. Tei S, Kitajima N, Takshashi K, Mishiro S. Zoonotic transmission of hepatitis E virus from deer to human beings. Lancet 2003;362(9381):371–3.
19. Tamada Y, Yano K, Yatsuhashi H, Inoue O, Mawatari F, Ishibashi H. Consumption of wild boar linked to cases of hepatitis E. J Hepatol 2004;40(5):869–70.
20. Murray K, Russell R, Selvey L, Selleck P, Hyatt A, Gould A, Gleeson L, Hooper P, Westbury H. A novel Morbillivirus pneumonia of horses and its transmission to humans. Emerg Infect Dis 1995;1(1):31–33.
21. Mackenzie J, Field H. Emerging encephalitogenic viruses: lyssaviruses and henipaviruses transmitted by frugivorous bats. Arch Virol Suppl 2004;(18):97–111.
22. Barclay A, Paton D. Hendra (equine morbillivirus). Vet J 2000;160(3):169–76.
23. Halpin K, Young P, Field H, Mackenzie J. Isolation of Hendra virus from pteropid bats: A natural reservoir of Hendra virus. J Gen Virol 2000;81(part 8):1927–32.
24. Field H, Mackenzie J, Daszak P. Novel viral encephalitides associated with bats (Chiroptera): host management strategies. Arch Virol Suppl 2004;(18):113–21.
25. Barker S. The Australian paralysis tick may be the missing link in the transmission of Hendra virus from bats to horses to humans. Med Hypotheses 2003;60(4):481–3.
26. Centers for Disease Control and Prevention. Hendra virus disease and Nipah virus encephalitis. Available at *www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/nipah.htm. Accessed July 30,2004*.
27. Love R, Philbey A, Kirkland P, Ross A, Davis R, Morrissey C, Daniels P. Reproductive disease and congenital malformations caused by Menangle virus in pigs. Aust Vet J 2001;79(3):192–8.
28. Bowden T, Westenberg M, Wang L, Eaton B, Boyle D. Molecular characterization of Menangle virus, a novel paramyxovirus which infects pigs, fruit bats, and humans. Virology 2001;283(2):358–73.
29. Chant K, Chan R, Smith M, Dwyer D, Kirkland P, and the NSW Expert Group. Probable human infection with a newly described virus in the family Paramyxoviridae. Emerg Infect Dis 1998;4(2):273–5.
30. Philbey A, Kirkland P, Poss A, Davis R, Gleeson A, Love R, et al. An apparently new virus (Family Paramyxoviridae) infectious for pigs, humans, and fruit bats. Emerg Infect Dis 1998;4(2):269–71.
31. Kirkland P, Love R, Philbey A, Ross A, Davis R, Hart K. Epidemiology and control of Menangle virus in pigs. Aust Vet J 2001;79(3);190–1.
32. Mohd N, Gan C, Ong B. Nipah virus infection of pigs in peninsular Malaysia. Rev Sci Tech 2000;19(1):160–5.
33. Chew M, Arguin P, Shay D, Goh K, Rollin P, Sheih W, et al. Risk factors for Nipah virus infection among abattoir workers in Singapore. J Infect Dis 2000;181(5):1760–3.
34. Centers for Disease Control and Prevention. Outbreak of Hendra-like virus–Malaysia and Singapore, 1998–1999. MMWR 1999;48(13):265–9.
35. Parashar U, Sunn L, Ong F, Mounts A, Arif M, Ksiazek T, et al. Case-control study of risk factors for human infection with a new zoonotic paramyxovirus,

Nipah virus, during a 1998–1999 outbreak of severe encephalitis in Malaysia. J Infect Dis 2000;181(5):1755–9.
36. ProMed Digest. Nipah virus-2004 Bangladesh., Volume 2004, Number 237. Posted on June 25, 2004.Available at *promed-digest-Owner@promed.isid.harvard.edu.*
37. Lam S. Nipah virus–a potential agent of bioterrorism? Antiviral Res. 2003: 57(1–2):113–9.
38. Goldsmith C, Whistler T, Rollin P, Ksiazek T, Rota P, Bellini W, et al. Elucidation of Nipah virus morphogenesis and replication using ultrastructural and molecular approaches. Virus Res 2003;92(1):89–98.
39. Chan Y, Chua K, Koh C, Lim M, Lam S. Complete nucleotide sequences of Nipah virus isolates from Malaysia. J Gen Virol 2001;82(pt 9):2151–5.
40. Goh K, Tan C, Chew N, Tan P, Kamarulzaman A, Sarji S, et al. Clinical features of Nipah encephalitis among pig farmers in Malaysia. N Eng J Med 2000;342(17):1229–35.
41. Tan C, Goh K, Wong K, Sarji S, Chua K, Chew N, et al. Relapsed and late-onset Nipah encephalitis. Ann Neurol 2002;51(6):703–8.
42. Paton N, Leo Y, Zaki S, Auchus A, Lee K, Ling A, et al. Outbreak of Nipah-virus infection among abattoir workers in Singapore. Lancet 1999;354(9186):1253–6.
43. Lam S, Chua K. Nipah virus encephalitis outbreak in Malaysia. Clin Infect Dis 2002;34 Suppl 2:S48–51.
44. Wong K, Sheih W, Kumar S, Norain K, Abdullah W, Guarnerc J, et al. Nipah virus infection: pathology and pathogenesis of an emerging paramyxoviral zoonosis. Am J Pathol 2002;161(6):2153–67.
45. Hooper P, Williamson M. Hendra and Nipah virus infections. Vet Clin North Am Equine Pract 2000;16(3):597–603.
46. Olsen J, Rupprecht C, Rollin P, An U, Niezgoda M, Clemins T, Walston J, Ksiazek T. Antibodies to Nipah-like virus in bats (Pteropus lylei), Cambodia. Emerg Infect Dis 2002;8(9):987–8.
47. Chau K, Lam S, Goh K, Hooi P, Ksiazek T, Kamarulzaman A, et al. The presence of Nipah virus in respiratory secretions and urine of patients during an outbreak of Nipah virus encephalitis in Malaysia. J Infect 2001;42(1):40–3.
48. Chong H, Kunjapan S, Thayaparan T, Tong J, Petharunam V, Jusoh M, Tan C. Nipah encephalitis outbreak in Malaysia, clinical features in patients from Seremban. Can J Neurol Sci 2002;29(1):83–7.
49. Ali R, Mounts A, Parashar U, Sahani M, Lye M, Isa M, et al. Nipah virus infection among personnel involved in pig culling during an outbreak of encephalitis in Malaysia, 1998–1999. Emerg Infect Dis 2001;7(4):759–61.
50. Chong H, Kamarulzaman A, Tan C, Goh K, Thayaparan S, Chew N, et al. Treatment of acute Nipah encephalitis with ribavirin. Ann Neurol 2001;49(6):810–3.
51. McCaughey C, Hart C. Hantaviruses. J Med Microbiol 2000;49(7):587–99.
52. National Center for Infectious Diseases. All about Hantaviruses. Available at www.cdc.gov/ncidod/diseases/hanta/hps/index.htm. Accessed August 3, 2004.
53. Bayard V, Kitsutani P, Barria E, Ruedas L, Tinnin D, Munoz C, et al. Outbreak of Hantavirus Pulmonary Syndrome, Los Santos, Panama, 1999–2000. Emerg Infect Dis 2004;10(9):1635–1642.
54. Howard M, Doyle T, Koster F, Zaki S, Khan A, Petersen E, Peters C, Bryan R. Hantavirus pulmonary syndrome in pregnancy. Clin Infect Dis 1999;29(6):1538–44.
55. Markotic A. Immunopathogenesis of hemorrhagic fever with renal syndrome and hantavirus pulmonary syndrome. Acta Med Croatica 2003;57(5):407–14.

56. Kilpatrick E, Terajima M, Koster F, Catalina M, Cruz J, Ennis F. Role of specific CD8+ cells in the severity of a fulminant zoonotic viral hemorrhagic fever, hantavirus pulmonary syndrome. J Immunol. 2004;172(5):3297–304.
57. Armien B, Pascale J, Bayard V, Munoz C, Mosca I, Guerrero G, et al. High seroprevalence of hantavirus infection on the Azuero peninsula of Panama. Am J Trop Med Hyg 2004;70(6):682–7.
58. Castillo C, Villagra E, Sanhueza L, Ferres M, Mardones J, Mertz, G. Prevalence of antibodies to hantavirus among family and health care worker contacts of persons with hantavirus cardiopulmonary syndrome: lack of evidence for nosocomial transmission of Andes virus to health care workers in Chile. Am J Trop Med Hyg 2004;70(3):302–4.
59. Houck M, Qin H, Roberts H. Hantavirus transmission: potential role of ectoparasites. Vector Borne Zoonotic Dis 2001;1(1):75–9.
60. Young J, Hansen G, Graves T, Deasy M, Humphreys J, Fritz C, et al. The incubation period of hantavirus pulmonary syndrome. Am J Trop Med Hyg 2000; 62(6):714–7.
61. Mills J, Corneli A, Young J, Garrison L, Khan A, Ksiazek T. Hantavirus pulmonary syndrome: Updated recommendations for risk reduction. MMWR 2002;51:1–12.
62. Ye C, Prescott J, Nofchissey R, Goade D, Hjelle B. Neutralizing antibodies and Sin Nombre virus RNA after recovery from hantavirus cardiopulmonary syndrome. Emerg Infect Dis 2004;10(3):478–82.
63. Mathiesen D, Oliver J, Kolbert C, et al. Genetic Heterogeneity of *Borrelia burgdorferi* in the United States. J Infect Dis 1997;175:98–107
64. Kazmierczak J, Davis J. Lyme disease: Ecology, epidemiology, clinical spectrum, and management. Adv In Peds 1992;39:207–55.
65. Steere A. Lyme disease. N Engl J Med 1989;321:586–596.
66. Steere A. Lyme disease. N Engl J Med 2001;345:115–125.
67. McAlister H, Klementowicz P, Andrews C, et al. Lyme Carditis: an important cause of reversible heart block. Ann Intern Med 1989;110:339–45.
68. Recommendations for Test Performance and Interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. MMWR 1995; 44:590–1.
69. Dressler F, Whalen J, Reinhardt B, Steere A. Western blotting in the serodiagnosis of lyme disease. J Infect Dis 1993;167:392–400.
70. Keirans J, Hutcheson H, Durden L, Klompen J. *Ixodes scapularis*: Rediscription of all active stages, distribution, hosts, geographical variation, and medical and veterinary importance. J Med Ent 1996;33:297–318.
71. Piesman J, Happ C. Ability of the lyme disease spirochete *Borrelia burgdorferi* to infect rodents and three species of human-biting ticks. J Med Ent 1997;34:451–6.
72. Apperson C, Levine J, Nicholson W. Geographic occurrence of *Ixodes scapularis* and *Ambylomma americanum* infesting white-tailed deer in North Carolina. J of Wild Dis 1990;26:550–3.
73. Fritz C, Kjemtrup A. Lyme Borreliosis. JAVMA 2003;223:1261–70.
74. Magnarelli L, Anderson J, Barbour A. The etiologic agent of Lyme disease in deer flies, horse flies and mosquitoes. J Infect Dis 1986;154:355–8.
75. Magnarelli L, Anderson J, Apperson C, et al. Spirochetes in ticks and antibodies to *Borrelia burgdorferi* in white-tailed deer from Connecticut, New York State, and North Carolina. J Wildlife Dis 1986;22:178–88.

76. Magnarelli L, Freier J, Anderson J. Experimental infection of mosquitoes with *Borrelia burgdorferi*, the etiologic agent of Lyme disease. J Infect Dis 1987;156:694–5.
77. Markowitz L, Steere A, Benach J, et al. Lyme disease during pregnancy. JAMA 1986;255:3394–6.
78. Gerber M, Shapiro E, Krause P, et al. The risk of acquiring Lyme disease or babesiosis from a blood transfusion. J Infect Dis 1994;170:231–4.
79. Nadelman R, Wormser G. Lyme borreliosis. Lancet 1998;352:557–65.
80. Klempner M, Hu L, Evans J, Schmid C, Johnson G, et al. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. N Engl J Med 2001;345:85–92.
81. Bakken J, Dumler J, Chen S, Eckman M, Van Etta L, Walker D. Human Granulocytic Ehrlichiosis in the Upper Midwest United States. JAMA 1994;272(3):212–18.
82. Keefe T, Holland C, Salyer P, Ristic M. Distribution of Ehrlichia canis among military working dogs in the world and selected civilian dogs in the United States. JAVMA 1982;181:236–8.
83. Anderson B, Dawson J, Jones D, Wilson K. *Ehrlichia chaffeensis*, a new species associated with human ehrlichiosis. J Clin Microbiol 1991;29:2838–42.
84. Belongia E, Gale C, Reed K, Mitchell P, Vandermause M, Finkel M, et al. Population based incidence of Human Granulocytic Ehrlichiosis in Northwestern Wisconsin 1997–1999. J Inf Dis 2001;184:1470–4.
85. Dumler J, Barbet A, Bekker C, et al. Reorganization of genera in the families Rickettsiaceae and Anaplasmataceae in the order Rickettsiales: Unification of some species of *Ehrlichia* with *Anaplasma, Cowdria* with *Ehrlichia* and *Ehrlichia* with *Neorickettsia*, descriptions of six new species combinations and designation of *Ehrlichia equi* and HGE agent as subjective synonyms of *Ehrlichia phagocytophila*. Int J Syst Evol Microbiol 2001;51:2145–65.
86. Buller R, Arens M, Hmiel S, Paddock C, Sumner J, Rikihisa Y, Unver A, et al. *Ehrlichia ewingii*, a newly recognized agent of human ehrlichiosis. N Engl J Med 1999;341:148–55.
87. Center for Disease Control and Prevention. Statewide surveillance for Ehrlichiosis: Connecticut and New York, 1994–1997. MMWR 1998;47(23);476–80.
88. Yabsley M, Varela A, Tate C, Dugan V, Stallnecht D, Little S, Davidson W. *Ehrlichia ewingii* infection in White-Tailed Deer (*Odocoileus virginianus*). Emerg Infect Dis 2002;8(7):668–71.
89. Mueller-Anneling L, Gilchrist M, Thorne P. Ehrlichia chaffeensis antibodies in White Tail Deer, Iowa, 1994 and 1996. Emerg Infect Dis 2000;6(4):397–400.
90. McQuiston J, McCall C, Nicholson W. Ehrlichiosis and related infections. JAVMA 2003;223(12):1750–6.
91. Belongia E, Reed K, Mitchell P, Kolbert C, Persing D, Gill J, Kazmierczak J. Prevalence of granulocytic ehrlichia infection among white tail deer in Wisconsin. J Clin Microbiol 1997;35:1465–8.
92. Walls J, Greig B, Neitzel D, Dumler J. Natural infection of small mammal species in Minnesota with the agent of human granulocytic ehrlichiosis. J Clin Microbiol 1997;35:853–5.
93. Hodzic E, Fish D, Maretzki C, et al. Acquisition and transmission of the agent of human granulocytic ehrlichiosis by *Ixodes scapularis* ticks. J Clin Microbiol 1998;36:3574–8.

94. Aguzzi A, Heikenwalder M, Miele G. Progress and problems in the biology, diagnostics, and therapeutics of prion diseases. J Clin Invest 2004;114:153–60.
95. Brown P, Will R, Bradley R, Asher D, Detwiler L. Bovine Spongiform Encephalopathy and variant Creutzfeldt-Jakob Disease: Background, evolution, and current concerns. Emerg Infect Dis 2001;7:6–16.
96. Southeastern Cooperative Wildlife Disease Study Briefs. Special CWD issue. 2002;18:1–16.
97. Current data and legislation at Department for Environment, Food and Rural Affairs (DEFRA): *http://www.defra.gov.uk/animalh/bse/index.html*
98. Cohen J, Duggar K, Gray G, Kreindel S. Evaluation of the potential for bovine spongiform encephalopathy in the United States. Harvard Center for Risk Analysis. Available at http://www.hcra.harvard.edu/pdf/madcow.pdf.
99. Center for Disease Control and Prevention. Bovine Spongiform Encephalopathy in a Dairy Cow: Washington State, 2003. MMWR 2004;52(53):1280–5.
100. United Kingdom Department of Health Monthly CJD disease statistics:*http://www.dh.gov.uk/PublicationsAndStatistics/PressReleases/fs/en*
101. Williams E, Young S. Chronic wasting disease of captive mule deer: A spongiform encephalopathy. J Wildlife Dis 1980;16:89–98.
102. Salman M. Chronic wasting disease in deer and elk: Scientific facts and findings. J Vet Med Sci 2003;65:761–8.
103. Center for Disease Control and Prevention. Fatal degenerative neurologic illness in men who participated in wild game feasts: Wisconsin, 2002, 2003. MMWR 2003;52(07):125–7.
104. Prusiner S. Novel proteinaceous infectious particles cause scrapie. Science 1982;216:136–44.
105. Collins S, Lawson V, Masters C. Transmissible spongiform encephalopathies. Lancet 2004;363:51–61.
106. Brown D, Qin K, Herms J, et al. The cellular prion protein binds copper in vivo. Nature 1997;390:684–7.
107. Collinge J, Whittington M, Sidle K, et al. Prion protein is necessary for normal synaptic function. Nature 1994;370:295–7.

30

Arthropod Bites and Stings

Mitchell S. Wachtel and Danny B. Pence

Key words: scabies, lice, ticks, spiders, insects

This chapter describes the diagnosis and treatment of the most common diseases arising from direct interactions of agricultural workers and arthropods.

When confronted by a complaint of an infestation, vigorous attempts to identify an etiologic agent will sometimes be fruitless; if presumptive treatment fails to provide relief, delusional parasitosis must be considered (1).

Scabies

The mite that causes scabies, *Sarcoptes scabiei*, is colorless and less than 1 mm long (2,3). It perpetuates solely in human skin, forming sinuous burrows in the stratum corneum. Adult females periodically emerge from their burrows to crawl over the skin surface. The mites die within two days of isolation from a human host; transmission results mostly from direct contact between human hosts rather than fomite transfer through contaminated clothing or bedding. Crowding, common in migrant labor housing, promotes outbreaks. Thirty-eight percent of household contacts experience a secondary attack, arguing for presumptive community treatment, which in the agricultural setting includes coworkers and fellow household members. Pandemics occur about every three decades (4), meaning physicians should again be prepared for a large number of patients with this disease. Scabies frequently burdens African villagers, but black people are generally less susceptible than are others (5). For the treating physician and his or her staff, scabies poses an occupational risk, particularly superscabies in anergic patients, which is highly contagious and lacks the characteristic pruritis.

Signs and Symptoms

Intense pruritis, often worse at night or after a hot shower, is the primary symptom (3). The resultant bleeding is a clinical clue to the diagnosis. Symmetric,

papulovesicular, 2 to 3 mm in diameter, lesions, may be accompanied by macules, pustules, and scaly plaques. The irregular, fine, black, thread-like, 3- to 15-mm long burrows are often difficult to find. Lesions are confined in two-thirds of patients to the flexor surfaces of interdigital spaces; nine-tenths of patients will have a lesion in this location. Also affected are breasts, periumbilicus, belt line, buttocks, thighs, penis, scrotum, elbows, feet, ankles, and anterior axillary folds. On occasion the infestation presents as a blistering eruption (6).

Superscabies in anergic individuals (Norwegian scabies) (7) presents as widespread erythema, hyperkeratosis, and crusting with little or no itching. No burrows are evident. Nail involvement is common. Alopecia, generalized hyperpigmentation, pyoderma, and eosinophilia may also occur. It may be induced by steroid administration but is most commonly seen in immunocompromised or mentally impaired patients (8,9). "Scabies of the cultivated," which develops in patients with a high level of hygiene (10), has burrows in only 7% of cases. Steroids may suppress the symptoms, resulting in a misdiagnosis of a fungal infection or impetigo. In nodular scabies, indurated, often pigmented, tumors lie in the groin or axilla; infestations may continue for more than a year despite therapy.

Aside from the specific variant of *Sarcoptes scabeie* that only affects humans, a number of specific variants infest a variety of domestic and companion animals. These include strains that occur on dogs and other canids, cattle, sheep, goats, llamas, camels, pigs, and horses. These strains of *S. scabeie*, while unable to produce full-blown scabies in the classic sense, can nonetheless produce a transient dermatitis in humans that can persist for several days to weeks. The usual lesions are erythematous pustules about the hair follicles that the mites enter (11).

Diagnosis

Given this polymorphic appearance, it is little wonder scabies has been called "the great imitator" in dermatology (12). Scabies should be suspected in any patient who presents with pruritis, particularly if more than one household or occupational contact suffers from the condition. By the same token, it should be noted that primary care physicians more frequently overdiagnose than underdiagnose scabies (13).

A diagnosis can be rendered after discovering burrows (2). Present in almost all patients, burrows should be sought in the web spaces between fingers, on wrists and elbows, on sides of hands, feet, and ankles, and in the external genitalia. Several diagnostic techniques exist (14–17). If, after liquid tetracycline has been applied for several minutes, alcohol is wiped over the lesion, burrows fluoresce yellow-gray with a Woods lamp. Mineral oil, by altering the refractive index of the stratum corneum, allows visualization of burrows. Applying India ink over affected areas and wiping away the excess shows burrows as diagnostic ink lines. Other techniques usually unavailable to occupational physicians include epiluminescence microscopy and videodermatoscopy.

Discovery of eggs, scybala, or mites is pathognomic (2). After placing a drop of sterile mineral oil at the anterior end of a suspected burrow, one may scrape the surface with a number 15 blade. Mites or eggs can be seen under the microscope amid the scrapings; a magnifying glass can detect the mite, an oval object, white with dark pigment caudally, within its burrow. Scrapings or shavings of papulovesicular lesions or, in the case of Norwegian scabies, the crust, is also diagnostic. A punch biopsy of skin, especially after treatment failure, can often be diagnostic as the corneal burrow is diagnostic on histopathologic examination. As always, a diagnosis of scabies does not exclude other conditions; other pruritic and non-pruritic disease may also be present. Scabies is often accompanied by a staphylococcal skin infection.

Management

A wide array of scabicides exists. As always, resistance must be borne in mind; resistance to ivermectin, the newest drug, has been reported (18). Reinfestation is a constant risk. Allergic reactions can persist months after the mites have been destroyed; treatment with calamine lotion or antihistamines is generally effective, but a brief course of steroids may be required. *Before applying steroids, secondary bacterial infection should be excluded. If found, it should be treated with topical antibiotics if localized or systemically if widespread or with adenitis*. Steroids may also be needed to treat Norwegian scabies.

Drugs(14), in order of effectiveness, include ivermectin, permethrin, lindane, benzyl benzoate, crotamiton cream, sulfur ointment, and monosulfiram. For Norwegian scabies or nail involvement, a keratolytic agent may be required. Combinations, such as oral ivermectin and permethrin cream, may be more effective than monotherapy, especially with crusted scabies.

Lice

Louse infestations comprise head lice (*Pediculusis humanus capitis*), body lice (*Pediculusis humanus humanus*), and pubic lice (*Pthirus pubis*) (10). The dorsoventrally flattened animals lack wings and infest only humans, although humans may be transiently affected by lice from other animals. The louse mouth is a toothed tubular structure that emerges from the head only when feeding begins; blood, the sole nutritional source, is obtained through a pair of stylets; a third stylet injects antigenic and antihemostatic saliva into the skin. During feeding copious defecation occurs, permitting transmission of louse-borne infectious diseases, such as typhus.

Head and body lice bear three clearly demarcated body regions, including a central thorax with six clawed legs and seven abdominal segments with lateral lobes. The crablike pubic louse, about as broad as it is long, is shorter than other lice, bears a more-fused body, and has slender claws on its forelegs,

enabling it to grasp pubic hairs with ease; but they can also grasp eyelash, facial, axillary, and, rarely, scalp hairs.

Signs, Symptoms, and Diagnosis

Head lice primarily infest children but do affect all ages (19). Of interest, in the Americas, blacks are less affected than others, whereas the reverse is true in Africa (20). A red, maculopapular rash on the scalp, the nape of the neck, and the shoulders may occasionally result, but most infestations lack symptoms. Excoriation may yield crust, matted hair, and bacterial infection. Eggs or nits are more easily found than lice; hair casts, seborrheic material, and other debris can closely mimic nits (21). Direct contact, not shared headgear and grooming implements, now appears to be the primary means of louse transfer. Treatment should only be performed when live lice are discovered; if live nits are found by a specialist (primary care physicians should not attempt to discriminate live from dead nits), treatment should also be initiated.

Body lice mainly infest indigent people who remain clothed for extended periods. The lice remain sequestered in the seams and between layers of clothing except when feeding (22). They are transmitted both by direct contact and by exchange of contaminated clothing and bedding. Body louse saliva induces an intensely pruritic, red, maculopapular eruption hours to days after feeding, often resulting in hives complete with flare and wheal formation. Excoriation can yield crusts, regional adenopathy, and bacterial infection. The saliva can itself induce a hemorrhagic reaction. Chronic infestation can incite lichenification with generalized hyperpigmentation, known as vagabond's disease.

Pubic louse saliva yields a pruritic rash mainly in pubic, inguinal, and lower abdominal sites, and occasionally also axillae and eyelids. The rash may present as blue-gray macules known as maculae ceruleae (23). Excoriation can yield crusts, but infection is less likely than with other lice. Nits are always present, and the lice can usually be seen with a magnifying lens. Infested eyelids have blepharoconjunctivitis with occasional serosanguinous discharge, and occasional adult lice at the eyelash roots. The diagnosis mandates considering other venereal diseases and evaluating all sex partners.

Management

Mechanical removal of head lice and their eggs with special fine-toothed combs or other implements is an established technique. Non-prescription pyrethrins can be applied twice with an interval of 10 days between doses. Pyrethrins kill adults and immatures, but not live nits, which must be combed out. Lindane and malathion can also be prescribed. As with all infectious diseases, resistance is increasing (19), and local information as to the most effective pediculucide must be obtained.

For body lice, the principal therapy lies in more frequent washing and changing of clothes and linens, which should be placed loosely in a clothes dryer for at least one-half hour at a temperature of at least 65° C. If lice or louse eggs lie amid body hair, head to foot treatment with pediculucides, either pyrethrin or lindane, is recommended.

Pubic lice are best eliminated by pyrethroid-containing shampoo, mechanical removal of lice and eggs, and shaving the affected region. Eyelid infestations have been treated by 1% yellow mercuric acid ointment, four times daily for two weeks (24), but, as this infestation is rare, no definite therapeutic recommendations can be made, and no specific FDA approval is now available. For all forms of louse infestation, ivermectin may soon become an important adjunct.

Ticks

Ticks are infectious-disease vectors *par excellence*; one was recently reported to simultaneously bear seven different pathogens (25). Although general statements about which agents occur within which species can be made, epidemiologic studies show regional variation (26,27). Excepting Africans who sleep on the floor, humans interact with hard (ixodid) ticks far more often than they do soft (argasid) ticks. Hard ticks embed into skin, through which they feed for 3 to 10 days; soft ticks attach lightly and feed for about 20 minutes.

Deer Ticks

Lyme disease, babesiosis, granulocytic ehrlichiosis, and tickborne encephalitis are carried by *Ixodes scapularis* (formerly *I. dammini*), in the eastern United States, *Ixodes pacificus*, in the western United States, and *Ixodes ricinus* and *Ixodes persulcatus*, in Europe (28,29). Tick larvae that quest for hosts from August through September and nymphs that quest for hosts from May to July feed on mice, where they obtain pathogens. Adults that quest for hosts from October through April feed upon deer. Humans are accidental hosts who may be attacked by larvae, nymphs, and adults wherever deer are numerous, particularly at brushy margins of forested sites. Rapid evaluation of ticks is vital to prevent disease transmission. Lyme disease and babesiosis pathogens wait for about two days of tick feeding before traveling through tick saliva to rest on the skin surface. Hence, within the first two days of a tick bite, firm traction applied with a forceps should remove as much of the tick as possible; tincture of iodine should then be applied to the skin to kill adherent pathogens. Established practice notwithstanding, leaving behind part of the tick's mouth is not problematic; neither will heat, burning, or chemical weaponry aid in tick removal. Dead ticks rarely, if ever, transmit disease. Any blood-engorged, 2 mm tick is considered infectious; promptly administered doxycycline helps prevent Lyme disease (30,35).

Wood and Dog Ticks

Wood ticks (*Dermacentor andersoni*) are common in the western mountains; dog ticks (*Dermacentor variables*) are common in the coastal regions. Adult wood ticks feed on woodchucks or marmots; adult dog ticks prefer dogs. Nymphs and larvae feed on voles and mice. All stages feed in early summer. Adult ticks, the only stage that attacks humans, are attracted to grassy sites and also to carbon dioxide sources, e.g., cars. Gentle traction with a forceps easily removes these ticks, which always remain intact; tincture of iodine should be applied to the bite area. As these ticks can transmit Rocky Mountain spotted fever, tularemia, Q fever, and Colorato tick fever, gloves must be worn when removing the tick; by the same token, these rare diseases do not require presumptive treatment. Except in the southeastern United States, summer-feeding ticks 6 mm or longer should be considered dog or wood ticks (36,37).

Lone Star Ticks

This tick, *Amblyomma americanum* (36,38), is identified by a white dot at the top of the back in females and white curved back markings in males, which allows relatively easy separation from deer ticks. Although native Texans, lone star ticks now range to the Atlantic coast and as far north as New York. They do not transmit Lyme disease but can produce a mild disorder that mimics it as well as a mild form of borreliosis. They can transmit tularemia and Rocky Mountain spotted fever. As these diseases are rare, prophylaxis is not indicated. Throughout their lives, the ticks feed on deer and other large herbivores; they can attack humans at any stage. They firmly attach to the skin, like deer ticks, and so must be treated in the same way. Walking near a deposited egg mass can result in an acute massive infestation, in which the chest and pelvis can appear to vibrate; pyrethroid shampoo, head to foot, and laundering of sheets and clothes are curative.

Tick Paralysis

Any of the above ticks can produce tick paralysis (39). A neurotoxin in tick saliva yields acute ascending paralysis without constitutional signs a few days after tick attachment. Hypoactive/absent deep tendon reflexes are common; ocular muscle abnormalities can occur. Tick removal usually yields rapid cure, but the disorder can be complicated by respiratory failure and is occasionally fatal.

Fire Ants

Fire ants (40), indigenous to tropical America, were imported into Alabama in the United States in 1918, but now are seen in such diverse locales as

Australia and Korea (41). In endemic areas, such as the southeastern United States, fire ants represent the leading cause of insect hypersensitivity (42) and, perhaps, of anaphylaxis (43). The 2 to 5 mm, red-brown ants, *Solenopsis richteri* and *Solenopsis invicta*, nest in up to 50-cm diameter mounds bearing up to 200,000 ants with tunnels to the outside world that can extend to 25 m from the mound center. Up to 10,000 stings can be inflicted on an individual who disturbs the mounds (44). The stinging ant first bites into the skin before pivoting about its head to deliver multiple stings through a stinging apparatus at its caudal end. The venom, a necrotizing toxin containing solenamine, produces a wheal and flare reaction within 30 minutes that resolves 30 minutes later; a sterile pustule forms about a day later, for which there is no effective treatment (45), but it does resolve on its own a few days later if undisturbed; bandage can help prevent excoriation. Steroid creams can help with allergic reactions. Topical antibiotics should be applied if local infection is suspected.

Systemic reactions occur in 16% and anaphylaxis in 2% of patients. The onset occurs within 45 minutes of a sting. It can include urticaria, chest tightness, pruritis, dysphagia, abdominal cramps, nausea, vomiting, diarrhea, wheezing, the changes of anaphylaxis (described later), syncope, convulsions, confusion, mononeuropathy and seizures (46–48). Therapy is directed towards the particular symptoms and signs the patient has. Immunotherapy is in its early stages but shows great promise (49,50).

Spiders

Of the over 30,000 kinds of described spiders, about 200 attack humans. Severe injuries are most often from bites by species of the genera *Latrodectus* (widow spiders) and *Loxoscleles* (violin spiders) (51), and a few others, such as the Brazilian banana spider (*Phoneutria* nigriventer) and Sydney's funnel web spider (*Atrax* robustus) (52), which are also highly venomous. Because 80% of reported spider bites may be due to other etiologies, the wise physician will limit diagnoses to cases in which the spider is observed, preferably by the physician; parts of spiders oft suffice for speciation.

Neurotoxic Arachnidism

In the United States, black (*Latrodectus. mactans, L. various, L. Hesperus*), red (*L. bishopi*), and brown (*L. geometricus*) widow spiders, in Australia and New Zealand, the red back (*L. hasselti*) widow spider, and in South and eastern Africa black (*L. mactans, L. geometricus*) widow spiders, attack people. The tarantula (*L. tredecimguttatus*) is also a member of this family.

Adult male (0.5 cm) and immature black widow spiders are more colorful than are adult females (1.0 cm). With the familiar red hour glass, females are mostly responsible for human bites. These eight-eyed creatures

spin variably-sized webs close to the ground and in such varied sites as logs, shutters, windows, doors, dumps, barns, and sheds. In infested outdoor privies, spiders bite penises of seated men who disturb the web with a urine stream. Most often injury results when a human limb disturbs the web or a body part traps the spider against it.

Local effects, except for *Latrodectus hasselti*, are usually quite mild, ranging from a sharp pinprick to nothing, leaving a small pair of red marks, and occasionally yielding slight redness and swelling. Within an hour, dull cramping and often severe pain and numbness spread from bite to the entire torso; the syndrome begins to wane after three hours, but can last for days. Sometimes, a surgical abdomen is mimicked, but the lack of tenderness and distension, the history, and the muscle spasms allow the correct diagnosis. Other symptoms include tachycardia, headache, diaphoresis, salivation, weakness, fever, vomiting, backache, respiratory distress, priapism, impotence, urinary retention, anxiety, increased deep tendon reflexes, proteinuria, parasthesia, hypertension, fetal positioning, and burning; these changes usually end after several days, but can last for months. Complications include shock, convulsions, and cerebral hemorrhage, as well as respiratory, cardiac, or renal failure.

Local treatment includes cleansing the wound, tetanus vaccination if not administered within the past ten years, and an ice cube on the wound. If the patient is less than 16 or more than 60 years old, pregnant, suffering from chronic disease, or subject to one of the more severe symptoms listed in the previous paragraph, hospitalization and antivenin are recommended (52,53).

Necrotic Arachnidism

Violin spiders, *Loxosceles*, most often produces necrotic arachnidism. *Loxosceles laeta* inhabits Latin America; *L. reclusa*, the brown recluse, in the United States, and *L. refuscens*, the Mediterranean and adjacent nations. Related species occur in Africa. The spider's outdoor preferences include the undersurfaces of rocks and boards, and caves; indoors, they prefer dark, dry locations, such as closets, storage spaces, drawers, and garages. Bites occur most often when the spider is trapped against a body part, usually while the patient dresses, on the face, neck, and hands (51,54).

The bite itself is often painless, but within a few hours the site becomes, in mild cases, mildly pruritic and painful with surrounding ischemic pallor; these changes resolve within a few days. In more severe cases, pruritis and pain last for 8 hours to a day before a blue-gray macular halo develops with or without a pustule or bulla at the inoculation site; red, swollen, purpuric skin often surrounds the halo. Necrosis, eschar, and ulceration often follow, accompanied sometimes by a swollen limb or portion of torso. These changes usually happen within the first to third days. Resolution by a scar can take half a year. Local complications include chronic pain, secondary infection, skin graft

failure, pyoderma gangrenosa, and limb function impairment (54,56). Treatment may involve surgery, which is beyond the scope of this text.

Necrotic areas narrower than 2 cm may require only pain medicine, antihistamines, sterile dressings, tetanus prophylaxis, ice, and elevation of the affected limb. Necrotic foci larger than 1 cm require screening for hemolysis, renal failure, and disseminated intravascular coagulation. Mild systemic reactions are usually apparent within 3 days and include leukocytosis, malaise, headache, arthralgia, myalgia, proteinuria, vomiting, diarrhea, and generalized urticaria. Severe reactions include anuria, delirium, shock, hemolysis, and coma. These reactions should prompt consideration of hospitalization.

Bees, Wasps, And Hornets

Stings from these flying insects are familiar to all. The stings, while painful, are of most concern in terms of anaphylaxis in hypersensitized persons. Honeybees (*Apus spp*.), who often lose their stingers when they envenomate, and bumblebees (*Bombes spp*.), who do not, usually will not bother people unless they are disturbed, excepting the easily provoked Africanized bees. Yellowjackets, paper wasps, and hornets (*Vespoidea*) feed on nectar as adults, but feed their larvae insects. Vespids are seen at picnics and garbage dumps, attack without much provocation and retain their stingers, permitting repetitive stings (38).

The diagnosis of hymenopterism is straightforward, with accurate historical recollection by almost all patients. The painful, red, swollen sting usually resolves spontaneously in a few hours. Cold compresses and analgesics help, as does removing bee stingers. More extensive local allergic reactions can develop within two days and last a week; NSAIDs, antihistamines, cold compresses, and, if necessary, prednisone, will relieve symptoms.

Imported fire ants and the stings of bees, hornets, and wasps together cause over half the reported anaphylaxis cases (57). The cardinal signs are bronchial spasm, larangeal spasm, and hypotension. Within minutes of the sting, upper or lower airway obstruction occurs, the latter more frequent in asthmatics. Usually, pruritic wheals with red, raised, curved edges and white centers appear, focal or diffuse, that may become giant hives; these usually resolve by the second day. Occasionally, soft tissue swelling, as angioedema, is also present. Shock is often present, with or without a secondary cardiac event. Aspirin, opioids, NSAIDs, and radiocontrast agents must be avoided, as they may worsen matters. Upon recognizing anaphylaxis, inject 0.2 to 0.5 mL of 1:1000 epinephrine subcutaneously. Remove any insect stinger. Initiate an intravenous line to administer at 5 to 10 minute intervals 1:10,000 epinephrine and, should hypotension ensue, volume expanders and vasopressor agents. Nasal oxygen may be useful, but intubation or tracheostomy must be used to treat progressive hypoxia (58). Rapid transit to a hospital is critical. Immunotherapy with insect venom effectively prevents future events; referral

to an allergist is vital (59). Patients must be provided and taught to use Epipens. Discussions with the employee and the employer are important to reduce the hazards and consider transfer to a job without such risk factors.

Scorpions

These eight-legged arthropods, with a stinging tail and a pair of anterior pincers, have a shape both familiar and frightening to all. The 1,400 species live on all continents except Antarctica; the varied colors and sizes do not correlate with the danger of the sting, which varies from a local noxious event to a fatal event (38). When confronted by, or preferably *before* being confronted by, a scorpion sting, one should contact local emergency rooms to discover the danger posed by scorpions in the area.

Recent publications list as local symptoms pain, often severe, lasting for several hours, numbness, edema, parasthesia, and erythema (60–62). The area may be blackened by hemorrhage; as with vespids, a wheal may also be seen—anaphylaxis may complicate matters. A local anesthetic may be of use. Ice packs and pressure dressings often help (38). Systemic symptoms without permanent damage include vomiting, headache, paleness, sweating, myoclonus, dysarthria and ataxia (60–62). Seizures, pulmonary edema, and cardiac damage can also ensue and be fatal (60–64). Scorpion venom has specific cardiotoxicity (63,64), the treatment of which is controversial. Antivenom has been advocated (65) but is also controversial. As stated before, wise treatment depends upon local knowledge. A general statement will not apply in all areas; but, where appropriate, a conservative approach may be wisest consisting of 6 hours of monitoring followed by hospitalization if systemic symptoms appear (66).

References

1. Koo J, Gambla C. Delusions of parasitosis and other forms of nomosymptomatic hypochondriacal psychosis. General discussion and case illustrations. Dermatol Clin 1996;14:429–438.
2. Mallenby K. Scabies. Hampton, England: EW Classey, 1972.
3. McCarthy JS, Kemp DJ, Walton SF, et.al. Scabies: more than just an irritation. Postgraduate Medical Journal 2004;80:382–387.
4. Orkin M, Maibach HI. Current concepts in parasitology. This scabies pandemic. N Engl J Med 1978;298:496–498.
5. Alexander AM. Role of race in scabies infestation. Arch Dermatol 1987;114:627.
6. Said S, Jay S, Kang J, et al. Localized bullous scabies. Uncommon presentation of scabies. Am J Dermatopathol 1993;14:590–593.
7. Scheinfeld N. Controlling scabies in institutional settings: a review of medications, treatment models, and implementation. Am J Clin Derm 2004;5:31–37.
8. Marleire V, Roul S, Labreze C, et al. Crusted (Norwegian) scabies induced by use of topical corticosteroids and treated successfully with ivermectin. J Pediatr 1999; 135:122–124.

9. Glover A, Young L, Goltz AW. Norwegian scabies in acquired immunodeficiency syndrome: Report of a case resulting in death from associated sepsis. J Am Acad Dermatol 1987;16:396–399.
10. Parish LC, Nutting WB, Schwartzman RM. Cutaneous infestations of man and animals. New York: Praeger Publishers, 1983.
11. Pence DB, Wecherman E. Sarcoptic mange in wildlife. Revue Scientific Office de Internationale Epizootologie 2002;21:385–398.
12. Arlian LG. Biology, host relations, and epidemiology of *Sarcoptes scabei*. Annu Rev Entomol 1989;34:139–161.
13. Pariser RJ, Pariser DM. Primary care physicians' errors in handling cutaneous disorders: a prospective survey. J Am Acad Dermatol 1987;17:239–245.
14. Chouela E, Abeldano A, Pellerano G, et al. Diagnosis and treatment of scabies: a practical guide. Am J Clin Dermatol 2002;3:9–18.
15. Haas N. A simple vital microscopy aid for the detection of scabies mites. Z Hautr 1987;62:1395.
16. Prins C, Stucki L, French L, et al. Dermoscopy for the in vivo detection of *Sarcoptes scabeii*. Dermatology 2004;208:241–243.
17. Micai G, Lacarrubba F, Tedeschi A. Videodermatoscopy enhances the ability to monitor efficacy of scabies treatment. J Eur Acad Dermatol Venereal 2004;18:153–154.
18. Currie BJ, Harumel P, McKinnon M, Walton SF. First documentation of in vivo and in vitro ivermectin resistence in *Sarcoptes scabiei*. Clin Infect Dis 2004:39:e1–9.
19. Downs AM. Managing head lice in an era of increasing resistance to insecticides. Am J Clin Derm 2004;5:169–177.
20. Lane AT. Scabies and head lice. Pediatr Ann 1987;16:51–54.
21. Pollack RJ, Kiszewski AE, Spielman A. Overdiagnosis and consequent mismanagement of head louse infestations in North America. Pediatr Infect Dis J 2000;19:689–693.
22. Green RW. Infestations: Scabies and lice. In: Brickner P, ed. Healthcare of Homeless People. New York: Springer-Verlag, 1985:33–55.
23. Weeden D. Arthropod induced diseases. In: Skin Pathology. New York: Churchill-Livingstone. 2002:737–746.
24. Ashkenazi I, Desatnik HR, Abraham FA. Yellow mercuric oxide; a treatment of choice for phthiriasis palpebrerarum. Br J Ophthalmol 1992;6:451–452.
25. Alekseev AN, Dubinina HV, Jushkova OV. First report on the coexistence and compatibility of seven tick-borne pathogens in unfed adult Ixodes persulcatus Schulze (Acarina: Ixodidae). Int J Med Microbiol 2004;293 suppl 37:104–108.
26. Oteo JA, Ibarra V, Blanco JR, Martinez de Artola V, et al. Dermacenter-borne necrosis erythema and lymphadenopathy: clinical and epidemiological features of a new tick-borne disease. Clin Microbiol Infect 2004;10:327–331.
27. Stanczak J, Gabre RM, Kruminis-Lozowska W, et al. *Ixodes ricinus* as a vector of *Borrelia burgdorferi sensu lato, Anaplasma phagocytophilum* and *Babesia microti* in urban and suburban forests. Ann Agric Environ Med 2004:11;109–114.
28. Spielman A. The emergence of Lyme disease and human babesiosis in a changing environment. Ann NY Acad Sci 1997;740:146–156.
29. Spielman A. Lyme disease and human babesiosis: evidence incriminating vector and reservoir hosts. In: Englund P, Scher A, eds. The biology of parasitism. New york: Alan R Liss, 1988:147–165.

30. Shih C-M, Pollack RJ, Telford SR, et al. Delayed dissemination of Lyme disease spirochetes from the site of deposition in the skin of mice. J Infect Dis 1992;166:827–831.
31. Matuschka FR, Spielman A. The vector of the Lyme disease spirochete. N Engl J Med 1992;327:542.
32. Treatment of Lyme disease. Med Lett 1989;31:57.
33. Smith RP, Lacombe EH, Rand PW, et al. Diversity of tick species biting humans in an emerging area for Lyme disease. Am J Public Health 1992;82:66–69.
34. Spielman A, Wilson ML, Levine JF, et al. Ecology of *Ixodes damini*-borne human bebesiosis and Lyme disease. Am J Public Health 1988;30:439–460.
35. Nadelman RB, Nowakowski J, Fish D, et al. Prophylaxis with single-dose doxycycline for the prevention of Lyme disease after an *Ixodes scapularis* tick bite. N Engl J Med 2001;345:79–84.
36. Beaver PC, Jung RC, Cupp EW. Clinical Parasitology. 9th Ed. Philadelphia: Lea & Febiger, 1984.
37. Spach DH, Liles WC, Campbell RE. et al. Tick-borne diseases in the United States. N Engl J Med 1993;329:936–947.
38. Goddard J. Physican's guide to arthropods of medical importance. Boca Raton, Florida: CRC Press. 2000.
39. Vedenarayanam V, Sorey WH, Subramony SH. Tick paralysis. Semin Neurol 2004;24:181–184.
40. Taber SW. Fire ants. College Station, Tex: Texas A&M University Press, 2000.
41. Pei-Chi Shek L, Siew Pei Ngiam N, Lee BW. Ant allergy in Asia and Australia. Curr Opin Allergy Clin Immunol. 2004;4:325–328.
42. Stablein JJ, Lockey RF. Adverse reactions to ant stings. Clin Rev Allergy 1998;5:161–175.
43. Caplan EL, Ford JL, Young PF, et al. Fire ants represent an important risk for anaphylaxis among residents of endemic region. J Allergy Clin Immunol. 2003;111:1274–1277.
44. Diaz JD, Lockey RF, Stablein JJ, et al. Multiple stings by imported fire ants (*Solenopsis invicta*) without systemic effects. South Med J 1989;82:775–777.
45. de Shazo RD, Butcher BT, Banks WA. Reactions to the stings of the imported fire ant. N Engl J Med 1990;323:462–466.
46. Stafford CT, Hutto LS, Rhoades RB, et al. Imported fire ants as a health hazard. South Med J 1989;82:1515–1519.
47. Adamski DB. Assessment and treatment of allergic response to stinging insects. J Emerg Nurs 1990;16:77–80.
48. Candiotti KA, Lamas AM. Adverse neurological reactions to the sting of the imported fire ant. Int Arch Allergy Immunol 1993;102:417–420.
49. Tankersley MS, Walker RL, Butler WK, et al. Safety and efficacy of an imported fire ant rush immunotherapy protocol with and without prophylactic treatment. J Allergy Clin Immunol 2002;109:556–562.
50. Brown SG, Heddle RJ. Prevention of anaphylaxis with ant venom immunotherapy. Curr Opin Allergy Clin Immunol. 2003;3:6–11.
51. Wong RC, Hughes SE, Voorhees JJ. Spider bites. Arch Dermatol 1987;123:98.
52. Isbister GK, White J. Clinical consequences of spider bites: recent advances in our understanding. Toxicon 2004:43:477–492.
53. Clark RK, Wethern-Kestner S, Vance MV, et al. Clinical presentation and treatment of black widow spider envenomation: a review of 163 cases. Ann Emerg Med 1992;21:782–787.

54. Diaz JH. The global epidemiology, syndromic classification, management, and prevention of spider bites. Am J Trop Med Hyg 2004;71:239–250.
55. King LE, Rees RS. Treatment of brown recluse spider bites. J Am Acad Dermatol 1986;14:691–692.
56. DeLozier JB, Reaves L, King LE, et al. Brown recluse spider bites of the upper extremity. South Med J 1988;81:181–184.
57. Hebling A, Hurni T, Mueller UR, et al. Incidence of anaphylaxis with circulatory symptoms; a study over a 3-year period comprising 940,000 inhabitants of the Swiss Canton Bern. Clin Exp Allergy 2004;34:385–390.
58. Austen KF. Allergies, anaphylaxis, and systemic mastocytosis. In: Braunwald E, Fauci AS, Kasper DL, et al. Harrison's Principles of Internal Medicine. 15th ed. New York: McGraw-Hill. 2001;1913–1922.
59. Mosbech H. Anaphylaxis to insect venom. Novartis Found Symp 2004;257: 177–188.
60. Isbister GK, Volschenk ES, Seymour JE. Scorpion stings in Australia: five definite stings and a review. Intern Med J 2004;34:427–430.
61. de Roodt AR, Garcia SI, Salomon OD, et al. Epidemiological and clinical aspects of scorpionism by Tityus trivittatus in Argentina. Toxicon 2003;41:971–977.
62. Pardal PP, Castro LC, Jennings E, et al. [Epidemiological and clinical aspects of scorpion envenomation in the region of Santarem, Para, Brazil] Rev Soc Bras Med Trop 2003;36:349–353.
63. Bahloul M, Ben Hamida C, Chtourou K, et al. Evidence of myocardial ischaemia in severe scorpion envenomation. Myocardial perfusion scintigraphy study. Intensive Care Med 2004;30:461–467.
64. Alan S, Ulgen MS, Soker M, et al. Electrocardiologic and echocardiographic features of patients exposed to scorpion bite. Angiology 2004;55:79–84.
65. Ghalim N, El-Hafny B, Sebti F, et al. Scorpion envenomation and serotherapy in Morocco. Am J Trop Med Hyg 2000;62:277–283.
66. Bentur Y, Taitelman U, Aloufy A. Evaluation of scorpion stings: the poison center perspective. Vet Hum Toxicol 2003;45:108–111.

31

Mammal Bites

Antonio Durazo and James E. Lessenger

Key words: animal bites, wound care, tetanus prophylaxis, antibiotics, rabies prophylaxis

Around the world mammals are encountered in agriculture as:

1. Livestock
2. Working animals, used on farms for production
3. Pets of farm families
4. Wild animals

Livestock includes cattle, sheep, goats, pigs, hogs, horses, bison, and other animals that are raised, slaughtered, dressed, and processed for food or leather. In some parts of the world, dogs, cats, and other small animals are used as food. Horse, dog, and other meats are also used as pet foods. In Australia, kangaroos are raised for their meat and hides. In northern climates in the United States, Canada, Scandinavia, and Russia, furred animals such as minks are raised for their pelts. In northern Europe, reindeer are raised for meat and hides. In many animals, not only are the meat and hides useful, but the endocrine organs are used for medications, the hooves and horns are used for glue and ornaments, and the hair or fleece is used for padding or textiles.

Livestock are also raised for sale as working animals. Horses, mules, donkeys, and camels are examples of animals raised for this purpose. Surplus animals are often slaughtered for their meat or hides.

Working animals are used for transportation, hauling loads, or pulling machinery or plows. They include horses, mules, donkeys, and camels. Many of these animals are also bred for sale or for other uses such as racing and recreation. Dogs are used extensively as working animals, especially in the raising of sheep, goats, and other herd animals. Cats are used on farms for rodent control and pets.

Pets are used on farms for personal recreation. In addition, animals such as dogs, cats, hamsters, prairie dogs, rats, mice, and monkeys may be raised on farms for sale as pets.

Wild animals such as deer, elk, caribou, bison, and wild pigs are hunted commercially for their meat, horns, hooves or hides. In addition, wild animals may threaten workers on farms and ranches, many of which are located in wild parts of the world. In India, for example, tiger attacks are not uncommon. In the United States, mountain lions have again become a threat to western farmers. In some parts of Africa, lions, tigers, and other animals still attack herds and herders. In fisheries and in the harvest of seaweed and other ocean crops, dolphin bites are not unheard of (1–4).

Incidence of Animal Bites

The incidence of animal bites varies around the world (see Table 31.1). Bites tend to occur in the summer months because people are interacting with the animals or out in the countryside. Household pet bites in male children are the most common bites, followed by human bites as a consequence of altercations, bites by farm animals, and bites by wild animals. Most bites are caused by farm and pet dogs, followed by cats, horses, cows, and other farm animals. Rarer bites such as tiger, squirrel, and bat do occur. The extremities are the most common area bitten, followed by the head, neck, thorax, abdomen, and genitals (Table 31.1) (1–15).

Clinical Presentation

Wounds caused by animal bites include:

1. Punctures
2. Lacerations
3. Tears and rips of tissue
4. Avulsions and amputations of tissue and extremities
5. Crush injuries to deep tissues

Bites may be single or multiple and may affect any part of the body. Wounds may be contaminated with infectious agents from saliva and foreign bodies such as teeth or dirt. Deeper structures such as tendons, nerves, and muscle may be injured or inoculated with bacteria. Bone may be fractured, crushed, or inoculated with bacteria. The transfer of zoonotic infections is possible (1,16,17).

Management

After the patient has been stabilized, an airway is assured (if necessary), and treatment for shock (if needed) is implemented, a careful initial examination of the wound and the surrounding structures needs to be performed to define the extent of the bite and injury to adjacent tissues. In children and in exten-

TABLE 31.1. Worldwide variety in animal wounds.

Location	Body part	Adult or child	Animal(s)
Indiana, USA	Abdomen (fatal) Neck (fatal) Arm and shoulder	Children	Dog Cats Dog Pet tiger
Illinois and Missouri, USA	Hands, arms and legs	Children Males>females	Pet dogs
Philadelphia	Limbs	Children and adults	Rats
San Francisco	Human genitalia	Adults	Dogs Humans
USA	Spinal cord	Children	Pet tiger
Czech Republic	Thorax (26.6%) Head (23.3%) Limbs (17.7%) Neck (17.3%) Abdomen (14.3%)	Mostly children	Dogs Cats Farm animals
Germany	Mostly limbs	Children and adults	Dogs Cats Horses Other farm animals
Great Britain	Limbs	Children and adults	Dogs Humans Squirrels Farm animals
Switzerland	Limbs	Children (home) Adults (farm animals)	Dogs Cats Farm animals
Brazil	Limbs, head, neck	Male adults more than females or children	Vampire bats
Thailand	Legs and foot 64.2% Hands and fingers 21.2%	Most are children	Dogs
Iran	Hands, arms, legs	Children and adults	Dogs Cats Rats Farm animals Jackals Foxes Wolves
South Africa	Entire body	Adults	Lion Leopard Zebra Musk elephant

Source: Data from Demetriades (1), Isotalo et al. (2), Durrheim et al. (3), Zeynali et al. (4), Mitmoonpitak et al. (5), Sinclair et al. (6), Clark et al. (7), Steinbok et al. (8), Hanna et al. (9), Baranyiova et al. (10), Matter (11), Hirshhorn et al. (12), Wyatt (13), and Schneider et al. (14).

sive injuries, local or general anesthesia may be necessary before a complete examination of the wound can be performed. It is important to examine the entire body because multiple bites are common, especially from wild animals. Hemostasis must be assured and the immune status of the patient documented. Diabetes, immunological disorders, chronic wasting, and malnutrition can delay the healing process and predispose to severe infections. Wound cultures should be taken, if possible, to guide long-term antibiotic therapy. Once the airway has been assured and the patient treated for shock, attention needs to be paid to wound care, tetanus prophylaxis, infection control, and rabies prophylaxis (16,17).

Wound Care

Wounds require careful irrigation with saline and povine iodine and debridement to remove saliva, teeth, dirt, oils, and necrotic tissue. Primary closure is possible in areas where cosmetic results are important, where the wounds are not deep and extensive, and in patients without immune compromise. Otherwise, most authorities recommend that wounds be treated open with packing and bulky dressings. Most authorities also recommend delaying tendon and nerve repair until after the threat of infection has been resolved. Primary surgical repair is indicated to repair structures critical for survival. Reimplantation by hand and plastic surgeons of amputated extremities or avulsed tissue such as the lips and nose have been attempted with mixed success (16–20).

Hand injuries are of special importance because of their extensive nerve, tendon, and vascular structures and the compartments they create. Wounds must be carefully and aggressively irrigated and antibiotics given to prevent or mitigate infection. Care may eventually involve hand surgeons, if available (16–20).

Antibiotic Prophylaxis

Particularly in persons with immune compromise, bites with extensive damage, bites that have been primarily closed, reimplantations, and bites to the hands, antibiotic prophylaxis is helpful. In addition to the staphylococcal and streptococcal species that typically colonize wounds, animal bites are complicated by a wide range of rare bacteria, summarized in Table 31.2. Antibiotic susceptibility is summarized in Table 31.3 and antibiotics should be selected to cover both aerobes and anaerobes (21–27).

Tetanus Prophylaxis

Tetanus is a life-threatening neuromuscular disease caused by the contamination of wounds with *clostridium tetani*. Both tetanus toxoid (Td) (typically mixed with diphtheria toxoid [DT]) and tetanus immunoglobulin (TIG) are used in trauma. The trauma immunization schedule recommended by the United States Center for Disease Control is shown in Table 31.4.

TABLE 31.2. Bacteria found in bites by species.

Animal	Bacteria
Siberian tiger	*Pasteurella multocida*
	Bergeyella zoohelcum
Pet tiger	*Pasteurella meningitis*
Dog	*Veillonella parvula*
	Pasteurella multocida, canis, dagmatis, stomatis
	Staphylococcus aureus
	Staphylcoccus intermedius
	Alpha hemolytic streptococci
	Capnocytophaga canimorsus
	Anaerobic bacteria
	Pseudomonas fluorescens
	Prevotella heparinolytica
	Corybacterium spp.
	Bergeyella zoohelcum
	Bacteroides spp.
Cat	*Veillonella parvule*
	Pasteurella multocida
Human	*Veillonella parvule*
	Eikenella corrodens
	Human immunodeficiency virus
	Alpha-hemolytic streptococci
	Haemophilus species
	Anerobic bacteria
	Bacteroides spp.
Rats	*Staphylococcus epidermidis*
	Bacillus subtillus
	Diptheroids
	Hemolytic streptococcus
	Escherichia coli
	Streptococcus milleri

Source: Data from Goldstein (22), Armstrong et al. (23), Rayan et al. (24), and Brook (25).

Contraindications to immunizations in trauma include a documented history of a severe allergic reaction leading to acute respiratory distress, or collapse with a prior immunization. Side effects include local reactions with erythema and induration, exaggerated local reactions, and, uncommonly, fever and systemic reactions (21).

Rabies Prophylaxis

Rabies is a zoonotic viral disease that infects domestic and wild animals. It is transmitted to other animals and humans through saliva from infected animals such by means of bites, scratches, or licks on broken skin and mucous membranes. Once the symptoms of the disease develop, rabies is typically fatal to both animals and humans. There are fewer than five reports of people surviving rabies with intensive medical care (28–31).

TABLE 31.3. Antibiotics recommended for bite management.

	Primary recommendation	Alternatives
Outpatient	Amoxicillin and clavulate potassium 875/125mg PO bid or 500/125 mg PO tid	- Clindamycin 300mg PO qid plus Ciprofloxacin, 500mg bid - Clindamycin 300mg PO qid plus TMP-SMZ, 160 mgTMP/800mg SMZ bid - cefurlxime 500 mg PO bid - doxycycline 100 mg PO bid (cannot use in children or pregnant women)
Inpatient	Ampicillin sodium and sulbactam sodium, 3 g IV q6h	- Piperacillin sodium and tazobactam sodium, 3.375 g IV q6h - Ticarcillin and clavulanate potassium, 3.1 g IV q6h - Cefriaxone sodium, 2 g IV q24 h, plus clindamycin, 600 to 900 mg IV q8h - Ciprofloxacin, 200-400 mg IV q12h, plus clindamycin, 600 to 900 mg IV q8h - TMP-SMZ, 8-10 mg/kg IV qd, divided, q6 to 12h, plus clindamycin, 600 to 900 mg IV q8h

Source: Data from Goldstein (22), Armstrong (23), Rayan et al. (24), Brook (25), and Medeiros (27).
Note: TMP-SMZ is trimethoprim-sulfamethoxazole. Fluroquinolones are not approved for children younger than 16 years.

TABLE 31.4. Indications for tetanus prophylaxis in wound management (Td: tetanus toxoid, TIG: tetanus immune globulin).

Number of previous tetanus vaccinations	Clean, minor wounds		All other wounds*	
	Give Td[†]	Give TIG	Give Td	Give TIG
Unknown, uncertain, or fewer than 3	Yes	No	Yes	Yes
3 or more[‡]	No[§]	No	No[‖]	No

*Such as, but not limited to: wounds contaminated with dirt, feces, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.
[†]For children ≤7 years of age DTaP or DTP (DT if pertussis vaccine is contraindicated) is preferred to tetanus toxoid alone. For persons ≥ 7 years of age, Td (tetanus-diphtheria toxoid for adult use) is preferred to tetanus toxoid alone.
[‡]If only 3 doses of fluid toxoid have been received, then a fourth dose of toxoid, preferably an adsorbed toxoid, should be given.
[§]Administer a booster if more than 10 years have elapsed since the last dose.
[‖]Administer a booster if more than 5 years have elapsed since the last dose. (More frequent boosters are not needed and can accentuate side effects.)
Source: Adapted from: Diphtheria, tetanus, and pertussis: recommendations for vaccine use and other preventive measures. *MMWR* 1991;40(No. RR-10):1-28 (21).

The first symptoms of rabies are usually non-specific, involving the respiratory, gastrointestinal, or central nervous system. In the acute stage, signs of hyperactivity (furious rabies) or paralysis (dumb rabies) predominate. In both furious and dumb rabies, paralysis eventually progresses to complete paralysis followed by coma and death due to respiratory failure. Without intensive treatment, death is within 7 days (28–31).

Worldwide incidence data are unreliable, but estimates range from 40,000 to 70,000 cases a year, mostly in Africa and Asia where rabies is endemic. It was thought that rabies had been eliminated from Europe, but recent cases found in animals have raised concern. In North America and Australia, bat rabies has emerged as an epidemiologic reservoir. Dramatic cases have been reported in China, Thailand, Sri Lanka, and Latin America where dogs remain the most common reservoir (with the exception of the Amazon region of Brazil where vampire bats have emerged as an important source). Humans are most frequently infected through bites of infected dogs, cats, wild foxes, raccoons, skunks, jackals, wolves, and bats. Recently, a rabies virus variant has been associated with the silver-haired (*Lasionycteris noctivagans*) and eastern pipistrelle *(Pipistrellus subflavus)* bats in North America. In Europe, North America, Japan, and other countries of low rabies incidence, a call to the health department may reveal which local animal species are currently at risk (28–31).

Post-exposure Prophylaxis

If the species is unlikely to be infected with rabies, treatment may be deferred pending the outcome of a laboratory diagnosis, provided that no more than 48 hours transpires before the results are available. The WHO has given recommendations and separated the risks into categories (see Table 31.5). If a biting dog is more than a year old and has a vaccination certificate indicating that it has received at least 2 doses of a potent vaccine, the first not earlier than 3 months of age and another within 6 to 12 months, the bitten patient may not need treatment and the dog should be observed for 10 days. If the dog shows any signs of illness, the patient should receive prophylaxis (30–31).

Vaccines and rabies immunoglobulin are available around the world for intrawound, intramuscular and intradermal administration. They include:

Human diploid cell vaccine (HDCV) (preferred)
Purified vero cell vaccine (PVRV)
Purified chick embryo vaccine (PCEV)
Purified duck embryo vaccine (PDEV)
Human rabies immunoglobulin (HRIG)
Equine rabies immunoglobulin (ERIG)

Before administrating any vaccine, the physician should carefully read the product insert or local health department information as vaccines and dosage regimens vary around the world. The intradermal route is more effective than

TABLE 31.5. WHO risk categories for rabies prophylaxis.

Category	Exposure history	Action
I	Touching or feeding of animals Licks on intact skin	No prophylaxis
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding Licks on broken skin	Administer vaccine
III	Single or multiple transdermal bites or scratches Contamination of mucous membrane with saliva (licks)	Rabies immunoglobulin Vaccine

Source: Data from World Health Organization (31).

intramuscular. Pregnancy and infancy are never contraindications to post-exposure rabies vaccination. In high risk bites and endemic areas, initiation of treatment should never await the results of a laboratory diagnosis. The vaccination schedule recommended by the World Health Organization is given in Table 31.6 (30,31).

People who have been previously vaccinated for rabies as a preventative measure or have had the series before must still receive a post-exposure vaccination, but not RIG. One dose is given at 0 and 3 days. Full treatment should be given to persons who received pre- or post-exposure treatment with vaccines of unproven potency and those who have not demonstrated acceptable rabies neutralizing antibody titer (30,31).

TABLE 31.6. Rabies vaccination schedule.

The intramuscular schedule for modern tissue-culture and duck embryo vaccines is:
Essen regimen: one dose of the vaccine administered on days 0, 3, 7, 14, and 28, given in the deltoid in adults or the anteriolateral thigh in children.
Alternative: 2 doses are given on day 0, followed by one dose on day 7 and day 21.
The intradermal schedule for modern vaccines is:

1. 2-site intraadermal method (PVRV and PDEV)
   Days 0, 3, 7: 1 intradermal dose of vaccine is given at each of 2 sites.
   Days 28 and 90: 1 dose given in one site.
2. 8-site intradermal method (HDCV and PCEC)
   Day 0: 0.1 ml of vaccine given at each of 8 sites using the contents of the whole vial.
   Day 7: 0.1ml given at 4 sites over deltoids and thighs.
   Day 28 and 90: vaccine given at one site in deltoid (30,31).

The method of administration of rabies immunoglobulin (RIG) is as follows:
Dose: 20 iu/kg body weight of HRIG
Or 40 iu/kg of ERIF
Infiltrate the wounds using sterile saline to dilute it 2- to 3-fold. Any remainder should be injected in the anterior thigh. A skin test may be performed, but a negative result does not assure lack of an immune reaction.

Source: Data from World Health Organization (31).

References

1. Demetriades D. Human and animal bites. S Afr J Surg 1989;27:185–7.
2. Isotalo PA, Edgar D, Toye B. Polymicrobial tenosynovitis with *Pasteurella multocida* and other Gram negative bacilli after a Siberian tiger bite. J Clin pathol 2000;53:871–2.
3. Durrheim DN, Leggat PA. Risk to tourists posed by wild mammals in South Africa. J Travel Med 1999;6:172–9.
4. Zeynali M, Fayaz A, Nadim A. Animal bites and rabies: Situation in Iran. Arch Int Med 1999;2:23–7.
5. Mitmoonpitak C, Tepsumethanon V, Raksaket S, Nayuthaya AB, Wilde H. Dog-bite injuries at the Animal Bite Clinic of the Thai Red Cross Society in Bangkok. J Med Assoc Thai 2000;83:1458–62.
6. Sinclair CL, Shou C. Descriptive epidemiology of animal bites in Indiana, 1990–92: A rationale for intervention. Public health Rep 1995;110:64–7.
7. Clark MA, Sundusky GE, Hawley DA, Pless JE, Fardal PM, Tate LR. Fatal and near-fatal animal bite injuries. J Forensic Sci 1991;36:1256–61.
8. Steinbok P, Flodmark O, Scheifele DW. Animal bites causing central nervous system injury in children: A report of three cases. Pediatr Neurosci 1985–86;12:96–100.
9. Hanna TL, Selby LA. Characteristics of the human and pet populations in animal bite incidents recorded at two Air Force bases. Public Health Rep 1981;96:580–4.
10. Baranyiova E, Holub A, Martinikova M, Necas A, Zatloukal J. Epidemiology of intraspecies bite wounds in dogs in the Czech Republic. Acta Vet Brno 2003;72: 55–62.
11. Matter HC. The epidemiology of bite and scratch injuries by vertebrate animals in Switzerland. Eur J Epidemiol 1998;14:483–90.
12. Hirshhorn RB, Hodge RR. Identification of risk factors in rat bite incidents involving humans. Pediatrics 1999;104:35–42.
13. Wyatt JP. Squirrel bites. BMJ 1994;309:1964.
14. Schneider MC, Santos-Burgoa C, Aron J, Munoz B, Ruis-Velazco S, Uieda W. Potential force of infection of human rabies transmitted by vampire bats in the Amazonian region of Brazil. Am J Trop Med Hyg 1996;55:680–4.
15. Wolf JS, Turzan C, Cattolica EV, McAnich JW. Dog bites to the male genitalia: Characteristics, management and comparison with human bites. J Urol 1993;149:286–9.
16. Wiley JF. Mammalian bites. Review and evaluation and management. Clin Pediatr (Phila) 1990;29:283–7.
17. Goldstein EJ. Management of human and animal bite wounds. J Am Acad Dermatol 1989;21:1275–9.
18. Brook I. Human and animal bite infections. J Fam Pract 1989;28:713–8.
19. Galloway RE. Mammalian bites. J Emerg Med 1988;6:325–31.
20. Hawkins J, Paris PM, Stewart RD. Mammalian bites: Rational approach to management. Postgrad Med 1983;73:52–64.
21. Center for disease control and prevention. Diphtheria, tetanus, and pertussis: Recommendations for vaccine use and other preventive measures. *MMWR* 1991;40(No. RR-10):1–28.
22. Goldstein EJ. Bite wounds and infection. Clin Infect Dis 1992;14:633–8.
23. Armstrong GR, Sen RA, Wilkinson J. *Pasteurella multocida* meningitis in an adult: Case report. J Clin pathol 2000;53:234–5.

24. Rayan GM, Downard D, Cahill S, Flournoy DJ. A comparison of human and animal mouth flora. JK Okla State Med Assoc 1991;84:510–5.
25. Brook I. Microbiology of human and animal bite wounds in children. Pediatr Infect Dis J 1987;6:29–32.
26. Krause M. Dog, cat and human bites. Schweiz Rundsch Med Prax 1998;87:716–8.
27. Medeiros I. Saconato H. Antibiotic prophylaxis for mammalian bites. Cochrane Database Syst Rev 2001;2:CD001738.
28. Hanlon CA, Smith JS, Anderson GR. Recommendations of a national working group on prevention and control of rabies in the United States. Article II: Laboratory diagnosis of rabies. JAVMA 1999;215:1444–7.
29. Hanlon CA, Childs JE, Nettles VF. Recommendations of a national working group on prevention and control of rabies in the United States. Article II: Rabies in wildlife. JAVMA 1999:215:1612–9.
30. Center for Disease Control and Prevention. Human Rabies Prevention: United States, 1999. MMWR 1999;48:1–23 (RR-1).
31. World Health Organization. WHO recommendations on rabies post-exposure treatment and the correct technique of intradermal immunization against rabies. Technical report series 824. Geneva: World Health Organization, 1992.

32

Reptile Bites

A. Nelson Avery

Key words: reptile bites, snakebite, rattlesnakes, copperhead snakes, coral snakes, exotic snakes, antivenin, agriculture

Reptiles are poikilothermic (cold blooded), and to warm themselves they lie in direct sunlight or absorb radiant heat from warm surfaces. For that reason, most reptile species are found between latitudes of 40˚N and 40˚S (1).

While reptiles can transmit various pathogens and toxins via bite wounds and cause trauma and pain by biting, the most common diseases in humans related to reptiles and amphibians are due to transmission of various species of Salmonella. As an example, an outbreak of *Salmonella enterica* occurred among visitors to a Colorado zoo reptile exhibit in 1996 that was associated with touching a wooden barrier around a Komodo dragon exhibit (1–3).

Reptiles are in the class Reptilia, which includes four orders: Squamata (snakes and lizards), Crocodylia (crocodiles, alligators, caimans, and gavials), Testudinata (tortoises and turtles), and Rhynchocephalia (tuatara). Depending on the classification scheme, there are 4 to 5 families of venomous snakes in the world: Viperidae, Elapidae, Colubridae, Atractaspididae (sometimes included with Columbridae), and Hydrophiidae (Table 32.1) (1,4–6).

Of the estimated 3,000 species of snakes in the world, there are only about 375 known species of venomous snakes, and even fewer that are capable of causing significant envenomation. There may be as many as 3 million snake bites annually worldwide, with estimates of death ranging from 30,000 to 150,000 (4,6–12).

Foreign Agricultural Data about Snakebites

Snakebite is mainly a rural and occupational hazard. The highest incidence of snakebite is in South America, West Africa, the Indian subcontinent, and Southeast Asia. In Mexico, they report 27,000 rattlesnake bites annually and 100 fatalities; the majority of patients are adults who work in agriculture or with cattle. In India with a large agricultural population there have been over

TABLE 32.1. Classification of venomous snakes in the world.

Classification						Examples
Class Reptilia	order Squamata (snakes and lizards)	suborder Serpentes (snakes)	Viperidae	Crotalidae (pit vipers)	*Crotalus*	rattlesnakes
					Agkistrodon	copperheads water moccasins (cottonmouths)
					Sistrurus	pigmy rattlesnakes massasaugas
				Viperinae		true vipers, adders
			Elapidae			coral snakes cobras, kraits, mambas, terrestrial Australian venomous snakes
			Colubridae			mangrove snake whip snake
			Atractaspididae			burrowing asps stiletto snakes
			Hydrophiidae			sea snakes

Source: Data from Davison, Schafer and Jones (4), Warrell (5), and White (6).

20,000 reported snakebite deaths annually for the last 100 years. Among Philippino rice farmers, cobra bites mostly afflict young males, with a death rate of 107 per 100,000 residents in one study. In parts of the Benue Valley in northeastern Nigeria, the incidence rate of bites is almost 500/100,000 annually with a mortality rate of more than 10%. In contrast, as Costa Rica transformed its rainforest into agricultural fields over four decades, its rate of snakebite deaths fell from 4.83 to 0.2/100,000 (5,13–15).

In tropical developing countries, snakebite is usually an occupational injury inflicted on the feet and ankles of agricultural workers, herders, and hunters who inadvertently step on a snake. It occurs most commonly during the summer in open fields, threshing yards, barns, irrigation channels and storage sheds. With night work, there is also risk from walking by thick grass or undergrowth. Special footwear that can deflect snakebites should be worn in high risk locations. In contrast to other agricultural areas, farmers in the Sucua canton of Ecuador had 72% of bites on upper extremities, due to their primitive farming technique of kneeling to plant or harvest (5,16–18).

United States Snakebite Data

American farmers are at high risk from animal-associated injuries. Surveys by the National Safety Council found animals accounting for 17% of all nonfatal farm injuries, second only to agricultural machinery. In an epidemiology study from 1979 to 1990, animals were responsible for 3.6% of all farm deaths, and there were 66 deaths from snakebites, accounting for 3.5% of all animal-related deaths (19,20).

About 45,000 snakebites are reported in the United States annually, with approximately 8,000 venomous bites, but only about 6 to 15 persons die each year. There were only two snakebite fatalities reported to poison control centers in 2002 (Table 32.2), and both were related to rattlesnake bites.

TABLE 32.2. Statistics on snakebites in United States, based on 2002 annual report of the AAPCC toxic exposure surveillance system.

Type of snake	No. of bites	% of venomous bites
Rattlesnake	1150	47%
Copperhead	889	36
Cottonmouth	173	7
Crotaline: unknown	25	1
Coral	88	4
Exotic snake–poisonous	125	5
Total venomous snakebites	2450	100%
Exotic (non-poisonous)	155	
Exotic (unknown if poisonous)	7	
Nonpoisonous	1976	
Unknown snake	2145	
Total snakebites reported	6733	

Source: Data from Watson WA et al. (29).

Crotalidae accounted for 91% of the reported venomous bites (4,9,10,20–29).

Herpetologists define an exotic snake as one out of its normal geographic range. Emergency physicians may have difficulty with an exotic snakebite because of erroneous reporting by the illicit collector, limited knowledge of the clinical presentation of the envenomation, and lack of locally available antivenin. Most estimates of poisonous snakebites by exotic nonnative species are in the 3% to 5% range (8,29,30).

The highest snakebite rates are found in southern states. Most bites occur from April to October. The optimal temperature range for snakes is 27°C to 32°C (80°C to 90°F), which occurs at night in the southwestern desert and in the evening in southern states. Snakebites are most common in young men who have purposely handled a venomous snake and often have consumed alcohol prior to the encounter. Of intentional exposures 35% occurred in an occupational setting such as professional snake handling and snake hunts (11,24,25,27,28).

Classification and Identification of Snakes and Characteristics of Bites

Crotalids: Rattlesnakes, Copperheads, Cottonmouths

In the United States, most venomous snakes are members of the subfamily Crotalidae, the pit vipers. The three main genera in this family are *Crotalus* (rattlesnakes), *Agkistrodon* (copperheads and cottonmouths), and *Sistrurus* (pigmy rattler and massasauga) (4,31,32).

Crotalids are called pit vipers because of depression or pit located midway between and below level of eye and nostril on each side of head. They sense

heat, which helps them detect prey. They are deaf and have poor vision but perceive vibration and odors. Other distinguishing characteristics of pit vipers include vertical elliptical pupils (also seen in a few non-venomous snakes), a single row of subcaudal scales, and a triangular head. Crotalids and viperids can be distinguished from non-venomous snakes by their two elongated, canaliculated, upper maxillary teeth, which can be folded against the roof of the mouth (4,26,27).

The rattlesnake's most distinguishing characteristic is the rattle at the end of the tail. The rattle is composed of loosely articulated, interlocking, keratinous rings that vibrate as a defensive warning, creating a distinctive buzzing sound. Copperheads have triangular orange to rust-colored heads, and cottonmouths, also known as "water moccasins," have a distinctive white mouth (4,27).

Crotalids have a well developed mechanism for erecting the fangs and introducing the venom into their prey. The muscles of the jaw cause ejection of the venom through the hollow penetrating fangs, and they can control the amount of venom ejected. About 25% to 75% of stored venom is discharged following a rattlesnake bite, and the entire supply is replenished in 3 to 4 weeks. The striking range is usually equivalent to half the length of the snake. The speed of the strike is approximately 8 feet per second. Crotaline (pit viper) venom is usually injected only into the subcutaneous tissue, although deeper, intramuscular (subfascial) envenomation may rarely occur. So-called "dry bites" may occur in about 20% of strikes for crotalids and 40% to 50% for elapids. Individuals may be envenomated by rattlesnakes thought to be dead, even up to 60 minutes after decapitation. A fatally injured rattlesnake may still produce serious or even multiple envenomations (4,9,26,27,32–34).

Elapids: Coral Snakes

There are two genera of coral snakes—*Micruroides* (the Sonoran coral snake found in Arizona, *Micruroides euryxanthus*) and *Micrurus* (two subspecies: the eastern coral snake, *Micrurus fulvius fulvius*, and the Texas coral snake, *Micrurus fulvius tenere*) (33).

Coral snake fangs are short, upper anterior maxillary teeth, fixed in an erect position. They also have rounded pupils and subcaudal scales in a double row. The body is small and slender with a bright three-color pattern of red, black, and white or yellow, which encircle the body without interruption. The head is small and rounded and has a black snout without facial pits (9,26,27).

The coral snake must rely on a chewing action to instill its venom. It is generally accepted that the snake must maintain its bite hold on its victim for some prolonged period of time in order to administer a significant amount of venom. Kitchens reported that in 85% of cases in their series, the snake had to be actively removed (33,35).

Pharmacology and Pathophysiology of Venom

This chapter is not intended to discuss, in detail, the properties of snake venoms; the reader is referred elsewhere for a thorough review. Snake venoms have greater biochemical complexity than any other toxin of animal origin and are probably the most highly concentrated secretion products found in vertebrates (7,12).

Crotaline venom is a complex heterogeneous solution and suspension of 30 to 40 different proteins, peptides, lipids, carbohydrates, and enzymes. Snake venoms can cause multiple clinical effects, including local tissue injury, edema, paralysis, muscle breakdown, and coagulopathy (Table 32.3) (6,7,23,27,36).

In coral snake venom, polypeptide neurotoxins predominate, with curare-like effects. They cause respiratory paralysis by interfering with nicotinic cholinergic neuromuscular receptors. The venom is not associated with hemostatic problems. Coral snake venom is rapidly absorbed via the venous system as opposed to the lymphatic system (12,23,33).

Clinical Presentation

Prognosis and Grading Severity of Envenomation

The symptoms, signs, and prognosis of envenomation are dependent on a number of factors, including species and size of the snake, nature of the bite (location, number of bites, character of clothing between fangs and skin,

TABLE 32.3. Snake venom properties.

Local tissue damage (necrotoxins)	Proteases and small peptides damage the epithelial cells and basement membranes of capillaries, altering blood vessel permeability, which leads to loss of blood and plasma into tissues, which causes edema, shock from fluid shifts
Coagulation defects (hemotoxins)	Capillary damage and DIC-like state lead to decreased platelets and fibrinogen, hemorrhage, and sometimes shock; not seen with elapid venom
Hemolysis	Phospholipases induce red cells to swell, causing hemolytic anemia, hemoglobinuria
Neurotoxins	Major components in Mojave rattlesnake and elapid venom, can cause flaccid paralysis of skeletal muscle by blocking transmission at the neuromuscular junction, lead to death by respiratory paralysis
Myotoxins	Can result in massive skeletal muscle breakdown, myoglobinuria, potential renal failure
Nephrotoxins	Cause primary and secondary damage to kidneys

Source: Data from White (6), Iyaniwura (7), Kitchens (23), Wingert (27), and Iyaniwura (36).

TABLE 32.4. Grade of envenomation.

Severity	Type of signs or symptoms
Grade 0 (no envenomation)	■ fang marks, minimal pain and erythema but no local swelling or hemorrhage ■ no systemic symptoms; normal coagulation and no bleeding
Grade I (minimal)	■ fang marks with swelling (1-5 inches), moderate pain, and ecchymosis ■ no systemic symptoms; normal coagulation and no bleeding
Grade II (moderate)	■ swelling (6-12 inches), pain and ecchymosis progressing rapidly beyond the site of the bite (such as elbow or knee) ■ decreased fibrinogen and/or platelets, but without clinical bleeding (may have minor hematuria, nosebleed) ■ nausea, vomiting, oral paresthesias, unusual tastes, weakness, mild hypotension, mild tachycardia
Grade III (severe)	■ swelling (>12 inches), pain and ecchymosis involving more than an entire extremity or threatening the airway ■ abnormal coagulation measures with hemorrhage ■ altered mental status, falling blood pressure, severe tachycardia, tachypnea, or respiratory insufficiency ■ seen with bite by a large or highly toxic snake (e.g., *C. atrox*), or multiple bites
Grade IV (very severe)	■ seen with bite of large rattlesnakes (eastern and western diamondback rattlers, timber rattler) ■ sudden pain and rapid local swelling that spreads proximally and may involve the ipsilateral trunk; ecchymoses follow rapidly; bleb formation with spontaneous rupture; areas of necrosis ■ rapid onset of weakness, vertigo, numbness, fasciculation, painful muscular cramping, and tingling about the face (particularly lips); shock may be apparent within a few minutes; nausea and vomiting often appear in the first 10 to 15 minutes; may lead to kidney shutdown, hepatic and cardiovascular damage; coma and death can occur within 30 minutes.

Source: Data from Kunkel et al. (9), Dart et al. (22), Parrish (25), Wingert (27,28), McCollough (32), Lawrence et al. (37), and Scharman and Noffsinger (38).

amount of venom injected), victim's age, size and sensitivity to venom, and subsequent medical care (26,27,32).

There is a fairly uniform system of grading envenomation that has evolved over the past 4 decades. It ranges from no envenomation to very severe, based on such factors as spread of edema, systemic signs (nausea, vomiting, hypotension, tachycardia), and coagulation status (Table 32.4) (9,22,25,27,28,32,37,38).

Crotalid Envenomation

A typical pit viper case involves an individual bitten on the dorsum of the hand or foot. The fangs penetrate the skin leaving visible marks, and venom is injected into the skin or subcutaneous tissue. Within minutes, proteolytic

enzymes cause pain and swelling. Edema is usually seen around the injured area within 5 to 30 minutes after the bite but may be delayed for several hours. It progresses rapidly and may involve the entire injured extremity within an hour. Generally, however, edema spreads more slowly, usually over a period of 8 to 36 hours, as a result of lymphatic drainage of the venom. The swelling is most severe after bites of the eastern diamondback rattlesnakes; least severe after bites by the Mojave rattlesnake, copperheads, massasaugas, and pigmy rattlesnakes. Antivenin often stops the progression of swelling but may not reverse it (4,26–28).

Crotalid envenomations also cause sweating and chills, paresthesias, faintness, weakness, muscle fasciculations, nausea, and coagulopathies. The diagnosis of intravascular envenomation is based on the extremely rapid onset of severe manifestations, a phenomenon rarely seen with North American rattlesnake dermal or subcutaneous envenomations (9,26,27,39,40).

The cause of death in humans is associated with destruction of the epithelial lining of blood vessels and of erythrocytes, especially in the pulmonary system. Hypovolemic shock and pulmonary edema appear to cause most fatalities. Curry described a death case that was complicated by disseminated intravascular coagulation, adult respiratory distress syndrome, renal failure, left ventricular dysfunction, and many other problems, 15 days after rattlesnake envenomation. This demonstrated the wide range of pathology that can follow a rattlesnake bite (21,27).

Hematologic Changes with Crotalid Envenomation

Blood in the local tissues is anticoagulated. Ecchymosis and discoloration of the skin often appear in the area of the bite within several hours. Vesiculations may be found within three hours. Hemorrhagic vesiculations and petechiae are common, and thrombosis may occur in superficial vessels. Necrosis develops in many untreated victims. Subcutaneous hemorrhage has been reproduced in mice with injection of venom damaging capillaries by a direct lysis of endothelial cells, which resulted in hemorrhage by rhexis (rupture of vessel) (26,41).

The proteolytic activity of some enzymes can activate the coagulation or fibrinolytic system. The Eastern diamondback rattlesnake can cause nearly total defibrination (with relative sparing of platelets), yet the patient rarely bleeds. Envenomation by the Southern Pacific rattlesnake (*C. viridis helleri*) is associated with rapid, severe thrombocytopenia with little evidence for fibrinogenolysis (23).

Laboratory evaluation after envenomation reveals hemoconcentration, coagulation abnormalities, with thrombocytopenia followed by decreased fibrinogen, increased fibrin split products from fibrinolysis, prolonged prothrombin time and partial thromboplastin time (4,42).

The mechanism of venom-induced thrombocytopenia is unclear, but is thought mainly to be secondary to the action of phospholipases contained in

the venom that damage platelet membranes and trigger platelet destruction. Prompt antivenin administration is usually followed by a sustained rise in platelet counts. Thrombocytopenia can be recurrent in a crotaline envenomation and can be resistant to antivenom therapy (43–46).

Neurotoxic Changes with Crotalid Envenomation

Fasciculations and paresthesias are frequent seen with rattlesnake envenomation, with respective occurrences of 33% and 63%. A common complaint following bites by the Southern Pacific rattlesnake (*C. viridis helleri*), and sometimes reported after other pit viper biters, is tingling or numbness over the tongue and mouth or scalp, fingers and toes, and around the wound. Two syndromes of neurotoxicity following rattlesnake envenomation have been described. Myokymia, or muscle fasciculations, may occur following envenomation by various species of rattlesnakes, including Southern Pacific rattlesnakes, western diamondback rattlesnakes (*C. atrox*), and timber rattlesnakes (*C. horridus horridus*) (26,47,48).

Another type of neurotoxicity, described following envenomation by certain populations of Mojave rattlesnakes (*C. scutulatus scutulatus*), may manifest with generalized weakness, cranial nerve palsies, and respiratory paralysis. Venom of the Mojave rattlesnake, unlike the venom of other rattlesnakes, does not usually produce a significant coagulopathy. It also produces far less tissue destruction than most other rattlesnake venoms (26,48,49).

Mojave venom A is found in snakes inhabiting California, Utah, and southwestern Arizona. It contains Mojave toxin, which can produce a systemic neurotoxic syndrome with lethargy, obtundation, neuromuscular weakness, cranial nerve dysfunction, and respiratory paralysis in the absence of local symptoms. Mojave toxin acts presynaptically, inhibiting the frequency of miniature endplate potentials and indirectly evoked muscle contraction without affecting muscle responses to direct stimulation or to acetylcholine (50–52).

Mojave rattlesnakes not expressing Mojave toxin (type B snakes, generally located in the area between Tucson and Phoenix) are characterized by hemorrhagic and proteolytic venom peptides that type A snakes lack, and they cause local tissue findings similar to those of other North American crotalids. Mojave toxin has also been isolated in venom of western diamondback rattlesnakes and prairie rattlesnakes (51,53).

Allergic Reactions to Snakebite Venom

Acute anaphylactic and anaphylactoid reactions have been previously reported following snake envenomations. The majority of these cases involved a minimum of at least two previous envenomations. However, anaphylactoid reaction can occur after first time envenomation without the patient having a previous exposure. Anaphylaxis can also occur from

immunogenicity across rattlesnake species. Patients with anaphylactic reactions should be warned of possible life-threatening reactions with further exposure to snake venom (54–56).

Extremity Problems: Compartment Syndromes and Long-term Complications

Most rattlesnake envenomations occur to the extremities and can result in large amount of swelling and discoloration along with the development of blebs and/or tissue necrosis. Despite the swelling and discoloration, increased compartmental or subcutaneous pressures usually do not play an important role in the development of myonecrosis or functional disabilities. Increased tissue pressures are not severe enough to cause ischemia of envenomated extremities in most patients bitten by rattlesnakes. Early surgical intervention is not recommended in patients who demonstrated only decreased skin temperatures (57).

Diamondback rattlesnake bites to the upper extremity consistently result in severe envenomations. Cowan looked at the long-term complications of snake bites to the upper extremity and found that 4 of 46 patients had continued pain and tissue atrophy at the bite site (58).

Copperhead Envenomation

Envenomation by copperheads usually gives rise to fewer systemic clinical manifestations than that of other North American pit vipers. The most clinically significant local effect is pain. Other local findings include swelling, fang marks, ecchymosis, and erythema. In a retrospective study on clinical severity of local effects in copperhead envenomation, clinically significant local effects (pain requiring parental analgesics, ecchymosis, swelling over one half of the bitten extremity) occurred in one third of the patients. Envenomation by either the cottonmouth or the copperhead is usually not characterized by gross hemostatic abnormalities (23,28,59,60).

In a series of crotalid bites, with the majority by copperheads, there were no deaths or amputations. However, there can be considerable long-term subjective morbidity from copperhead envenomation, including limb dysfunction with recurrent pain and edema (60–62).

Coral Snake Envenomation

Coral snake bites appear as teeth marks that ooze blood. Unlike pit viper venoms, coral snake venom lacks significant proteolytic enzymatic function, so there are few local signs and symptoms following envenomation. Systemic

signs and symptoms are often delayed in onset. Coral snake envenomation is not associated with hemostatic problems (23,27,33,35).

Coral snake (elapid) envenomation usually progresses along a neurotoxic course, with occasional early numbness or weakness of the bitten extremity. It can cause tremors, drowsiness, or euphoria, and marked salivation within four hours. After 5 to 10 hours, cranial nerve involvement leads to slurred speech, diplopia, fixed contracted pupils, ptosis, and dysphagia. Curare-like effect of venom can cause total paralysis and death in untreated patients. The major cause of death is respiratory paralysis (9,26,27,33,35).

Exotic Snakes

Emergency physicians face an increased likelihood of treating exotic envenomation due to private collections. The clinical presentation of a victim envenomated by a cobra or other elapid that causes neurotoxicity is the development of cranial nerve palsies manifested by ptosis, ophthalmoplegia with blurred vision or diplopia, dysphagia with increased secretions, dysarthria, and facial muscle weakness. This can be followed by drowsiness and confusion, flaccid paralysis, coma, and respiratory paralysis. Cholinesterase inhibitors such as neostigmine are effective in temporarily reversing neurotoxicity in some Asiatic species of *Naja* (63).

Management of Snakebites

Death from snakebite in the United States is rare, currently estimated to be approximately 1% or less of cases. Antivenin is the specific and most important therapeutic measure responsible for the decrease in fatalities from snakebites (27,62).

Management in the Field

It is important to try to identify the snake if it is available but not to try to capture the snake at risk of being bitten again. Patients can be shown pictures of snakes later. It is important to transfer the bite victim to a medical facility as rapidly as possible. The patient should lie down and remove constricting clothing and jewelry. Tourniquets, incision, and suction are best avoided.

Tokish concluded that field management is largely ineffective and may be detrimental to the outcome of the envenomated patient. Helicopter transport services are overused and should be reserved for patients whose current (not anticipated) clinical condition requires the immediate administration of antivenin or ICU support (64).

Management in the Emergency Department

Wingert suggested a multi-step guideline for treatment of snakebite envenomation, beginning with establishing a physiologic baseline. This includes rapid evaluation of signs and symptoms and obtaining laboratory tests (CBC and platelet count, INR and PTT, fibrin split products, fibrinogen, CPK, urine dipstick for occult blood, electrolytes, BUN and creatinine, and type and cross for possible transfusion) (27).

Next, determine the severity of the envenomation (Table 32.4). An unremarkable physical and laboratory exam at presentation does not reliably indicate an insignificant envenomation. It is recommended that physicians observe patients with a history of crotalid snakebite for at least 6 to 8 hours and for Mojave rattlesnake (*C. scutulatus*) or an elapid bite monitor for 12 to 24 hours, before the bite is termed non-envenomated (9,65).

Intravenous lines are started to infuse fluids and antivenin if necessary (see below). Do not start IV in affected extremity. Treat bleeding complications first with antivenin, then with fresh frozen plasma and blood. Treat hypotension with crystalloid fluids and rhabdomyolysis with fluids and sodium bicarbonate. Monitor oximetry and arterial blood gases as necessary. Treat pain, but avoid potent narcotics because of possible respiratory depression. Give tetanus toxoid or human immune tetanus globulin if immunization status is questionable.

Monitor local swelling at 20 to 60 minute intervals with measurements of limb circumference at the point of edema and assessment of circulation, and repeat laboratory tests. Splint the extremity in a position of function. Clean the wound and debride if necessary. Prophylactic antibiotics are not indicated in patients with rattlesnake bites (66).

Antivenin Therapy for Rattlesnake and Cottonmouth Envenomation

The previously available antivenin, derived from horse serum product, was antivenin (Crotalidae) polyvalent (ACP). Acute reactions occurred in 20% to 25% of patients, and serum sickness in 50% to 75% of patients treated with the equine product (22).

In December 2000, Crotalidae polyvalent immune Fab (ovine) (CroFab ®; FabAV) became commercially available in the United States. FabAV is derived from sheep hyperimmunized against *Crotalus atrox (western diamondback)*, *C. adamanteus (eastern diamondback)*, *C. scutulatus (Mojave rattlesnake)*, and *Agkistrodon piscivorus (cottonmouth)*. Similar to digoxin Fab, these antibodies are treated with papain to cleave off the Fc portions of the molecule. The possibility of hypersensitivity reactions still exists, but these reactions may be easily treated and additional Fab antivenom products can

be safely given along with histamine receptor blockers and epinephrine as needed (67,68).

FabAV was shown in the clinical studies to be effective when given within 6 hours of snakebite, but recently, FabAV has been shown to be effective starting at 52 hours after envenomation from a rattlesnake (*C. concolor*). The recommended initial dose is 4 to 6 vials. The patient should be observed for up to 1 hour following the completion of this first dose to determine if initial control has been achieved (complete arrest of local manifestations and return of coagulation tests and systemic signs to normal). If initial control is not achieved by the first dose, an additional dose of 4 to 6 vials should be repeated until initial control of envenomation has been achieved. Recurrence of effects of venom after completion of the FabAV treatment, including limb swelling and hypofibrinogenemia, has been observed. Additional 2-vial doses of FabAV at 6, 12, and 18 hours after achieving initial control has effectively prevented recurrence (68–70).

FabAV can neutralize the toxic effects of all North American *crotalidae* venoms. Southern Pacific rattlesnake (*Crotalus helleri*) venom is not one of the four venoms used to produce FabAV. In standard treatment doses though, it was efficacious for bites of this species (71).

Postmarketing experience with FabAV found that control of coagulopathy was difficult, and delayed-onset hematotoxicity was common. Because hypofibrinogenemia and prothrombin time prolongation in patients experiencing rattlesnake bites do not result in spontaneous bleeding, observation might be all that is needed in the absence of active bleeding. When managing coagulopathy and thrombocytopenia, a trend toward normalization of laboratory values might be a more reasonable end point for FabAV treatment than actual attainment of normal reference values. Every effort should be made to repeat coagulopathy studies within 2 to 3 days after treatment with FabAV (72,73).

Copperhead Envenomation

In a series covering over 40 years (1952 to 1992), with 64% copperhead bites, 7% cottonmouth bites, 3% rattlesnake bites, and 26% unidentified, no first aid measure significantly affected the outcome. Therefore, no first aid measures are recommended for pit viper bites due to copperheads and cottonmouths except immobilization and elevation of the injured extremity (37).

Envenomation of copperheads tends to be less severe than either rattlesnake or water moccasin envenomation and usually requires only conservative local treatment without antivenin. In a retrospective review of copperhead bites, when FabAV was administered, 88% had cessation of the progression of local injury within 4 hours; there were some treatment failures (74,75).

Coral Snake Envenomation

It is difficult to judge which patients bitten by coral snakes are envenomated. The venom has rapid venous absorption, but symptoms may have delayed onset for 12 or more hours after the bite and are difficult to reverse or may even progress after administration of antivenin. If a patient has been bitten by a snake positively identified as a coral snake, with a history of the snake having chewed the affected area and fang marks present, administration of antivenin is warranted, even without any other signs or symptoms (33,35).

Eastern coral snake envenomation requires antivenin (*Micrurus fulvius*). It is derived from horses, and can cause allergic reactions immediately in someone with previous sensitization, or later cause serum sickness. The Arizona coral snake (*Micruroides*) is not associated with human fatality and has no specific antivenin (76).

Envenomation by the Eastern coral snake can result in major neurologic dysfunction, including cranial nerve paralysis. Elective endotracheal intubation is recommended if any signs of bulbar paralysis develop (including slurred speech and diplopia) to minimize the potential of aspiration before respiratory paralysis develops (35).

Elapidae venom can produce respiratory compromise followed by death within 10 minutes. The neurotoxic-acting polypeptides are known to act as a curare-like nondepolarizing paralytic agent. A therapy to consider in patients envenomated by cobras are the acetylcholinesterase inhibitors; a test dose of edrophonium followed by an infusion of neostigmine has occasionally been successful (77).

Compartment Syndrome

Local reaction to rattlesnake envenomation on an extremity may mimic compartment syndrome, however, it is an unusual complication. Current evidence suggests surgery does not improve outcome and should be limited to refractory cases. If pressure exceeds 30 mm Hg, Gold recommends giving additional vials of antivenom and 20% mannitol as an osmotic diuretic. Antivenin administration is clearly effective in preventing death after envenomation, plays a significant role in preventing local muscle necrosis, and is not augmented by fasciotomy and debridement (78,79).

Exotic Snake Envenomation

An emergency physician in an urban hospital in the eastern or midwestern United States is almost as likely to be confronted with a bite of an exotic venomous snake as with that of a species native to North America. A number of these snakes have no locally available antivenin, leaving the emergency physi-

cian trying to find available antivenin. The best resource is the local poison control center, using the *Antivenom Index*. Internet search for locating resources for management can start with site such as *www.herpetology.com* (8).

Alligator Bites

Alligators are found throughout Florida, inhabiting rivers, wetlands, lakes, ponds and canals. The alligator population significantly increased with protection under the Federal Endangered Species programs. Alligators normally avoid humans, but human development of former wilderness areas has placed alligators and humans in close proximity and humans have encroached on them in the alligator farming industry and in hunting season in some states (80).

Alligator attacks are most common during daylight hours, in warm weather months, during the mating season and when protecting their nests. Most attacks occur in water, and the attacking alligators are usually large (81,82).

Soft tissue infections are common after alligator bites, and broad-spectrum antibiotics should be administered prophylactically. A variety of gram-negative aerobes, including *Aeromonas hydrophila,* which is endemic in Florida's lakes and ponds, have been cultured from the mouth of alligators. Aeromonas infection may present as bullae with areas of erythema and cellulitis at the site of injury and even distant sites. Large areas of necrosis rapidly develop in these areas with progressive cutaneous and subcutaneous necrosis and separation (80,82,83).

Lizard Bites

The exotic pet industry in the United States is growing rapidly, with an estimated 7.3 million pet reptiles owned by 3% of all U.S. households. Today, reptile trade is increasingly dominated by lizards. The most popular choice is the common green iguana (*Iguana iguana*). They can deliver significant injury with their teeth, claws, and tails (84).

The only venomous lizards in the world are found in North America. The Gila monster (*Heloderma suspectum*) is endemic to the southwestern United States, and the closely related Mexican beaded lizard (*Heloderma horridum*) is found along the west coast of Mexico. Although docile and sluggish, the Gila monster can suddenly become aggressive if handled (9,85,86).

Gila monsters may hang on during a bite, and mechanical means may be required to loosen the grip of the jaws. Bites of Gila monsters result in significant tissue trauma and even retention of fractured and avulsed teeth in tissue. The teeth of the Gila monster are sharp, recurved, poorly anchored, and periodically shed. Soft-tissue radiographs are unlikely to demonstrate retained

teeth, so the wound must be explored for foreign bodies, after it is cleansed with a bactericide and irrigated copiously with normal saline (9,85–87).

Pain begins almost immediately, can be excruciating, peaks at 15 to 45 minutes, and is minimal at 6 to 10 hours. Local injections of lidocaine will relieve the intense pain. Bleeding from the wound may be profuse (9,85,86).

The venom delivery system is primitive (rigid teeth) and true envenomations are rarely reported. The Gila monster is unique among lizards in having venom glands. All the teeth are grooved and venom flows by simple capillary action up these grooves. Venom flow is augmented by the chewing motions characteristic of Gila monsters once attached to the victim. The chewing bite potentially causes more envenomation than the slashing bite. Systemic complaints of nausea, diaphoresis, and dizziness last about 1 hour. Patients also have hypotension, tachycardia, and generalized weakness, nausea, and vomiting. No antivenin is available, but only one death was recorded from Gila bites during the period from 1929 to 1969 (9,85–87).

References

1. Centers for Epidemiology and Animal Health. The reptile and amphibian communities in the United States. USDA, Animal and Plant Health Inspection Service, Veterinary Services. January 2001.
2. Kelsey J, Ehrlich M, Henderson SO. Exotic reptile bites. Amer J Emerg Med 1997;15(5):536–7.
3. Eidson M, Bender JB, Currier RW, et al. Compendium of measures to prevent disease and injury associated with animals in public settings, 2003. National Association of State Public Health Veterinarians.
4. Davidson TM, Schafer SF, Jones J. North American pit vipers. J Wilderness Med 1992;3:397–421.
5. Warrell DA. Venomous bites and stings in the tropical world. Med J Australia 1993;159(11–12):773–9.
6. White J. Bites and stings from venomous animals: A global overview. Therapeutic Drug Monitoring 2000;22(1):65–8.
7. Iyaniwura TT. Snake venom constituents: Biochemistry and toxicology (part 1). Vet Human Toxicol 1991;33(5):468–74.
8. Jasper EH, Miller M, Neuburger KJ, et al. Venomous snakebites in an urban area: What are the possibilities? Wilderness Environ Med 2000;11(3):168–71.
9. Kunkel DB, Curry SC, Vance MV, et al. Reptile envenomations. J Toxicol Clin Toxicol 1983-1984;21(4,5):503–26.
10. Langley RL. Fatal animal attacks in North Carolina over an 18-year period. Amer J Forensic Med Path 1994;15(2):160–167.
11. Parrish HM. Analysis of 460 fatalities from venomous animals in the United States. Am J Med Sci. 1963;245:129–141.
12. Meier J, Stocker K. Effects of snake venoms on hemostasis. Critical Rev Toxicol. 1991;21:171–182.
13. Cruz NA, Alvarez RG. Rattlesnake bite complications in 19 children. Pediatr Emerg Care 1994;10(1):30–33.

14. Watt G, Padre L, Tuazon ML, et al. Bites by the Philippine cobra (*Naja naja philippinensis*): an important cause of death among rice farmers. Amer J Tropical Med Hygiene 1987;37(3):636–639.
15. Rojas G, Bogarín G, Gutierrez JM. Snakebite mortality in Costa Rica. Toxicon 1997;35(11):1639–43.
16. Kumar P. Drudgery, accidents and injuries in Indian agriculture. Industrial Health 2004;42:149–62.
17. Dumavibhat B. A study of epidemiology, risk factors and preventive measures against snake bites. J Med Assoc Thailand 1997;80(9):547–56.
18. Praba-Egge AD, Cone SW, Araim O, et al. Snakebites in the rainforests of Ecuador. World J Surg 2003;27(2):234–40.
19. Langley R. Physical hazards of animal handlers. Occup Med 1999;14(2):181–94.
20. Langley RL, Morrow WE. Deaths resulting from animal attacks in the United States. Wilderness Environ Med 1997;8:8–16.
21. Curry SC, Kunkel DB. Death from a rattlesnake bite. Am J Emerg Med 1985;3(3):227–35.
22. Dart RC, Seifert SA, Boyer LV, et al. A randomized multicenter trial of Crotalinae polyvalent immune Fab (ovine) antivenom for the treatment for crotaline snakebite in the United States. Arch Intern Med 2001;161(16):2030–6.
23. Kitchens CS. Hemostatic aspects of envenomation by North American snakes. Hematol Oncol Clin North Am 1992;6(5):1189–95.
24. Morandi N, Williams J. Snakebite injuries: Contributing factors and intentionality of exposure. Wilderness Environ Med 1997;8(3):152–5.
25. Parrish HM. Incidence of treated snakebites. US Public Health Rep 1966;81: 269–76.
26. Russell FE, Carlson RW, Wainschel J, et al. Snake venom poisoning in the United States: experience with 550 cases. JAMA 1975;233:341–4.
27. Wingert WA. Poisoning by animal venoms. Top Emerg Med 1980;2(3):89–118.
28. Wingert WA, Chan L. Rattlesnake bites in southern California and rationale for recommended treatment. West J Med 1988;148:37–44.
29. Watson WA, Litovitz TL, Rodgers GC Jr, et al. 2002 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med. 2003;21(5):353–421.
30. Bey TA, Boyer L, Walter FG, et al. Exotic snakebite: Envenomation by an African puff adder. J Emerg Med 1997;15:827–31.
31. Clement JE, Pietrusko RG. Pit viper snakebite envenomation in the United States. Clin Toxicol 1979;14(5):515–38.
32. McCollough NC, Gennaro JF. Evaluation of venomous snake-bite in the southern United States from parallel clinical and laboratory investigations. J Florida Med Assoc 1963;49:959–67.
33. Norris RL, Dart RC. Apparent coral snake envenomation in a patient without visible fang marks. Am J Emerg Med 1989;7:402–5.
34. Suchard JR, LoVecchio F. Envenomations by rattlesnakes thought to be dead. N Engl J Med 1999;340(24):1930.
35. Kitchens CS, Van Mierop LHS. Envenomation by the eastern coral snake (*Micrurus fulvius fulvius*): A study of 39 victims. JAMA 1987;258(12):1615–8.
36. Iyaniwura TT. Snake venom constituents: Biochemistry and toxicology (part 2). Vet Human Toxicol 1991;33(5):475–80.

37. Lawrence WT, Giannopoulos A, Hansen A. Pit viper bites: Rational management in locales which copperheads and cottonmouths predominate. Ann Plast Surg 1996;36:276–85.
38. Scharman EJ, Noffsinger VD. Copperhead snakebites: Clinical severity of local effects. Annals Emerg Med 2001;38(1):55–61.
39. Davidson TM. Intravenous rattlesnake envenomation. West J Med 1988;148:45–7.
40. Schaeffer RC, Pattabhiraman TR, Carlson RW, et al. Cardiovascular failure produced by a peptide from the venom of the Southern Pacific rattlesnake, Crotalus viridis helleri. Toxicon 1979;17:447–53.
41. Ownby CL, Kainer RA, Tu AT. Pathogenesis of hemorrhage induced by rattlesnake venom. Am J Pathol 1974;76(2):401–8.
42. Hasiba U, Rosenbach L, Rockwell D, et al. DIC-like syndrome after envenomation by the snake, *Crotalus horridus horridus*. N Engl J Med 1975;292(10): 505–7.
43. Tanen DA, Ruha AM, Graeme KA, et al. Epidemiology and hospital course of rattlesnake envenomations cared for at a tertiary referral center in central Arizona. Academic Emerg Med 2001;8(2):177–82.
44. Riffer E, Curry SC, Gerkin R. Successful treatment with antivenin of marked thrombocytopenia without significant coagulopathy following rattlesnake bite. Ann Emerg Med 1987;16:1297–9.
45. Bond GR, Burkhart KK. Thrombocytopenia following timber rattlesnake envenomation. Ann Emerg Med 1997;30:40–4.
46. Offerman SR, Barry JD, Schneir A, et al. Biphasic rattlesnake venom-induced thrombocytopenia. J Emerg Med 2003;24(3):289–93.
47. Brick JF, Gutmann L. Rattlesnake venom-induced myokymia. Muscle Nerve 1982;5(suppl):98–100.
48. Bush SP, Siedenburg E. Neurotoxicity associated with suspected Southern Pacific rattlesnake (*Crotalus viridis helleri*) envenomation. Wilderness Environ Med 1999;10(4):247–49.
49. Corrigan JJ, Jeter MA. Mojave rattlesnake (*Crotalus scutulatus scutulatus*) venom: In vitro effect on platelets, fibrinolysis, and fibrinogen clotting. Vet Hum Toxicol 1990;32(5):439–41.
50. Glenn JL, Straight RC, Wolfe MC, et al. Geographic variation in *Crotalus scutulatus scutulatus* (Mojave rattlesnake) venom properties. Toxicon 1983;21(1):119.
51. Jansen PW, Perkin RM, Van Stralen D. Mojave rattlesnake envenomation: Prolonged neurotoxicity and rhabdomyolysis. Ann Emerg Med 1992;21(3):322–5.
52. Gopalakrishnakone P, Hawgood BJ, Holbrooke SE, et al. Sites of action of Mojave toxin isolated from the venom of the Mojave rattlesnake. Br J Pharmac 1980;69:421–31.
53. Farstad D, Thomas T, Chow T, et al. Mojave rattlesnake envenomation in southern California: A review of suspected cases. Wilderness Environ Med 1997;8(2):89–93.
54. Nordt SP. Anaphylactoid reaction to rattlesnake envenomation. Veterinary Human Tox 2000;42(1):12.
55. Ryan KC, Caravati EM. Life-threatening anaphylaxis following envenomation by two different species of Crotalidae. J Wilderness Med 1994;5:263–8.
56. Tanen DA, Ruha AM, Graeme KA, et al. Rattlesnake envenomations: unusual case presentations. Arch Intern Med 2001;161(3):474–9.

57. Curry SC, Kraner JC, Kunkel DB, et al. Noninvasive management of rattlesnake envenomations to extremities. Ann Emerg Med 1985;14(11):1081–4.
58. Cowan DJ, Wright T, Cowan JA. Long-term complications of snake bites to the upper extremity. J Southern Ortho Assoc 1998;7(3):205–11.
59. Keyler DE, Vandevoort JT. Copperhead envenomations: Clinical profiles of three different subspecies. Vet Human Toxicol 1999;41(3):149–52.
60. Thorson A, Lavonas EJ, Rouse AM, et al. Copperhead envenomations in the Carolinas. J Toxicol Clin Toxicol 2003;41(1):29–35.
61. Burch JM, Agarwal R, Mattox KL, et al. The treatment of crotalid envenomation without antivenin. J Trauma. 1988;28(1):35–43.
62. Spiller HA, Bosse GM. Prospective study of morbidity associated with snakebite envenomation. J Toxicol Clin Toxicol 2003;41(2):125–30.
63. Gold BS, Pyle P. Successful treatment of neurotoxic king cobra envenomation in Myrtle Beach, South Carolina. Ann Emerg Med 1998;32(6):736–8.
64. Tokish JT, Benjamin J, Walter F. Crotalid envenomation: The southern Arizona experience. J Ortho Trauma 2001;15(1):5–9.
65. Hurlbut KM, Dart RC, Spaite D. Reliability of clinical presentation for predicting significant pit viper envenomation. Ann Emerg Med 1988;17(4):438–9.
66. LoVecchio F, Klemens J, Welch S, et al. Antibiotics after rattlesnake envenomation. J Emerg Med 2002;23(4):327–8.
67. Clark RF, McKinney PE, Chase PB, et al. Immediate and delayed allergic reactions to Crotalidae polyvalent immune Fab (ovine) antivenom. Annals Emerg Med. 2002;39(6):671–6.
68. CroFab, Crotalidae Polyvalent Immune Fab Ovine. Nashville, TN: Protherics, Inc., 2000. [package insert]
69. Bebarta V, Dart RC. Effectiveness of delayed use of Crotalidae polyvalent immune Fab (ovine) antivenom. J Toxicol Clin Toxicol 2004;42(3):321–4.
70. Gold BS, Dart RC, Barish RA. Bites of venomous snakes. N Engl J Med 2002;347(5):347–56.
71. Bush SP, Green SM, Moynihan JA, et al. Crotalidae polyvalent immune Fab (ovine) antivenom is efficacious for envenomations by Southern Pacific rattlesnakes (*Crotalus helleri*). Ann Emerg Med 2002;40(6):619–24.
72. Boyer LV, Seifert SA, Clark RF, et al. Recurrent and persistent coagulopathy following pit viper envenomation. Arch of Intern Med. 1999;159(7):706–10.
73. Ruha AM, Curry SC, Beuhler M, et al. Initial postmarketing experience with crotalidae polyvalent immune Fab for treatment of rattlesnake envenomation. Annals Emerg Med 2002;39(6):609–15.
74. Whitley RE. Conservative treatment of copperhead snakebites without antivenin. J Trauma 1996;41:219–21.
75. Lavonas EJ, Gerardo CJ, O'Malley G, et al. Initial experience with Crotalidae polyvalent immune Fab (ovine) antivenom in the treatment of copperhead snakebite. Ann Emerg Med 2004;43(2):207–8.
76. Juckett G, Hancox JG. Venomous snakebites in the United States: Management review and update. Am Family Physician 2002;65(7):1367–74.
77. Britt A, Burkhart KK. *Naja naja* cobra bite. Am J Emerg Med 1997;15:529–31.
78. Gold BS, Barish RA, Dart RC, et al. Resolution of compartment syndrome after rattlesnake envenomation utilizing non-invasive measures. J Emerg Med 2003;24(3):285–8.

79. Stewart RM, Page CP, Schwesinger WH, et al. Antivenin and fasciotomy/debridement in the treatment of severe rattlesnake bite. Am J Surg 1989;158:543–7.
80. Flandry R, Lisecki EJ, Domingue GJ, et al. Initial antibiotic therapy for alligator bites: Characterization of the oral flora of Alligator mississippiensis. Southern Med J 1989;82(2):262–6.
81. Burgess GH, Callahan MT, Howard RJ. Sharks, alligators, barracudas, and other biting animals in Florida waters. J Florida Med Assoc. 1997;84(7):428–32.
82. Howard RJ, Burgess GH. Surgical hazards posed by marine and freshwater animals in Florida. Amer J Surgery 1993;166(5):563–7.
83. Raynor AC, Bingham HG, Caffee HH, Dell P. Alligator bites and related infections. J Florida Med Assoc 1983;70(2):107–10.
84. Kelsey J, Ehrlich M, Henderson SO. Exotic reptile bites. Am J Emerg Med 1997;15(5):536–7.
85. Hooker KR, Caravati EM. Gila monster envenomation. Annals Emerg Med 1994;24(4):731–5.
86. Stahnke HL, Heffron WA, Lewis DL. Bite of the Gila monster. Rocky Mt Med J 1970;67:25–30.
87. Strimple PD, Tomassoni AJ, Otten EJ, Bahner D. Report on envenomation by a Gila monster (Heloderma suspectum) with a discussion of venom apparatus, clinical findings, and treatment. Wilderness Environ Med. 1997;8(2):111–6.

33

Heat, Cold, and Water Immersion Injuries

Karl Auerbach

Keywords: frostbite, heat stroke, heat exhaustion, hypothermia

Humans have a remarkable ability to function in a wide range of ambient temperatures and have practiced agriculture in tropical, semi-arid and sub-arctic regions to varying degrees. Despite the ability of humans to exist in these environments, the human body has a relatively narrow range in which its core temperature can function. When the core temperature is outside of this range, the efficiency of the person decreases, and serious consequences, including death, can occur.

The body keeps the central temperature within the appropriate range through several physiologic methods that serve to add or remove heat from the core. We supplement these physiologic processes by use of protective gear or techniques. When disease is present, the body may not be able to maintain the central core temperature within a viable range. Medications, nutrition, alcohol, and drugs may impact the ability of the body to maintain normal temperature. Activity can add to the stress on the temperature regulating mechanisms.

This chapter will discuss heat- and cold-related stressors, methods for responding to the stressors, and situations that affect the body's ability to function under these stressors. Signs and symptoms of heat- and cold-related problems will also be discussed.

Heat-Related Injury

Normal human oral temperature is 37˚C (98.6˚F), but it can range between 36.3˚C (97.3˚F) and 37.1˚C (98.8˚F) in the morning. Oral temperature is normally 0.5˚C (.9˚F) lower than rectal temperature. Hyperthermia is defined as the elevation of the core body temperature above the normal diurnal range of 36˚C (96.8˚F) to 37.5˚C (99.5˚F) due to failure of thermoregulation. There is a spectrum of core body temperature at which symptoms will occur. Some individuals will have core temperatures higher or lower than normal without

symptoms. Measured temperatures, especially skin or oral, will show a wider range of variation than true core temperature. Table 33.1 summarizes heat effects on the body, their prevention and their treatment (1,2).

TABLE 33.1. Heat effects.

Condition	Characteristic	Prevention	Treatment
First Degree Burn	Superficial skin	Avoid contact	Nothing or bland moisturizing topical
Second Degree Burn	Into dermis of skin, blister	Avoid contact	Local wound care, topical antibiotics, protective cover
Third Degree Burn	Through the dermis, nerve endings destroyed	Avoid contact	Fluids, debridement, systemic antibiotics
Fourth Degree Burn	Muscle, bone involved	Avoid contact	Hospitalization, fluid replacement, treat shock, debridement, reconstruction, antibiotics
Heat Rash	Rash from eruption of the sweat glands	Keep skin dry, clean	Seek cool, powders
Sunburn	Ultraviolet ray damage to skin	Avoid exposure, sun block	Treat as per burn depending on degree
Dehydration	Loss of water	Acclimatization. Fluid and electrolyte intake	Fluid replacement
Heat Cramps	Water and sodium depletion, muscle cramps, sweating, mildly elevated body temp	Acclimatization. Maintain fluid and electrolyte intake. Rest. Proper clothing.	Fluid replacement and electrolyte replacement. Oral usually adequate.
Heat Exhaustion	As for Heat Cramps with further depletion. Higher elevation body temperature, irritability, malaise, confusion	As for Heat Cramps, removal to a cool environment.	Fluid and electrolyte replacement, oral and possible intravenous. Cooling, typically external.
Heat Stroke	As for Heat Exhaustion but sweating often ceases, organ shut down, cardiac irregularity or arrest, muscle break down, core temperature over 40.5 degrees C	As for Heat Exhaustion, more urgent	Immediate need for intravenous fluid and electrolyte replacement, immediate need for cooling including core cooling. Cardiac monitoring, monitor kidney and urine.
Malignant Hyperthermia	Reaction to anesthetics but can be seen with heat exposure. Life threatening hyper-metabolic syndrome	Obtain family and personal history of possible prior events and avoid triggers	As for Heat Stroke.

Thermoregulation in Hot Environments

Maintaining core temperature is a balance between heat production and loss. Heat is produced by muscular exercise, digestion, and cellular processing of glucose. The body absorbs heat from the environment through convection and radiation, especially from sunlight. Heat is lost from the body by radiation, conduction, convection, and vaporization of water in the respiratory passages and on the skin through perspiration. The balance between heat production and heat loss determines the body temperature, a process called thermoregulation (1).

Paradoxically, cold environments can also cause heat gain. The body's defense mechanisms against cold include shivering. Shivering can cause a net heat gain through muscle contractions, hence heat-related injuries can occur in cold weather, especially if accompanied by other causes of heat gain (3).

Factors that can impact the increased production of heat include muscular conditioning, timing and type of food intake, and the factors that impact basal metabolism. These factors include thyroid hormone status, gender, age, race, and the presence of illness. Pregnancy can increase heat production and impact regulation as well. Drugs, such as cocaine or other stimulants, can increase the metabolic rate and create heat. Infections can cause fever that not only creates heat but also decreases the body's ability to adjust for heat (3,4).

A rise in the blood temperature of less than 1˚C (2˚F) activates peripheral and brain heat receptors that signal the hypothalamus thermoregulatory center. In turn, the afferent signals from this center increase the delivery of heated blood to the surface of the body. These signals activate nerve endings that act on blood vessel smooth muscles to cause vasodilatation that increases blood flow in the skin by up to 8 L per minute. An increase in the blood temperature also initiates perspiration. If the air surrounding the surface of the body is not saturated with water, perspiration will evaporate and cool the body surface. At maximal efficiency in a dry environment, sweating can dissipate about 600 kcal of heat per hour. The evaporation of sweat is critical for the transfer of heat from the body to the environment. An elevated blood temperature also causes tachycardia, increased cardiac output, and increased respiratory rate. As blood flow is transferred from the core circulation to the muscles and skin to facilitate heat dissipation, blood flow to the internal organs is reduced, particularly in the intestines and kidneys (4).

Dermal Thermal Effects

When the body is unable to rid itself of heat, the core temperature rises and a spectrum of heat-related illness can occur. Unrecognized and/or untreated, serious and life threatening problems can develop.

Thermal Burns

Thermal burns of the skin occur when the temperature of the object touching or radiating to the skin exceeds the ability of the skin's vascular system to carry away the heat. This is made worse by pressure on the skin, which reduces circulation. The pressure effect is multiplied as the area and time of contract increase. Even temperatures as low as 45˚C to 49˚C (114˚F to 120˚F) have caused third degree burns of the skin (5,6).

Burns are described by degree:

1. First degree burns involve only the superficial epidermis. The skin is dry, red, and may be hypersensitive.
2. Second degree burns destroy the epidermis and penetrate into the dermis. The skin is edematous, red, wet, and painful since nerve endings are involved. Blistering may occur. Second degree burns can be further classified by the depth into the dermis.
3. Third degree burns penetrate the dermis. The skin is pale, contracted, and leathery. Sensation is lost because the nerve endings are destroyed.
4. Fourth degree burns involve deeper structures such as muscle, bone or other tissue. Charred bone or muscle may be visible (7).

Burns are also described in terms of involved surface area. The body is divided into regions, each considered as a percentage of the body. In this system, the head is one region of 9%, each arm is 9% and each leg is 18% and the torso is 36%. There is an inverse relationship between percentage of the body burned and survival potential. However, modern burn units and aggressive care of burns have increased the survivability of serious burns (7,8).

Burns continue to be a significant cause of injury in agriculture. Hot engines and exhausts, heating devices for the livestock, hot liquids, and fires are but some of the causes. Children who live and/or work on the farm are particularly at risk because many devices are moving and children are attracted to them (9).

Heat Rash

Heat rash is a skin manifestation of heat. Typically seen in children more than adults, it can occur at any age. Sometimes called prickly heat, miliaria rubra is often seen in conditions of high heat and humidity. It is a papulovesicular rash caused by eruption of the sweat glands.

Sunburn

Sunburn is damage to the skin from ultraviolet radiation. It is a significant problem in hot, sunny environments. Sunburn can occur in cold, sunny environments

as well and even on cloudy days, so long as ultraviolet rays penetrate the cloud cover. It can also cause actinic skin changes (see Chapter 18) (10).

General Heat-related Problems

Under conditions of high heat and activity, up to 60% of the cardiac output may pass through the skin for cooling and sweat production. Loss of fluid occurs by sweating. To prevent dehydration in hot environments, workers should drink at least an extra cupful of water every hour, an extra 1.5 to 2 L a day (Table 33.2). Because rapid weight loss in the heat means water loss and not fat loss, people losing weight should drink more water, possibly even 10 L, to maintain body weight. The urine should be plentiful and light colored. Urine that is dark, strong smelling, or of reduced volume indicates a large fluid deficit (3).

Dehydration

As water is lost, dehydration and its effects can occur. This can result in shifts of concentrations of several electrolytes in the body. Usually, salts become more concentrated but sodium is lost in sweat and can be reduced. The blood also becomes thicker as the circulating volume of water drops. These changes can lead to fatigue and reduced physical and mental performance. However, often there are no symptoms until significant changes have occurred. Then the symptoms can develop rapidly, resulting in giddiness, fatigue, irritability, fainting, and cramps (3).

Heat Cramps

Heat cramping is often the earliest manifestation of heat-related illness and forms a continuum of severity from mild to life threatening. Heat cramps are typically seen following exercise in the heat. Symptoms include painful muscle cramps, thirst, sweating, elevated body temperature and

TABLE 33.2. Fluid requirements for hot work in liters/hour.

WBGT Index	Easy Work	Moderate Work	Hard Work
78-82	1/2	3/4	3/4
82-85	1/2	3/4	1
85-90	3/4	3/4	1
Over 90	3/4	1	1

Source: Adapted from the U.S. Army Field Manual FM21-10 "Field Hygiene and Sanitation."
Notes: Maximum hourly intake 1 1/4 liters.
Max daily intake: 12 liters.
WGBT Index is a measure of heat based on influence of ambient temperature, wind speed, and relative humidity.

tachycardia. Typical locations of muscle spasms are the calves or the abdominal muscles (10).

Heat Exhaustion

If exercise continues without adequate fluid and electrolyte replacement, water and sodium depletion occurs and increasing symptoms develop. This is known as heat exhaustion. The time it takes to develop this condition depends on many factors including ambient temperature, level of exercise, relative humidity and conditioning. The time to exhaustion at 10.5˚C (51˚F) is about 93 minutes. At 30.5˚C (87˚F), the time is about 51 minutes (11).

In addition to the symptoms of heat cramps, headaches and lightheadedness are common as well as muscle cramps, a general myalgia, malaise, and irritability. As the process continues, lack of coordination, confusion, nausea, and vomiting develop. The kidneys may decrease the amount of urine they produce reaching the point of producing no urine at all. Hypotension may occur as the process continues. Some or all of these symptoms may be present, and they do not necessarily present in a given order. If recognized, fluid and electrolyte replacement can stop the process. However, if symptoms such as nausea and vomiting occur, the ability to replace fluids and sodium by mouth is lost. The person can become too confused or weak to adequately recognize the need to take fluids and sodium, compounding the problem (10).

Heat Stroke

Usually by the late stages of heat exhaustion, the person is unable to exercise effectively, but if exercise or heat exposure continues, heat stroke can occur. In addition to the findings of heat exhaustion, a complex of symptoms develops in heat stroke that tends to worsen rather than improve the clinical situation. Initially sweating can be profuse but often stops. The kidneys shut down, and hyperventilation and pulmonary edema develop. The heart can develop irregular rhythms that compromise circulation. Liver damage develops. Muscles break down releasing products that can worsen kidney status and heart rhythm. Blood clots develop in the vascular system and shock can develop. Core body temperature is typically above 40.5˚C (105˚F) (2–4,10).

Heatstroke can occur in the absence of exercise. Classic heat stroke takes place when the ambient temperature is high and the person has a medical condition that impairs thermoregulation. These conditions include cardiovascular disease, neurological disorders, diabetes, and obesity. The very old and very young are especially susceptible to heat stroke. Psychiatric conditions that impact the intake of fluids and medications such as anticholinergic agents or diuretics can contribute to heat stroke (1,2,12).

Malignant Hyperthermia

Malignant hyperthermia is an autosomal dominant genetic condition that is typically triggered by certain anesthetics, for example sevoflurane. Calcium metabolism in skeletal muscles is impacted and a life-threatening hypermetabolic syndrome develops. Stress can also trigger this syndrome; some cases that have been called heat stroke may actually have a component of the malignant hyperthermia syndrome present (13).

Prevention of Heat-related Injury

Agricultural activities often place the worker in a setting of heat and intense exercise. Even in colder settings, there are significant heat exposures in settings such as barns, animal shelters, and storage sheds. Heat also contributes to other injuries, for example in tobacco farming it has been shown that extreme heat contributes to falls resulting in musculoskeletal injuries (14).

Avoidance

The first line of defense is avoidance of heat. Assuming one cannot move the location of the job task to a cooler climate, appropriate scheduling of activities to avoid the extreme heat in the middle of the day is a good strategy for prevention of heat-related problems.

Recognition

Another means of prevention is recognition of the problem. A variety of heat stress measures have been proposed to help individuals recognize when they might be at risk for heat-related illnesses. Ultimately, the supervisor, foreman, or someone monitoring the heat and humidity must realize that the conditions may be above human tolerance. Whether or not a person can recognize these conditions depends on a variety of factors including the perception of heat. Studies have shown that heat perception is far from a perfect system. In a study on trained and untrained individuals, it was found that while untrained individuals were able to perceive heat stress fairly closely to measured parameters, trained individuals underestimated the heat stress on their bodies. Thus while training may overall improve heat stress, it may also prevent appropriate recognition (15).

Acclimatization

Acclimatization is a key factor in improving heat tolerance. A period of 8 to 14 days of repeated exposure to heat and exercise result in a number of changes that improve heat transfer, including the initiation of cooling mechanisms and a lower core temperature. To be effective, the acclimatization

must have enough heat and exercise stress to elevate both core temperature and elicit profuse sweating (16,17).

Fluid Intake

In addition to improving cooling mechanisms, acclimatization can increase plasma volume up to 30%. An increase in plasma volume gives the body more leeway in terms of maintaining body fluids. No matter what the increase, there will come a time when fluid replacement is needed. How much fluid and what should be in that fluid is a topic of ongoing investigation. While some of the literature is based on good scientific work, some is based on perceived experience including out-dated information. Some is also based on the claims of manufacturers with a product to sell. Caution is advised (17,18).

Increasing plasma volume, either by acclimatization or by increased pre-exposure fluid intake has been proposed as a way of improving performance in the heat. While it is true that plasma volume may expand in acclimatization, studies have shown that plasma volume expansion alone is not adequate to improve tolerance to heat. In fact, over-expansion can result in dilution of vital electrolytes and can worsen the clinical situation (18).

Salt tablets have long been recommended as a means of preventing heat-related illness, but their use is controversial. Problems arise when salt tablets are taken without adequate fluid intake, which is counterproductive in terms of preventing heat-related illness. Far more effective are pre-mix solutions containing both water and electrolytes. Many studies have been done on various fluid–electrolyte combinations. The results appear to depend on what is hypothesized and who is doing the study. A balanced electrolyte solution is likely the best way to replace fluids. As a general guide to fluid replacement, at temperatures less than 82˚C, one-half to three-quarters quart water per hour is recommended, depending on workload. As the temperature rises above 90˚C, at least a quart of fluids per hour is needed (Figure 33.1) (19–25).

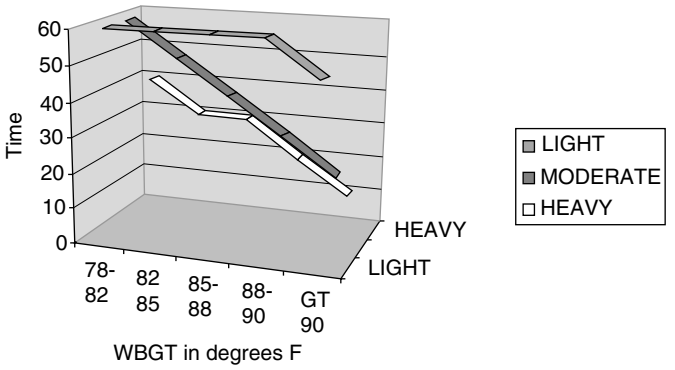


FIGURE 33.1. Times of exposures to heat in an hour under various conditions of work-rest cycles. (Data from U.S. Army Research Institute of Environmental Medicine (24).

Work-rest and Work-cool Cycles

If acclimatization is not possible or is not sufficient, then consideration needs to be given to work-rest cycles or work-cool cycles. For ambient temperatures below 28˚C (82˚F and in heavy labor, 40 minutes work followed by 20 minutes rest is advisable. As the temperature rises to above 32˚C (90˚F), even light work status needs a 10-minute rest period for each hour of labor. Heavy work requires 10 minutes of work with 50 minutes of rest (Figure 33.1) (22–24).

Clothing

Clothing can make a big difference in heat tolerance. Remembering that a major way the body rids itself of heat is by sweating and evaporation, the clothing chosen should foster that process. Loose fitting garments with "breathable" fabrics will do better for control of heat then impervious garments. Unfortunately, in agriculture, protective gear may be needed to protect against chemical exposure (25).

Management of Heat-Related Illness

The first step in treatment is recognition. Individuals and supervisors must be on the look out for heat-related illness. Since the illness can impact judgment, it is often necessary to have some way of monitoring exposure and status.

Heat Cramps

When heat cramps occur, the person should be given plenty of electrolyte balanced fluids, at least enough to satisfy their thirst. If the worker is performing at even moderate level of activity, he or she should stop that activity until the cramping has resolved and, if possible, move to a cooler area.

Heat Exhaustion

As the seriousness of the heat-related condition increases, close attention needs to be paid not only to fluid intake but also to the nature of that fluid. Cooling becomes even more critical. Techniques such as spraying with cool water can be used, although care must be taken not to overcool the worker.

Heat Stroke

Heat stroke often goes unrecognized until it has progressed to a level where treatment in a hospital emergency room or clinic will be needed. Measures in the field include giving fluid if the person can swallow it safely without aspiration, as well as loosening clothing and cooling. However, field treatment should not delay transfer to an appropriate medical facility where resuscitation with fluids such as normal saline will be necessary.

The effects of heat-related illness can last for several days beyond the acute event. During that time, adequate hydration and electrolyte balance should be maintained. Avoidance of heat and heavy labor, if possible, is an important step in long-term recovery (24).

Cold-Related Injury

Agricultural work involves cold exposure during the cold months when dealing with equipment, preparing fields, caring for livestock, or creating or repairing buildings. Hunting and fishing are two situations in which cold exposure plays a key role. A particular problem arises when there is a need to go from one temperature extreme to another in the course of the work day. Both acclimatization and protective clothing issues have to be considered. Table 33.3 summarizes the effects of cold as well as prevention and treatment (25,26).

TABLE 33.3. Cold effects.

Condition	Characteristic	Prevention	Treatment
Chilblains	Superficial skin from cool temperature, high humidity and winds	Protective gear, avoid exposure	Removal from cool environment and rewarming
Frostnip (1st degree frostbite)	Superficial skin damage from temperatures near freezing	Protective gear, avoid exposure	Local care. Removal from cold environment and rewarming
Second degree frostbite	Into the dermis, can blister	Protective gear, avoid exposure	Topical antibiotics, removal from cold, rewarming
Third Degree frostbite	Through the dermis, nerve endings destroyed, potential for damage to deeper structures and gangrene	Protective gear, avoid exposure	Hospitalization, fluid replacement, treat shock, debridement, reconstruction, antibiotics
Early hypothermia	Fatigue and clouded thinking; shivering, irritability	Acclimatization. Maintain fluid and nutritional intake. Avoidance. Appropriate gear.	Rewarming. Nutritional and fluid supplement.
More advanced hypothermia	As for early plus uncoordination, social withdrawal and paradoxical clothing removal	As for early	Rapid external rewarming, Nutritional and fluid supplement
Extreme hypothermia	As for more advanced hypothermia plus organ shutdown and cardiac arrest	As for early	Immediate need for in hospital care including core rewarming and fluids and cardiac resuscitation if needed.

Thermoregulation in Cold Environments

Hypothermia is defined as a core temperature below 35˚C (95˚F). It can be considered mild (32˚C to 35˚C) (89.6˚F to 95˚F), moderate (28˚C to 32˚C) (82˚F to 89.6˚F), or severe (below 28˚C)(82˚F). When body tissue is exposed to cold, the cell membranes no longer function properly, fluid leaves the cell, cellular processes stop, and an electrolyte imbalance occurs. Cell death occurs as the water in and around the cells crystallizes. In response to cold, the brain attempts to stimulate heat production by the mechanisms of shivering, increased metabolism, and the reduction of blood flow to peripheral tissue to minimize heat loss (27).

In many ways, issues of cold exposure parallel those of heat exposure. Local and generalized injuries can occur. It is also critical to remember that cold-related problems can occur even with mild outdoor temperatures. For example, amenorrhea has been reported in female workers in poultry slaughterhouses who work in the cold. Death of a farm worker due to hypothermia has been reported from immersion in cold water, even in warm weather (28,29).

Wind can multiply the effect of cold. What may be a perfectly safe situation in calm air can result in significant cold-related injury in windy conditions. To assist in evaluating the effect of wind, the National Weather Service publishes a wind chill index (Figure 33.2) (30,31,32).

Dermal Cold Effects

Chilblains

Chilblains (erythema pernio) are a superficial tissue injury that occurs after prolonged or ongoing intermittent exposures to temperatures above freezing and with high humidity and winds. Chilblains can occur with temperatures between 0˚C (32˚F) and 12.8˚C (55˚F). Exposure lasting for hours can cause this condition. It usually does not cause permanent damage, but acutely there can be local soreness, swelling, redness and itching. If recurrent, blistering and skin damage can occur (32,33).

Treatment is removal from the cool environment and/or protection from the exposure. Rewarming is needed to prevent progression to deeper tissue injuries. Following rewarming, there may be increased redness and itching. The effects are usually self-limiting (33,34).

Frostnip

Frostnip is a transient tingling and numbness that does not cause any permanent injury. This is sometimes referred to as first degree frostbite.

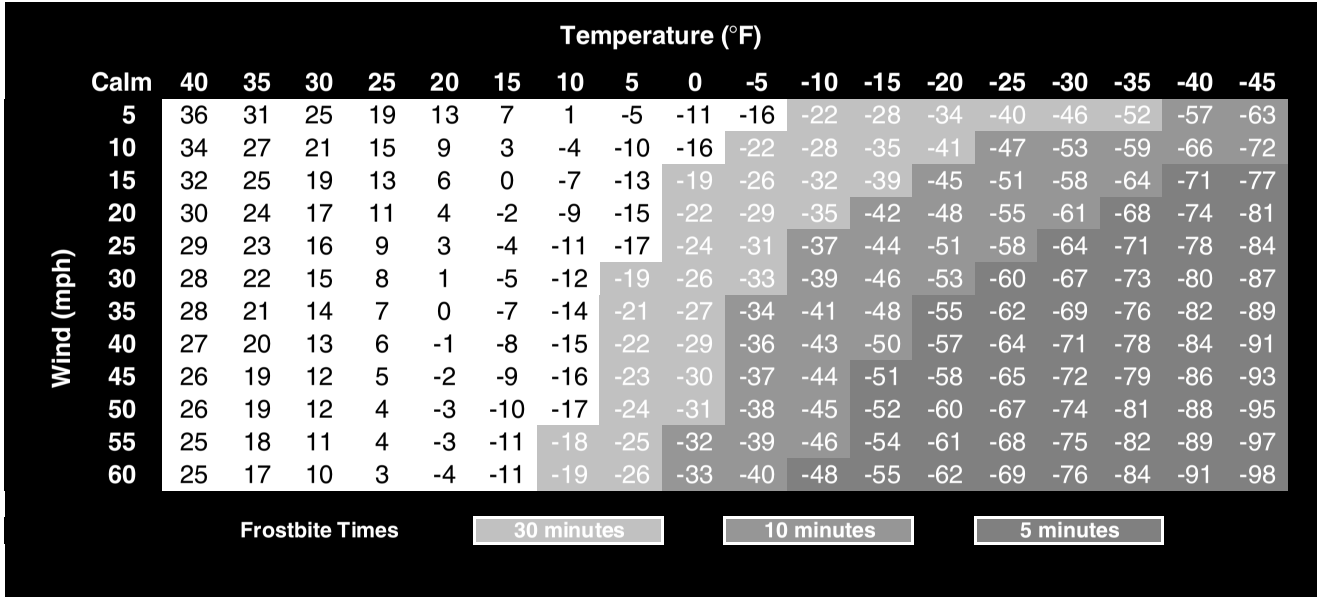


FIGURE 33.2. Wind chill temperature index. (Courtesy of National Weather Service (30).)

Frostbite

Cold exposure below freezing can cause local injury due to hypothermia. Cold burns or frostbite particularly impact exposed areas but potentially any area of the body. Fingers, ear lobes and toes are particularly susceptible to these types of injuries. Skin freezes at –2°C (28°F). Depending on how long the skin remains at that temperature will influence the degree of damage. Superficial frostbite injuries can either be second or third degree depending on depth. Deeper frostbite injuries can involve the joints, bone, and muscle tissue. Ulceration and gangrene can occur with deep third degree or deeper injuries. Unlike burns, which frequently cause the person to withdraw from the heat source, the exposure to cold can continue. Thus frostnip needs to be taken seriously because it can progress to full frostbite including all the complications (27,32,33,34).

Frostbite injuries are generally treated much by rewarming with warm, but not hot, water to minimize the tissue effects. Local care, antibiotics, debridement, and, in severe cases, reconstruction, may be necessary for appropriate treatment of frostbite injuries. As in the case of burns, fluid replacement is important, especially in blistering forms (35,36).

Generalized Effects of Cold

Maintaining core temperature is a balance between heat lost and heat produced. When exposed to cold weather, the body's regulatory mechanisms induce measures to increase heat production. Shivering is one of the main ways that heat production is increased. Increased muscle activity generates heat as a byproduct. Other methods for increasing metabolism tend to take longer periods of time to develop and be of value.

Acclimation to the cold can help maintain function in the face of the cold exposure. However, the improvement is not as good as it is for heat. As exposure goes on, other mechanisms to increase body heat become useful, such as increased metabolism and skin circulation adaptations (33).

Performance decreases with body cooling, much as it does for hot temperatures. The very old and the very young are most sensitive to cold, just as they are to heat. Various medical conditions, hypothyroidism for example, make a person more sensitive to cold-related illness. Alcohol intake dilates skin blood vessels, making the person more sensitive and likely to develop significant cold-related problems (35).

The earliest manifestations of cold-related illness may be non-specific and include fatigue and clouded thinking. Increased muscle tone and shivering are an early part of the body's response to cold and attempt to maintain core temperature. The person may develop altered vision, social withdrawal, irritability, and uncoordinated movements. One paradoxical symptom is removing clothing despite the cold.

If the cold-related illness is left untreated, shivering may cease as the body fatigues and organs shut down. Cardiac arrest may develop leading to death. The timing and sequence of events depend on a number of factors but once started require immediate medical attention (33).

While cold-related problems are the result of cold exposure, overheating and heat-related problems can develop if the person over-exerts in the cold or has overdressed for the situation. This situation can lead to increased perspiration, dampness of clothing, and body cooling (34).

Prevention of Cold-related Injury

Adequate nutrition and hydration are important general measures. Acclimatization, though not as pronounced as in heat, can help increase metabolism over a period of days to weeks. Warm fluid replacement is important in cold weather. Adequate nutrition is equally important given the increased metabolic cost of cold exposure even in the absence of exercise. Caloric requirements can be 25% to 50% higher in cold weather as compared to warm weather (33).

The mnemonic "C-O-L-D" can help remind people of what will help prevent cold-related injury. C is for cleanliness and care because clothing will tend to stay warmer when clean and dry. O is for overheating. Preventing overheating will keep down perspiration which can lead to dampness and further cooling. L is for layers and looseness. Clothing that is loose and in layers will create air spaces that hold body heat. It also can allow for removal of some clothing when appropriate to prevent overheating. D is for dampness. When clothing is wet, heat loss is increased (34).

Proper insulation is important in prevention, through the use of layers of loose clothing and waterproof outer gear to keep the clothing from becoming wet. Various materials that have insulation properties, yet are light in weight and relatively low bulk, are desirable for work in cold weather.

Management

When hypothermic symptoms begin, the most important treatment step is recognition. Re-warming, through use of additional layers of clothing, removal and replacement of wet clothing, or use of blankets is critical. Rest and reduction of surface area for heat loss can slow the process. Shelter from the cold, the wind, and wetness is likewise important (33).

What should be avoided is paradoxical behavior as can be seen in hypothermia where the individual removes rather than adds clothing. Also to be avoided is rubbing of the area or use of snow to deal with frostbite. Local rubbing destroys damaged skin tissue (34).

When more severe hypothermia occurs, external rewarming through the use of forced air heating blankets, radiant heat, or hot packs may be needed. In the most extreme cases, active core rewarming with heated humidified oxygen and heated intravenous fluids may be necessary. Treatment of severe hypothermia may also include appropriate treatment of impaired organ systems, including full cardiopulmonary resuscitation (37).

Despite the effects that cold can have, there are numerous cases of individuals recovering from severe hypothermia. This is particularly present in cold water drowning. There is an old saying in emergency medicine: "The person isn't dead until he is warm and dead." Thus, aggressive and continued therapy of hypothermia is warranted (37).

Immersion Injuries

Immersion is the placing of some or all of the body in fluid, typically water. Unless there is special equipment for breathing, submersion lasting more than a few minutes results in drowning.

Whole Body Immersion

There is an extensive literature on the body's response to submersion in activities such as self-contained underwater breating apparatus (SCUBA) diving. There are a whole host of physiologic changes that take place due to pressure, the work of breathing, and the gas mixture breathed. The main issue is heat transfer because water conducts heat at a rate 200 times that of air. Thus changes in core temperature are more rapid and more difficult to control when the person is immersed or submerged. Even in tropical water, the temperature is typically below that of air so there is a net cooling effect.

Situations may also arise where the issue is net heat flow into the body raising the core temperature. This might take place in a heated body of water, in farm effluent, or in a processing plant. Another example of potential hyperthermia in submersion is with the use of hot tubs or Jacuzzis where a drop in blood pressure and syncope have been reported (38–40).

In addition to the conduction effects of fluids, there can be local effects. Prolonged or repeated exposure to water, especially if combined with agents that replace oils of the skin, can result in dyshidrosis. The skin develops a rash of small papules or blisters that can crack and become infected. Typically the hands are involved, but the same process can occur in the feet. Exposure to mud or sludge has been associated with skin disease that may be from bacterial, viral, or parasitic infections. The condition is made worse if there are abrasions of the skin (41,42).

Cold Water Immersion Foot Syndromes (Trench Foot)

The immersion foot syndromes are a group of skin effects of moisture or immersion that typically involve the lower extremity. Trench foot, so called from military experience in trench warfare, is the result of wet and cold conditions without immersion typically over a period of days. Patients present with pain, numbness, and paresthesia, and the condition can become severe, lasting for weeks to months. Various pathological change occur, including thrombosis and capillary rupture. Treatment includes removal from wet conditions, dry clothing, elevation of feet, and rewarming. Antibiotics are often given (42).

Immersion foot typically occurs with cold water immersion for hours to a day, as in working in bogs without appropriate rubber boots. Symptoms and treatment are as for trench foot (42).

Warm Water Immersion Syndromes

Paddy Foot

Tropical immersion foot, some times called paddy foot occurs after continuous or near continuous exposure of the foot to water or mud at temperatures above 22˚C (71.6˚F) for 2 or more days. Burning and itching are the first symptoms, but walking becomes increasingly painful. The foot is swollen, and if the shoe is removed, it may not be able to be replaced. There is redness of the dorsum of the foot. Papules or vesicles, lymph node involvement into the groin, and fevers can develop. Treatment is to allow the feet to dry until the symptoms subside (42).

Moon Boot

Warm water immersion foot is also seen in use of insulated boots without water exposure: the moon boot syndrome. The skin on the soles and sides of the foot become thickened, wrinkled, and macerated. Pain develops, and walking becomes difficult. Treatment includes allowing overnight drying of the feet and barrier gels (42).

References

1. Soultanakis-Aligianni H. Thermoregulation During Exercise in Pregnancy. Clin Ob and Gyn. 2003;45:442–55.
2. Mechem C. Severe hyperthermia: Heat stroke; neuroleptic malignant syndrome; and malignant hyperthermia. UpToDate;2004 (online).
3. Lloyd E. ABC of sports medicine: Temperature and performance II: Heat. Brit Med J. 1994;309:587–9.
4. Bouchama A, Knochel J. Medical Progress: Heat Stroke. New England J of Med. 2002;346:1978–88.

5. Pirko M, Palmieri T, Greenhalgh D. Car seat heaters: A potential hazard for burns. J of Burn Care & Rehabilitation. 2003;24:315–6.
6. Rosenfield L, Pitlyk P. Intraoperative burns secondary to warmed IV bags: A warning. Anesthesiology. 1999;90:616–8.
7. Kao C, Garner W. Acute burns. Plastic & Reconstructive Surgery. 2000;105:2482–93.
8. Sheridan R. Burns. Critical care medicine. 2002;30:S500–14.
9. Ada S, Bora A, Ozerkan F, Kaplan I, Arikan G. Rolling belt injuries in children. J of Hand Surgery-Brit. 1994;19:601–3.
10. Wexler RK. Evaluation and treatment of heat-related illness. Amer Fam Physician. 2003;67:1349–50.
11. Galloway SD, Maughan RJ. Effects of ambient temperature on the capacity to perform prolonged cycle exercise in man. Med Sc Sports Exerc. 1997;29:1240–9.
12. Ellis FP. Heat illness II: Pathogenesis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1977;70:412–8.
13. Tobin J, Jason D, Challa V, Nelson T, Sambuughin N. Malignant hyperthermia and apparent heat stroke. JAMA. 2001;286:169–73.
14. Pugh K, Pienkowski D, Gorczyca JT. Musculoskeletal trauma in tobacco farming. Orthopedics. 2000;23:141–3.
15. Tikuisis P, Mclellan T, Selkirk G. Perceptual versus physiological heat strain during exercise-heat stress. Med & Science in Sports & Exercise. 2002;34:1454–61.
16. Gaie M. Olympic athletes face heat, other health hurdles. JAMA. 1996;276: 178–80.
17. Sawka M. Convertino V, Eichner E, Schnieder S, Young A. Blood Volume: Importance and adaptations to exercise training, environmental stresses, and trauma/sickness. Med Sc Sports Exerc. 2000;32:332–6.
18. Watt M. Garnham M, Febbraio A, Hargreaves M. Effect of acute plasma volume expansion on thermoregulation and exercise performance in the heat. Med Science Sports Exerc. 2000;32:958–62.
19. Allison S, Lobo D. Fluid and electrolyte in the elderly. Clin Nutr Metabolic Care. 2004;7:27–33.
20. Maughan RJ. Exercise in the heat: Limitations to performance and the impact of fluid replacement strategies. Introduction to the symposium. Canadian J of Applied Physiology. 1999;24:149–51.
21. Maughan RJ. Fluid Balance and Exercise. Int J Sports Medicine. 1992;13: S132–5.
22. Sawka M, Latzka W, Montain S, Cadarette B, Kolka M, Kraning K, Gonzalez R. Physiologic tolerance to uncompensable heat: Intermittent exercise, field vs laboratory. Med Sc Sports Exerc. 2001;33:442–30.
23. Department of the Army. FM 21-10-Field Hygiene and Sanitation, Chapter 3: Leaders' Preventive Medicine Measures. Virtual Navel Hospital. http://www.vnh.org/FM21-10/ch3.html.
24. U.S. Army Research Institute of Environmental Medicine. Management of Heat Illness. Virtual Naval Hospital. http://www.vnh.org/HeatIllness/manageht.html.
25. Bishop PA, Pieron RE, Smith JF, Constable SH. Limitations to heavy work at 21 degrees centegrade of personnel wearing the U.S. military defense ensemble. Aviat Space Environ Med. 1991;62:216–20.
26. Tuure VM. Cold working environments on dairy farms in Finland. Int J Circumpolar Health. 2003;62:190–203.

27. Mechem C. Accidental hypothermia. UpToDate 2004.
28. Messing K, Saurel-Cubizolles MJ, Bourgine, M, Kaminski M. Menstrual-cycle characteristics and work conditions of workers in poultry slaughterhouses and canneries. Scandinavian J of Work, Environment and Health. 1992;18:302–9.
29. Mallet M. Pathophysiology of accidental hypothermia. Quarterly J of Med. 2002;95:775–85.
30. National Weather Service, Office of Climate, Water, and Weather Services. Wind Chill Chart. 2004; online. http://www.nws.noaa.gov/om/windchill/.
31. Center for Disease Control and Prevention. Extreme Cold: A prevention guide to promote your personal health and safety. National Center for Environmental Health, Atlanta GA, 2001.
32. Department of the Navy Bureau of Medicine and Surgery. Cold Injuries. General Medical Office (GMO) Manual: Clinical Section: Environmental Injuries. Virtual Naval Hospital. 1999; http://www.vnh.org/GMO/ClinicalSection/*17ColdInjuries.html.
33. Young A, Roberts D, Scott D, Cook J, Mays M, Askew E. Sustaining Health & Performance in the Cold, Technical Note No. 92–2. Natick, MA: US Army Research Institute of Environmental Medicine, 1992.
34. Department of the Army, GTA 8-6-12 Adverse Effects of Cold. Virtual Naval Hospital. 1985; http://www.vnh.org/GTA/GTA6812.html.
35. Curtis R. Outdoor Action Guide to Hypothermia and Cold Weather Injuries. National Ag Safety Database, 1995. http://www.cdc.gov/nasd/docs/d001201-d001300/d001216/do1216.html.
36. Cold Injury. In: Merck Manual. Rahway, NJ: Merck and Company, 1995–2004.
37. Graber M. Emergency Medicine: Burns, cold, and thermal injury. Iowa City, IA: University of Iowa Family Practice Handbook, 4th edition, 1992–2004.
38. Doubt T. Cardiovascular and thermal responses to SCUBA diving. Med Sc Sports Exerc. 1996;28:551–86.
39. Sykes J. Fortnightly Review: Medical aspects of SCUBA diving. Brit Med J. 1994;308:1483–8.
40. Shin T, Wilson M, Wilson T. Are hot tubs safe for people with treated hypertension? Canadian Med Assoc J. 2003;169:1265–8.
41. Adler A, Altman J. An outbreak of mud-wrestling-induced pustular dermatitis in college students: Dermatitis palaestrae limosae. JAMA. 1993;269:502–4.
42. Adnot J, Lewis C. Immersion foot syndromes. In: Military Dermatology. Washington, DC: Office of the Surgeon General, Armed Forces Institute of Pathology, 1994.

34

Injuries from Electromagnetic Energy

Stephen A. McCurdy

Key words: electrocution, electromagnatic energy, non-ionizing radiation, ionizing radiation

Injury occurs when body tissues are subjected to levels of energy outside the normal tolerance bands. Excessive energy damages tissues, potentially beyond repair, and disrupts normal physiologic functioning. Injury may also occur when inadequate energy is available, such as extreme cold leading to frostbite injury, or disruption of normal cellular energy systems such as asphyxiation. Energy may be in the form of mechanical energy (e.g., moving parts of machinery), chemical energy (e.g., caustic substances), heat, potential energy (e.g., working at heights; with a fall, the potential energy is converted into mechanical energy as the subject strikes the ground), and electromagnetic energy (e.g., electricity, radiation). The agricultural work environment contains many sources of energy, and agriculture is widely recognized as one of the most hazardous industries in the United States (1–4).

Electromagnetic Energy

Electromagnetic energy is carried at low frequencies in electrons. The energy supplied by electrons is determined by the voltage (the force acting to push electrons through a conductor) and the flow of electrons, known as current. Current flow is measured in amperes or milliamperes (mA). Common residential and industrial machinery uses alternating current, indicating that the flow of electrons alternates in direction, typically at a frequency of 60 cycles per second, or 60 hertz (Hz). A battery, in contrast, supplies direct current, indicating that the flow of electrons proceeds in only one direction.

When the frequency of alternation of current flow is high, the electromagnetic energy can escape its conductor and radiate into space, traveling at the speed of light. Here the energy is carried by photons rather than electrons. The behavior and properties of this electromagnetic energy are determined largely by its frequency. The electromagnetic spectrum includes, in order of

increasing frequency, radio waves, microwaves, infrared (heat) radiation, visible light, ultraviolet radiation, X-rays, and gamma rays.

X-rays and gamma rays have extremely high frequency and energy content. As a result, this radiation can strike molecules in the body, knocking away electrons and leaving a damaged, electrically charged (i.e., ionized) remnant. Ionized molecules raise the risk of subsequent mutations and cancer. Accordingly, such high-frequency radiation is termed *ionizing radiation* and has been associated with increased cancer risk. Lower frequency radiation, such as radio waves, visible light, and microwaves, does not cause ionization, and is termed *nonionizing radiation*. Damage from nonionizing radiation is usually due to simple heating of tissues.

Nonionizing Electromagnetic Energy Sunlight

The most abundant form of environmental electromagnetic radiation is sunlight. The sun emits a broad spectrum of radiant electromagnetic energy. Frequencies in the visible light range penetrate the atmosphere and allow us to see. Radiation at frequencies just above the violet, or high-frequency, end of the visible light spectrum can have important health effects. Such ultraviolet radiation can cause acute sunburn. Chronic exposure to ultraviolet radiation prematurely ages the skin and increases the risk for skin cancers. Sunlight-related injuries are an important problem for agricultural workers because of the need to work outdoors.

Prevention of Sunlight Injuries

Reduction of exposure to direct sunlight is the simplest and most effective protection against sunlight-related injury. When work must be done in direct sunlight, workers should wear protective clothing, including long pants, long-sleeved shirts, gloves, and broad-brimmed hats to shade the face and neck. This may be uncomfortable on hot days, and workers should be careful to drink plenty of fluids and rest as needed so as to avoid heat exhaustion and sunstroke. Sunscreen should also be used.

Welding Flash Burns

Welding is a common activity in the agricultural work environment; its health effects have recently been thoroughly reviewed. Welding involves heating pieces of metal such that they liquefy and join together. Energy to raise the temperature of the metals may come from electricity (electric arc welding) or from the burning of gases such as acetylene. Temperatures reach several thousand degrees Celsius, and the process generates electromagnetic radiation across a wide frequency spectrum. Electric arc welding generates large

amounts of ultraviolet radiation. This can lead to an acute keratoconjunctivitis ("arc eye"), acute skin burns ("flash burns") similar to sunburn, and chronic skin damage. The most commonly affected body parts are the face, neck, hands, and forearms. Radiant heat carried by infrared electromagnetic energy may also cause burns and skin damage (5).

Prevention of Welding Flash Burns

Welders should wear protective equipment to shield from ultraviolet radiation. Long-sleeve upper-body clothing, gloves, and a welding helmet with ultraviolet filter plates for arc welding will minimize exposure and injury. Welding equipment should be well maintained and properly grounded to prevent electrocution injury.

Electrocution Injury

The most common source of severe electromagnetic injury on the farm is electricity carried in conducting wiring and used for machinery, light, and heating. Electricity causes injury through several mechanisms. Voltage and current flow disrupt nerve and muscle function. Electrical current stimulates contractions in both flexor and extensor muscles. At currents above 16 mA, the stronger flexor muscles predominate, rendering the victim unable to let go of an energized object they have grasped. Currents of 20 mA may lead to paralysis of respiratory muscles and death. Current at 100 mA leads to ventricular fibrillation, lower currents may also lead to fatal cardiac arrhythmias. Current at 2 Amperes and above leads to cardiac standstill and internal organ damage (6).

Conduction through the body is facilitated by moist conditions, such as contact with standing water and wet skin or clothing. Under dry conditions, the resistance of the body may be sufficient to limit current flow from a 120-volt source to 1 mA, a barely perceptible amount. Under wet conditions, resistance may be lowered to allow over 100 mA of current flow, sufficient to cause cardiac fibrillation. Skin damaged by electrical burns suffers further reduction in resistance, leading to increased current flow and injury (6).

Epidemiology of Electrocution in Agricultural Workers

Data from the United States Bureau of Labor Statistics Census of Fatal Occupational Injuries (CFOI) for 1992 to 1999 show a total of 2,525 occupational electrocution deaths among all occupations, yielding a mortality rate of 0.23 deaths/ deaths/10^5 worker-years. With respect to ethnicity, the highest rate was seen among Hispanics (0.30 deaths/10^5 worker-years), an important observation because a majority of hired workers in agriculture are Hispanic. Of all occupational electrocution deaths, 320 (12.7%) occurred in agricul-

tural, forestry, and fishing occupations. The number of such deaths in agricultural, forestry, and fishing occupations was exceeded only by those in the construction trades (988 deaths) and transportation and material moving occupations (517 deaths). When these deaths are expressed as mortality rates, the rate for agriculture, forestry, and fishing occupations (1.16 deaths/10^5 worker-years) is exceeded only by extractive (mining) occupations (2.38 deaths/10^5 worker-years) and construction trades (2.10 deaths/10^5 worker-years) (7,8).

Within agriculture, the majority of deaths occurred among farm workers (92 deaths, 1.24 deaths/10^5 worker-years) and groundskeepers and gardeners (91 deaths, 1.50 deaths/10^5 worker-years). While only 11 deaths occurred among supervisors of farm workers, this group demonstrated the highest mortality rate within agriculture (3.41 deaths/10^5 worker-years) (7,8).

Common Electrocution Injury Scenarios in Agriculture

Electrocution injury occurs when a worker comes into contact with an electrically energized source. Risk for electrocution rises when electrical networks and equipment are improperly designed, built, or maintained. Poorly grounded machinery and tools are a common source of electrocution. Workers come into physical contact with the faulty machinery, which carries an electric charge that flows to the ground through the worker's body. Risk is heightened for work in standing water, such as around pumps or on damp ground.

A second common scenario involves accidental contact with power lines. Overhead power lines typically carry between several hundred to several thousand volts, which is stepped down through transformers at various stages to bring either 220 or 110 volts to the point of use. Accidental contact can occur when lines are insufficiently elevated above ground or drop due to wind, storms, or inadequate maintenance. Electrocution injuries also have occurred when workers accidentally brush against the lines with metal ladders, pipes, or other tools. Damaged or weathered line insulation may prove inadequate to prevent current flow through the metal tool and ultimately to the ground through the worker's body. Metal booms and cranes may also contact lines and electrocute workers who come in to contact with them. Grain augers, when moved in an elevated position, may be able to contact high-voltage lines (6,9).

Prevention of Electrocution Injury

NIOSH described a series of 224 fatal electrocution incidents from 1982 to 1994 and noted that at least one of five factors was present for all cases. These included:

1. Failure to follow safe work procedures
2. Failure to use required personal protective equipment

3. Failure to follow lock-out/tag-out procedures
4. Failure to comply with existing OSHA, or recognized electrical safety code regulations
5. Inadequate safety training (10).

Prevention of electrical injury requires involvement by employers and employees. Electrical equipment should be inspected for safety and proper grounding on a periodic basis. This is especially important for equipment used for water or wet circumstances, such as pumps. Failsafe mechanisms that automatically shut off power to machinery when casings are opened should be incorporated in the design and not defeated by the operator. Workers should be certain that power is shut off before beginning maintenance work on electrical equipment. Electrical hand tools should be in good repair and properly grounded with a three-wire electrical system or have doubly insulated casings. Ground-fault circuit interrupters, which halt current flow when current to ground is detected (e.g., through the body of the tool operator), add further protection. Workers should wear dry gloves when operating electrical machinery, especially hand tools such as drills and sanders. In some settings, rubber insulated gloves are appropriate. Grain augers should be in the lowered position when moving to prevent contact with overhead high-voltage wires. Metal ladders should not be used in areas where there is a risk of contact with power lines. Request that the power company de-energize lines, if feasible, where there is risk of contact (6).

A comprehensive description of electrical safety regulations and recommendations is available in Subpart S 29 CFR 1910.302 through 1910.399 of the General Industry Safety and Health Standards. Subpart K of 29 CFR 1926.402 through 1926.408 of the OSHA construction safety and health standards address electrical equipment and installations used to provide electric power and light at the jobsite. The United States National Electric Code and National Electrical Safety Code comprehensively address electrical safety regulations. Most other countries have similar codes (11,12).

Lightning Injury

Lightning injury is an extreme form of electrocution injury. Tremendous voltages build up between the atmosphere and the earth, typically discharging in a spark striking high points, such as buildings or trees. The arcing electricity causes instantaneous superheating of the air, resulting in an explosive flash of visible lightning and thunder.

Agricultural workers are at risk for lightning strikes because of their outdoor work. Lightning may cause injury through a direct strike, which is usually fatal, or indirectly through current flows that occur in the vicinity of a strike. Indirect electrocution from lightning often causes burns but is not necessarily fatal.

Outdoor work should be halted during lightning storms. Workers caught outdoors in a lightning storm should take shelter in a building or car. If shelter is unavailable, they should seek low ground, such as gullies, and keep low. Workers should not remain on farm machinery such as tractors and should get out of the water if swimming or boating. It is unwise to seek shelter under lone or prominent trees or other objects. Tools, especially long tools like hoes or metal ladders, should not be carried.

Lightning may also cause injury indirectly by downing trees, power lines, or starting fires. Downed power lines should not be handled. If a downed power line strikes a car, the occupant should avoid contact with metal in the car and drive away if possible. If this is not possible, it is safest to remain in the car, avoiding contact with metal, until the line is deenergized.

Ionizing Radiation

Ionizing radiation is uncommon in agricultural settings. Ionizing radiation may be used in food sterilization and decontamination procedures. Excessive exposure to ionizing radiation may lead to acute or chronic radiation sickness. Rapidly dividing cells, such as the lining of the gastrointestinal tract and blood-generating cells in the bone marrow, are particularly sensitive to radiation exposure. Hence, acute radiation sickness is characterized by gastrointestinal disturbances, bleeding due to platelet loss, infections due to immune-system damage, and anemia. Exposed skin may suffer acute burns and subsequent scarification. Chronic radiation exposure may be associated with cancer and reproductive abnormalities. Prevention of illnesses and injuries from ionizing radiation involves eliminating or minimizing exposure. Radiation sources should be properly shielded and radiation exposures monitored. Persons not educated in working around such sources should not have access.

References

1. Robertson LS. Injury Epidemiology. New York, NY: Oxford University Press, 1992.
2. Hard DL, Myers JR, Gerberich SG. Traumatic injuries in agriculture. J Agric Saf Health 2002;8:51–65.
3. McCurdy SA, Carroll DJ. Agricultural injury. Am J Ind Med 2000;38:463–80.
4. Rautiainen RH, Reynolds SJ. Mortality and morbidity in agriculture in the United States. J Agric Saf Health 2002;8:259–76.
5. Antonini JM. Health effects of welding. Crit Rev Toxicol 2003;33:61–103.
6. National Institute for Occupational Safety and Health. Preventing Electrocution of Workers Using Portable Metal Ladders Near Overhead Power Lines. DHHS (NIOSH) Publication No. 89–110. Morgantown, WV: NIOSH, 1989.
7. Taylor AJ, McGwin G Jr., Valent F, Rue LW 3rd. Fatal occupational electrocutions in the United States. Inj Prev 2002;8:306–12.

8. Meister JS. The health of migrant farm workers. In: Cordes DH, Rea DF, eds. Occupational Medicine State of the Art Reviews: Health Hazards of Farming. Philadelphia, PA: Hanley and Belfus, Inc., 1991;6:503–18.
9. National Institute for Occupational Safety and Health. Preventing Grain Auger Electrocutions. DHHS (NIOSH) Publication No. 86–119. Morgantown, WV: NIOSH, 1986.
10. National Institute for Occupational Safety and Health. Worker Deaths by Electrocution: A Summary of NIOSH Surveillance and Investigative Findings. DHHS (NIOSH) Publication No. 98–131. Morgantown, WV: NIOSH, 1998.
11. National Fire Protection Association. National Electric Code. Quincy, MA: National Fire Protection Association, 2005.
12. American National Standards Institute. National Electrical Safety Code. New York, NY: American National Standards Institute, 2002.

35

Acoustic Injuries in Agriculture

James E. Lankford and Deanna K. Meinke

Key words: noise hazards, hearing loss, hearing tests, equipment noise reduction

It is paradoxical that the quiet rural farm is also the same environment where periods of high intensity noise may result in hearing loss among agricultural workers. The U.S. National Institute of Occupational Safety and Health (NIOSH) estimates that noise is a significant occupational health hazard for 84% of the agricultural workforce. Since health and safety professionals may encounter agricultural workers with concerns about hearing loss prevention, hearing loss identification and hearing rehabilitation, this chapter was written to inform the reader about these issues as they relate to farming (1).

Noise Hazards

Typically, sound becomes hazardous to the inner ear when the intensity and duration of the exposure exceed a particular criterion level. In industry, the levels of 85 to 90 dBA are considered hazardous to workers exposed to noise for an 8-hour work. However, high level sounds (>100 dBA) are especially hazardous even for brief periods of time (< 15 minutes). Agricultural workers may find themselves at an increased risk for noise-induced hearing loss (NIHL) during the long hours of equipment operation at certain times of the year due to seasonal demands on work schedules (2,3).

Farmers operate a variety of equipment capable of producing hazardous sound levels. Table 35.1 is compiled from research studies and investigations and lists most of the common noise sources and levels (in dBA) reported in the farm environment (4–7). Farmers rank ordered the loudest noise sources on the farm as follows: tractors, grain dryers, combines, chainsaws, grain grinding, and animals. One agricultural noise source rarely catalogued but frequently associated with farming is firearm noise. The majority (84% to 90%) of farmers do report having firearm noise exposures. These peak sound pressure levels (SPL) can range from 143 dB to 173 dB depending on the gauge or

TABLE 35.1. Typical noise sources and sound levels in farming.

Noise source	Noise levels (dBA)
Tractor	74–112
Grain dryer	81–102
Combine	80–105
Chainsaw	77–120
Grain grinding	93–97
Pig squeals	85–115
One-row beet puller	94
Orchard sprayer	85–106
Pneumatic conveyor	100
Riding mower	79–89
Garden tractor	88–94
Shotguns and rifles	143–173 (Peak)
Crop dusting aircraft	83–116

Sources: Data from Lankford, Zurales et al. (6), Dobie (5), and Lankford et al. (7).

caliber fired. These findings indicate that in addition to the typical farm noises, firearm noise is a component of most farmers' noise exposure profile. In addition, farmers (58%) commonly reported high levels of noise exposures outside the farm. These additional exposures include noise from non-agricultural employment settings as well as hobbies or entertainment (4–9).

Hearing Test Results

Numerous studies documenting NIHL in the farming population have been published. The NIHL is characteristically bilateral, sensory-neural (due to inner ear/cochlear damage) in nature with a greater degree of hearing loss in the higher frequencies than the lower test frequencies. It is common to find a notched audiometric configuration (noise notch) with greater loss at 3000, 4000, or 6000 Hz than at the adjacent frequencies. Figure 35.1 shows the hearing sensitivity of 2,695 males from a large farming community, by age decade, which were obtained in a 10-year cross-sectional study conducted in the Midwestern United States. The majority of the farmers came from Illinois, Iowa, and Indiana, but 34 states and 4 foreign countries were represented. The characteristic notched configuration disappears from the audiometric profile for most farmers at age 70 years and beyond as the hearing loss at 8000 Hz progresses. This is attributed to the presumed accelerated aging effect (presbycusis) in the later years. Between the ages of 20 to 60 years, farmers show dramatically more high frequency hearing loss than would be expected for their non-noise exposed peers after subtracting an age correction factor for each frequency as identified by OSHA 29CFR 1910.95 or ISO 1990: B.5. Unfortunately, the ability to differentiate the magnitude of NIHL from farm noise versus all other sources of noise exposure is more complex (2,4,9,10–16).

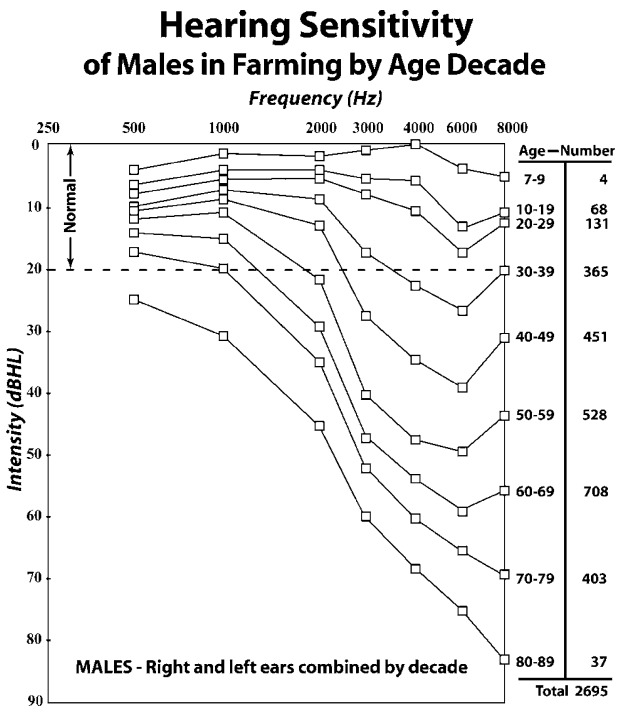


FIGURE 35.1. Progression of noise-induced hearing loss for males in farming over lifespan. (From Lankford, Zurales, Garrett & DeLorier, *Advance for Audiologists* 4(5):34–37, 2002 by permission of Merion Publications Inc.)

Another intriguing characteristic of the NIHL of farmers is an apparent difference in the magnitude of the loss at the higher frequencies (2000 to 8000 Hz) between ears. On average, there is about 3 dB more hearing loss noted for the left ear than for the right ear. Three explanations have been offered for this observed difference. First, is the left ear position relative to the noise source. For example, on a tractor without a cab, it is not unusual for the farmer to position the left ear forward while looking backward to monitor the pulled implement (plow, disc, rake, hoe, etc.). This places the left ear in a more direct exposure path to the noise from the engine. In addition, cab doors (until recently) on tractors and combines have been traditionally on the left side and provide a potential avenue for sound leakage from that direction. Several equipment manufacturers are now producing tractors with doors on both sides of their equipment. Second, the ear difference may be due to the high incidence (90 %+) of firearm noise exposure among this population. Because most individuals are right handed and long guns (rifles and shotguns) place the left ear in a position facing the muzzle blast, the left ear is at greater risk than the right ear, which may be partially shielded due to a head-shadow effect from the blast. Lastly, the third reason

might relate to a possible anatomical/physiological difference which may make one ear more sensitive and/or vulnerable to damage than the other (8).

Women and adolescents engaged in farming activities are also at risk for NIHL. In general, the audiometric configuration and progression of the hearing loss is similar to that of males, but the magnitude is significantly reduced. Theiler reported that 75% of females in her study reported high-intensity noise exposure from farm machinery, some beginning as young as 10 years of age. It was also noted that women may be receiving increased exposures due to greater involvement in the noisy work on the modern farm. Early reports of NIHL among children and adolescents on the farm indicate that noise notches can be seen in this younger population as well. The distinction between home and work noise exposures can be ambiguous for the rural farm family. It is not uncommon for young children to accompany their parents on tractors or for adolescents, especially males, to begin operating large noisy machinery at a young age (17,18).

Equipment Noise Reduction

Noise control or the elimination of hazardous noise from the farm environment is the ideal solution for the prevention of NIHL. To their credit, many equipment manufacturers have incorporated quiet design specifications in recent years, some in response to the need for regulatory compliance with national or international standards such as the European Union Directive 98/37/EC. For example, cabs on farm equipment are both a source of comfort and safety for the farmer. Essentially, all contemporary combines have cabs though many older and smaller tractors do not. An important cab enclosure benefit is the exclusion of hazardous noise. Most comparative sound level assessments demonstrate a 20 dB reduction in noise levels for equipment with original cabs, which are well maintained and kept in good working condition. However, for older equipment many small farm operations or those in more underdeveloped countries, economics may preclude the upgrade to newer and quieter equipment. Consequently, personal hearing protection (earplugs/earmuffs) is the realistic alternative for many farmers (19,20).

Personal Hearing Protection

The majority of male farmers do not report using hearing protection on a regular basis. Initial survey results from 1989 indicate only 30% reported using hearing protection devices (HPDs). This percentage rose to 44% when resampled 10 years later. Only 24.6% of high school students reportedly used hearing protection in an agricultural safety intervention study. However, in the Theiler study, a fairly high percentage of women (78%) were using HPD's in noisy environments. Engstrand, investigated the usage of hearing protec-

tors and whether they were reducing the amount of hearing loss among male farmers. Fifty farmers who consistently used HPD's were paired with a group of non-users; the results showed that significantly less hearing loss occurred for farmers who had worn protectors. Since firearm noise exposure is quite pervasive in the farming population and the exposure levels are so high, HPDs should be utilized for this activity as well. There are specialized HPDs designed for firearm noise sources that afford protection while maintaining adequate communication during shooting activities. These devices include passive earmuffs, electronic earmuffs, and both passive and electronic custom earplugs. Although the costs for the electronic and custom protectors are relatively high, the benefits should be considered priceless (21,22).

For some farmers, the issue may not be whether to wear hearing protection but rather which type of hearing protector to choose. With over 400 varieties of hearing protection databased on the electronic NIOSH Hearing Protector Device Compendium, the need for technical and practical guidance for proper selection is evident. In general, the laboratory-based Noise Reduction Rating (NRR) is a poor guide to real-world protection. Ideally, the best hearing protector is the one the individual will wear routinely because it is comfortable, effective, and compatible with working conditions as well as communication demands (23).

Intervention Strategies

Farmers are often located in rural, isolated environments. Therefore their access to information and services concerning hearing loss prevention is geographically restricted. One approach that has proven successful in reaching farm families is to make information and services available at state and county fairs, regional farm shows, and health screenings sponsored by farm agencies, medical clinics, universities, and hospitals.

One successful U.S. outreach program was held at the Farm Progress Show over a 10-year period. This show attracted over 250,000 annually during the 3-day event. The primary attraction for farmers included the equipment manufacturers, seed companies, chemical producers, university agricultural school displays, and various demonstration plots. However, coordinated efforts by health and safety professionals allowed for respiratory, blood pressure, cholesterol, vision, skin, and hearing assessments. Mobile audiometric testing facilities made the hearing assessments personal, convenient, efficient, and valid. It also afforded the opportunity to distribute sample hearing protectors, hearing loss prevention literature, and hearing test results. Farm family members were immediately counseled regarding their hearing status and advised of any referrals for medical and/or rehabilitative hearing services. One additional outcome of this particular intervention program was the enhanced usage of hearing protectors as documented by Pytko (24). When male participants were surveyed one

year after the farm show intervention program, the utilization of HPDs had increased from 37% to 73% (6,24).

Another intervention approach has been used in Canada. Hearing loss prevention literature was mailed to farmers in rural areas in Saskatchewan. For those who inquired, hearing tests were subsequently provided at a local community site. During the hearing test appointments, health professionals were able to provide additional information about noise exposure, hearing loss prevention strategies, and the proper use of hearing protectors (25).

Two other recent approaches designed to disseminate hearing loss prevention information include the farm safety camp and the Internet. Farm safety camps are designed to reach farm youth. Hearing safety can be one of the many sessions offered during these interactive camps, and it can be formatted into an entertaining, game activity. Certainly the Internet affords the farming community with new and ever-changing opportunities to access educational materials and health information. As with most internet topics, the reliability, validity, and continuity of these hearing loss prevention materials are varied. The National Hearing Conservation Association (NHCA) website (*www.hearingconservation.org*) offers professional educational opportunities and a variety of resources for hearing loss prevention efforts (26).

Recommendations

It is apparent and not surprising that NIHL is a very large part of the personal lives of most farmers. Therefore, annual hearing tests should begin in the rural farming communities at 10 years of age. Hearing should be monitored on an annual basis throughout a farmworker's life. It is recommended that educational programs regarding hearing loss prevention should start in elementary school and continue through the 12th grade. It is also suggested that audiologists provide hearing tests at farm shows and other public agricultural events as a way of identifying individuals with existing hearing loss or those with a potential risk for NIHL.

Free earplug samples and hearing protection literature should be included in most intervention programs targeting farmers. This introduces the farm family to HPDs and allows them to use a protector the next time they are exposed to high intensity noise. It is important that the farmers be informed of local, regional or mail-order resources for purchasing additional hearing protection once the outreach effort is completed.

A large percentage of farmers have substantial NIHL hearing loss and will experience the personal and social consequences of the impairment. Consequently, it is important that any outreach effort include strategies to motivate farmers to accept their hearing loss and seek rehabilitative help, including the purchase of hearing aids. Local medical and audiological professional resources should be identified in advance of the intervention effort.

Female members of the farm family appear to have the most influence on the acquisition and utilization of health services for their spouses and children. Therefore, hearing loss prevention and hearing rehabilitation education should directly involve the woman in the farm family. She may be in the best position to encourage family members to practice better health protective behaviors, such as the regular and proper use of hearing protectors. Encouragement and praise appear to be needed to reinforce healthful behaviors (27).

Ultimately, each of us has a potential role to play in the effort to identify hazardous agricultural sound, decrease individual noise exposures, and minimize the long-term personal, social, and financial impact of hearing-impairment on farm workers. Every farmer, regardless of age, deserves the opportunity to appreciate the rural farm soundscape, filled with early morning bird songs, wheat beards brushing in an afternoon breeze, and cricket chirps signaling the end of a long day in the field.

Acknowledgment. Portions of this chapter were published in *Advance for Audiologists* 4(5): 34–37 and are reprinted here with permission of Merion Publications Inc.

References

1. Franks JR, Stephenson MR, Merry CJ, ed. Preventing Occupational Hearing Loss – A Practical Guide. DHHS Publication No. 96–110. Cincinnati, OH: NIOSH, 1996.
2. Occupational Noise Exposure; Hearing Conservation Amendment; Final Rule. 29CFR 1910.95 Fed. Register.1983; 46 (162):42622–42639.
3. Criteria for a recommended standard: Occupational Noise Exposure Revised Criteria, DHHS Publication No. 98–126. Cincinnati, OH: NIOSH, 1998.
4. Lankford JE, Zurales SM, Garrett BRB. Hearing conservation for the agricultural community. In: Franks J, Casali J, ed. Proceedings Hearing Conservation Conference III/XX 1995 March 22–25, Cincinnati, OH. Des Moines, IA: Nat'l Hearing Conservation Association, 1995.
5. Dobie R. Medical-Legal Evaluation of Hearing Loss. 2nd ed. San Diego, CA: Singular, 2001.
6. Lankford JE, Zurales SM, Garrett BRB, DeLorier J. 10-year study of agricultural workers. Advance for Audiologists 2002; 4(5):34,36–37.
7. Lankford JE, Meinke D, Hotopp M. Need for hearing loss prevention for agricultural aerial application service personnel. Journal of Agromedicine, 2000; 6(2):25–39.
8. Kale D. Hearing loss among farmers: The effects of farm equipment and firearm noise. [Master's thesis], DeKalb (IL): Northern Illinois University, 1992.
9. Beckett WS, Chamberlain D, Hallman E, May J, Hwang S, Gomez M, Eberly S, et al. Hearing conservation for farmers: Source apportionment of occupational and environmental factors contributing to hearing loss. J of Occ Environ Medicine. 2000;42(8):806–13.

10. Lierle DM, Reger SN. The effect of tractor noise on the auditory sensitivity of tractor operators. Annals of Otology, Rhinology, Laryngology 1958;67:373–88.
11. Theilin JW, Joseph DJ, Davis WE, Baker DE, Hosokawa MD. High frequency hearing loss in male farmers in Missouri. Public Health Reports 1963; 98(3): 268–73.
12. Karlovich R, Wiley T, Tweed T, Jensen D. Hearing sensitivity in farmers. Public Health Reports 1988;103(1):61–71.
13. Plakke B, Dare E. Occupational hearing loss in farmers. Public Health Reports 1992;107(2):188–92.
14. Holt J, Broste S, Hansen D. Noise exposure in the rural setting. Laryngoscope 1993;103:258–62.
15. Stewart M, Scherer J, Lehman M. Perceived effects of high frequency hearing loss in a farming population. J of the Am Acad Audiology 2003;14(2):100–08.
16. International Organization for Standardization (1990a). Acoustics: Determination of occupational noise exposure and estimation of noise-induced hearing impairment. Geneva: International Organization for Standardization, 1990.
17. Theiler M. Hearing sensitivity of women in the farming community [Master's thesis]. DeKalb, IL: Northern Illinois University, 1996.
18. Broste S, Hansen D, Strand R, Stueland D. Hearing loss among high school farm students. Am J Public Health 1989;79:619–22.
19. Directive 98/37/EC of the European Parliament and of the Council of 22 June 1998 on the approximation of the laws of the Member States relating to machinery, Official Journal L 207, 23/07/1998, 0001–46.
20. Pessina D, Guerretti M. Effectiveness of hearing protection devices in the hazard reduction of noise from used tractors. J Agric Engineering Research 2000;75:73–80.
21. Reed DB, Kidd PS, Westneat S, Rayens MK. Agricultural disability awareness and risk education (AgDARE) for high school students. Injury Prevention 2001;7(Supp I):i59–62.
22. EngstrandL. Usage of hearing protective devices in farming: Do they work? [Master's thesis]. DeKalb, IL:Northern Illinois University, 1995.
23. NIOSH.gov [database on Internet] Cincinnati (OH): Centers for Disease Control; Hearing Protector Compendium. c2003 – [cited 2004 Aug 20]. Available from: *http://www.cdc.gov/niosh/topics/noise/hpcomp.html*
24. Pytko CM. Diffusion of hearing conservation into the farming community [Master's thesis]. DeKalb, IL: Northern Illinois University, 1990.
25. Lupescu C, Angelstad B, Lockinger L, McDuffie HH, Hage LM, Dosman JA, et al. Hearing conservation program for farm families: An evaluation. J Agric Safety Health 1999;5(3):329–37.
26. Lankford J, DeLorier J, Meinke D. Farm safety camp: Hearing loss prevention. Spectrum 2000;17(4):6–9.
27. McCullagh M, Lusk S, Ronis DL. Factors influencing use of hearing protection among farmers: A test of the pender health promotion model. Nursing Research 2002;51(1):33.

36

Reproductive Hazards

Robert L. Goldberg and Sarah Janssen

Key words: reproduction, biological, infertility, spontaneous abortion, preterm delivery, birth defects, low birthweight

Men, women, and children who live or work on farms around the world are exposed to many different types of potentially harmful agents that can interfere with reproductive development and function. Exposures to physical, chemical and biological hazards can occur during normal farm work from handling animals or their bodily fluids, working with chemicals or working in areas where chemicals have been used, and operating farm equipment.

Fertility, gestation, and pregnancy outcome are dependent on complex biological processes beginning early in life. Disruption of these processes can happen with environmental exposures *in utero* and throughout childhood development, as well as in adulthood through occupational and environmental exposures. Interference with development or functioning of the reproductive tract in males and females can result in diminished fertility, infertility, adverse pregnancy outcomes, congenital malformations, and childhood cancer.

Studies have documented associations between living or working in an agricultural area and adverse reproductive outcomes. Exposure to chemicals, mainly pesticides, has been linked to infertility and diminished fertility, spontaneous abortion, birth defects, and childhood cancer. A large number of studies suggest pesticide exposure is associated with these adverse reproductive outcomes, but few studies quantify the type of pesticide or measure exposure levels. Biomarkers of pesticides exposure have been measured in both male and female reproductive tracts, breast milk, and semen. Pesticides have also been measured in amniotic fluid, meconium, and cord blood, indicating the fetus is exposed to pesticides throughout development. These measurements provide some evidence to strengthen the association between pesticide exposure and reproductive outcomes but do not prove causality (1–6).

It is plausible that pesticides in semen may have direct effects on sperm or can be transmitted to the woman and fetus. Likewise, pesticides in the female reproductive tract could interfere with oocyte development, ovulation, fertilization, implantation, pregnancy, and development of the fetus. However,

there are no studies to date linking these biological measurements with adverse reproductive outcomes (1–6).

The term *pesticides* includes a wide variety of chemicals (see Chapters 13 and 16). In addition, many pesticide formulations contain solvents that have also been associated with reproductive toxicity. Adverse reproductive outcomes including decreased sperm count, infertility, testicular cancer, cryptorchidism, and hypospadias have been linked to widespread use of chemicals with hormonal properties, the so-called endocrine disruptors. A number of pesticides, especially organochlorines, have been identified as endocrine disruptors. In developing countries, workers are exposed to increasing amounts of pesticides, including some banned in prosperous countries. Prevention should include decreased total exposure by the elimination or reduction of chemicals, integrated pest management, proper personal protective equipment, and improved work practices (7–10).

Chemical Reproductive Hazards

Infertility in Males

Occupational and environmental chemical exposures in an agricultural environment have been associated with infertility in men. A number of pesticides have been associated with poor semen quality, including dibromochloropropane (DBCP), ethylene dibromide, carbaryl, chlordecone (Kepone), and 2, 4-D. The use of many of these pesticides has been banned or severely restricted (11–15).

There are a number of studies linking poor semen quality with pesticide exposure. In one well-designed study of environmental pesticide exposure, urine metabolites of pesticides were correlated to semen quality in known fertile men. Decreased semen quality was associated with exposure to the herbicides atrazine and alachlor and the insecticide diazinon. A study of men seeking infertility treatment in Argentina found pesticide exposure was associated with lower sperm counts and poor semen quality, although specific pesticides were not identified or measured. In a study of patients undergoing in vitro fertilization, high paternal pesticide exposure was associated with decreased fertilization rates. A study in Mexico demonstrated urinary metabolites of organophosphates were associated with an increased frequency of sperm sex-null aneuploidy and alterations in sperm chromatin structure. While there are no studies of semen pesticide levels and reproductive outcomes, it is plausible that poor semen quality could result in infertility or an increased time-to-pregnancy. Sperm chromosomal abnormalities could result in infertility, spontaneous abortion or birth defects (11,13,16,17,18).

High levels of pesticide exposures in pesticide applicators and greenhouse workers have been associated with increased time-to-pregnancy. The use of

pyrethoids has been similarly associated. However, a large multicenter study found no difference in time-to-pregnancy between traditional and organic farmers. Other studies have found no differences between time-to-pregnancy in greenhouse workers who use personal protective equipment compared to unexposed workers. Differences in working conditions, types of pesticides used, and levels of exposure may account for the discrepancis in these studies (19–22).

Infertility in Females

Although there are some reported associations between female infertility and agricultural work, there are no studies using direct exposure data to assess outcomes. Biomarker studies have measured pesticide residues in the female reproductive tract, indicating exposures and uptake are occurring in critical tissues, but there are no studies to date linking these measurements with infertility. High levels of p,p′-DDE, a metabolite of the pesticide DDT, were found in sera and follicular fluid samples of women attending an infertility program and were associated with poor fertilization rates (1).

There are a number of small studies where associations between working with pesticides and infertility or increased time-to-pregnancy were found. Fuortes found women were at an increased risk of infertility if they had worked in the agricultural industry or resided on a farm. In the same study, the risk of being diagnosed with an ovulatory or tubal cause of infertility was increased 4- to 16-fold among those working in agriculture (23–25).

Pregnancy Outcomes

Spontaneous abortion, defined as termination of pregnancy before 20 weeks gestation, has been associated with both maternal and paternal pesticide exposures. However, most studies have small numbers of subjects and do not classify or quantify pesticide exposure. A 3-fold increase in spontaneous abortions was found for paternal exposure to DBCP. A preliminary study of Chinese women found a weak association between serum DDE levels and increased incidence of spontaneous abortion. Studies in Ontario have suggested an increase in spontaneous abortions with paternal use of dithiocarbamates and carbaryl. A retrospective cohort study of farming households in the Phillipines found an increased risk of spontaneous abortion with increased pesticide use. A moderate increase in spontaneous abortion was observed in both female workers and the wives of male workers in the floriculture industry in Colombia. Other studies have found no association (26–31).

There are limited studies of the pregnancy outcomes of pre-term labor, small-for-gestational age, or low birth weight babies. The Ontario Farm Family Health Study found a weak association for mixing or applying herbicides and pre-term labor. However, other studies have not found any association

between parental pesticide exposure and pre-term labor. A recent study measuring maternal urinary and cord blood organophosphates and cholinesterase levels found a small decrease in gestational age but no association with intrauterine growth retardation (IUGR). A preliminary study found IUGR was associated with elevated levels of atrazine and other herbicides in drinking water in rural Iowa. A small but significant decrease in birth weight was associated with maternal pyrethoid use. Other studies have found no association with agricultural occupations and low birthweight (28–33).

Birth Defects

There are conflicting studies of the associations of agricultural work and pesticide exposure with birth defects. As in most studies examining reproductive outcomes and pesticide exposure, incomplete data are available on the types of pesticides associated with these defects and biomarkers of exposure. One large study of the Norway birth registry from 1967 to 1991 found activities involving high pesticide exposure and conception during times of high pesticide use (April to June) were associated with an increased risk of central nervous system defects, neural tube defects, limb reductions, and the genitourinary birth defects of hypospadias and cryptorchidism. Some studies have supported these findings while others have found risk estimates close to unity. Other studies have found an association with oral clefts and agriculture work. One difficulty in these studies is that the number of birth defects reported is very small and must be pooled for statistical power. Most of the studies on the risk of birth defects for paternal occupational exposures to pesticides do not find any associations or only small increased risks (31,34–40).

In Spain, maternal pesticide exposure during the first trimester was associated with an increased risk of central nervous system defects and oral clefts. Conventional pesticide use in the Phillipines was associated with increased risk of birth defects compared to low pesticide use (29,41).

Childhood Cancer

Although there is no strongly consistent evidence, a number of studies have found associations between childhood cancer and parental agricultural occupations or exposures. A large international study found associations between childhood brain tumors and various farm-related activities including maternal exposure to farm animals, working on a farm and pesticide exposure. In the same study, maternal exposure to pigs was associated with a 4-fold increase in risk of primitive neuroectodermal tumors. Other studies have found similar results. Chemicals, such as those found in a farm environment, and microbes that could be found in farm animals have been hypothesized to

cause childhood brain tumors. However, there is no direct evidence for this association (42–44).

Occupational parental pesticide use is associated with leukemia, childhood brain cancer, Wilm's tumor, and Ewing's sarcoma. Use of pesticides in gardens has been associated with childhood leukemia in Northern Germany and other countries. Other studies have found no association with paternal exposures to pesticides and childhood cancer. A large study of males born to parents engaged in agricultural activity between 1952 to 1991 in Norway found specific fertilizers were associated with an increased rate of testicular cancer, in particular, seminoma. Renal cancer has been associated with paternal exposure to pesticides in one small study (45–50).

Biologic Reproductive Hazards

A variety of organisms found in the agricultural setting have been associated with adverse reproductive outcomes, including miscarriage, stillbirth, congenital infections, and birth defects. These organisms include viruses, bacteria, and parasites associated with farm animals or working outdoors (51).

Toxoplasmosis

Toxoplasmosis gondii is passed to humans through contact with infected animal feces, usually cats, or ingestion of contaminated meat. Direct contact with cats does not usually result in infection; however, stray cats or cats roaming on farms may contaminate the environment with *T. gondii oocysts*. In 1977, an outbreak of acute toxoplasmosis occurred in a riding stable in Atlanta that was linked to inhalation of aerosolized oocysts shed by cats in the stable. A multicenter case-control study in Europe found contact with soil was a strong risk factor for toxoplasmosis infection, attributed to 6% to 17% of primary infections in humans.

Infections during pregnancy are transplacentally transmitted to the fetus and can cause fetal death or permanent neurological damage. In the United States, sero-positivity is about 15%, but in some African countries the prevalence approaches 80%. Reports of stillbirth caused by toxoplasmosis in developed countries are rare. However, in developing countries where the prevalence may be much higher the contribution is unknown. Pregnant women should avoid contact with cat feces and wear gloves when working in soil (51).

Q Fever

This rickettsial infection is caused by the bacteria *Coxiella burnetti* and is transmitted to humans during contact with infected parturient products, tick bites, and ingestion of infected dairy products. Cattle, sheep, and goats are

considered the primary reservoirs from which human infections occur. Human infections have been described worldwide and infections during pregnancy have been associated with abortion, stillbirth, low birthweight, and preterm labor. Atypical pneumonia and hepatitis are common presentations. A review of reported cases found two-thirds of untreated cases during the first trimester resulted in fetal death, while infection during the second trimester was associated with pre-term labor. Primary infection during the first 6 months of pregnancy is also associated with chronic infection. Long-term co-trimoxazole treatment can prevent fetal death but not the development of chronic infection. The overall contribution of Q Fever to poor pregnancy outcomes is unknown. Other rickettsial infections, such as Rocky Mounted Spotted Fever, have not been associated with poor pregnancy outcomes (51–54).

Psittacosis

A flu-like systemic infection caused by *Chlamydia psittaci*. Most cases of psittacosis result from inhaling infectious material from diseased birds. Infection can also result from contact with infected birth fluids and membranes of goats and sheep. Although human infection is rare, infections in pregnant women have been reported after exposure to birth fluids of otherwise healthy-appearing infected sheep and goats or through contact with birds. The majority of these cases resulted in fetal death due to spontaneous abortion or premature delivery (55–56).

Maternal infection can be severe, but full recovery usually occurs once the infant is delivered, although maternal death has been reported. Favorable outcomes can be achieved with prompt diagnosis and treatment, including emergency delivery of the infant when appropriate. Neonates are not always infected. Prevention includes avoidance of contact with membranes or birth fluids of sheep and goats or contact with birds during pregnancy. Strict personal hygiene should be practiced as the primary route of infection is oropharyngeal (56).

Brucellosis

This is caused by various species of the *Brucella* bacterium. Brucellosis is found worldwide and is transmitted to humans through direct contact with infected animals. Major reservoirs include goats and sheep (*B. melitensis*), swine (*B. suis*), cattle (*B. abortus*), and dogs (*B. canis*). Outcomes associated with infection during pregnancy are not well known and transmission to the fetus is speculated to occur through the placenta. Whether infection leads to fetal death is controversial. Manifestations of neonatal brucellosis include

low birth weight, fever, failure to thrive, jaundice, and hepatosplenomegaly. Antibiotic treatment during pregnancy may prevent abortion and premature delivery (57).

Leptospirosis

The causative organism, *Leptospira interrogans*, is a spirochete commonly found in Latin America. It is excreted in urine of infected animals and enters humans through non-intact skin, mucous membranes, and by inhalation and ingestion. It is usually a self-limiting disease, and, although rare in pregnancy, the organism has been detected in the placenta and amniotic fluid. Infections have been associated with fetal death in up to 50% of cases as well as active disease in newborn infants. Early diagnosis with urine and serological tests and treatment with antibiotics is critical (58).

Swine Influenza

This viral infection is thought to have been responsible for the worldwide pandemic that caused an estimated 40 million deaths in 1918 to 1919. During this epidemic, pregnancy was associated with a high mortality rate of over 50% if pneumonia was present. Since this pandemic, reports of swine influenza cases have been rare, with only sporadic case reports of human illness in the United States, Europe, and Russia. There is a case report of a previously healthy pregnant woman who acquired swine influenza while visiting a swine barn at a county fair. The swine were reported to exhibit influenza-like symptoms. The infection resulted in maternal respiratory failure and death, but the infant survived and was asymptomatic. There is no increase in influenza morbidity and mortality among pregnant women during non-pandemic years. Based on the few case reports and historical information from the swine flu pandemic of 1918, pregnant women are advised to avoid contact with swine that exhibit signs of respiratory illness (59).

Malaria

Infections during pregnancy result in a range of adverse pregnancy outcomes, especially pre-term delivery and IUGR. More than 40% of all births worldwide occur in areas with endemic malaria. Pregnant women experiencing a malaria infection for the first time are at high risk for stillbirth. Prevention is based primarily on environmental control, avoidance of mosquitoes, use of repellents, and bed netting. Repellents with DEET are considered safe for pregnant women (51).

West Nile Virus

West Nile Virus (WNV) is transmitted by infected mosquitoes. The reservoir exists in migratory birds and horses. Based on a limited number of cases, it is not possible to know if WNV infection in pregnancy results in neonatal infection or medical problems. Although one of the first reported cases of WNV infection transmitted via the placenta resulted in an infected infant with severe medical problems, it is unclear whether WNV infection caused these problems or whether they were due to other causes. A registry has been set up by the U.S. Centers for Disease Control to monitor cases of WNV infection in pregnant women. As of May 10, 2004, of the 74 women who acquired WNV while pregnant, 62 had delivered live infants, 2 had elective abortions, 5 miscarried in the first trimester, and 5 had not yet delivered. Because of ongoing concerns that intrauterine transmission can occur with possible adverse health effects, pregnant women are advised to take precautions to reduce their risk of infection by avoiding mosquitoes, especially during peak feeding times of dawn and dusk, wearing protective clothing, and using repellents. No specific treatment exists for WNV, and the consequences during pregnancy have not been well defined. Accordingly, it is not recommended that asymptomatic women be screened (60).

Lyme Disease

Caused by the tick-borne spirochete, *Borrelia burgdorferi*, Lyme disease is found in North America, Europe, Australia, China, Japan, and Africa. People who live or work in residential areas surrounded by tick-infested woods or overgrown brush are at risk. Lyme disease is a systemic illness that has been associated with stillbirth. The first cases were described in the mid-1980s, and the organism has been found in fetal organs. However, a large serological series found few adverse reproductive outcomes associated with Lyme disease. Preventive measures and early recognition of the disease are important. Early treatment with antibiotics decreases the morbidity from Lyme disease. In endemic areas, Lyme disease can be diagnosed if the typical "target" skin lesion is present even if serological tests are negative. Pregnant women should be treated with penicillin (51).

Physical Reproductive Hazards

Physical hazards in an agricultural setting that can impact reproductive outcomes are primarily associated with activities during pregnancy. Few studies have looked specifically at physical hazards in an agricultural occupation. A number of studies have associated poor pregnancy outcomes with activities

that are common in agricultural work: physical labor, heavy lifting, long hours, and shift work.

Jobs that involve an increase in abdominal pressure (bending and lifting), standing 6 or more hours per day, working more than 40 hours per week, and performing heavy lifting have been consistently associated with an increased incidence of spontaneous abortion and pre-term delivery. Shift work has also been associated with pre-term delivery. Outcomes of low birth-weight have not been as consistently associated with physically strenuous work. One study found long weeks of physically demanding work could result in a decrease in fetal weight, but no association was found for pre-term delivery. Occupational noise exposure at levels of 85 dB has been inconsistently associated with low birth-weight. Heat stress can also contribute to adverse fetal outcomes in the last trimester of pregnancy (32,61–64).

Whenever possible, heavy work duties should be modified and frequent rest periods taken throughout pregnancy to lower the risk of adverse pregnancy outcomes. If not possible, then more frequent clinician visits and placement in pre-term birth prevention classes may be valuable.

Conclusion

There is ample evidence that agricultural workers and those who reside in agricultural areas have an increased risk for a variety of adverse reproductive health outcomes. Both paternal and maternal exposures to biologic and chemical agents and maternal exposure to physical factors must be recognized and controlled to prevent these adverse effects on fertility and on the next generation of children. Strategies should include reduction or elimination of chemical agents whenever possible, proper personal protective equipment, improved work practices and hygiene, worker education, avoidance of biologic exposures, and reduction in the intensity and duration of maternal physical labor.

References

1. Younglai EV, Foster WG, Hughes EG, Trim K, Jarrell JF. Levels of environmental contaminants in human follicular fluid, serum, and seminal plasma of couples undergoing in vitro fertilization. Arch Environ Contam Toxicol 2202;43:121–26.
2. Arbuckle TE, Schrader SM, Cole D, Hall JC, Bancej CM, Turner LA, Claman P. 2,4-Dichlorophenoxyacetic acid residues in semen of Ontario farmers. Reprod Toxicol 1999;13:421–29.
3. Kunisue T, Someya M, Monirith I, Watanabe M, Tana TS, Tanabe S. Occurrence of PCBs, organochlorine insecticides, tris(4-Chlorophenyl)methane, and tris(4-chlorophenyl)methanol in human breast milk collected from Cambodia. Arch Environ Contam Toxicol 2004;46:405–12.

4. Anwar WA. Biomarkers of Human Exposure to Pesticides. Environ Health Perspect 1997;105:801–6.
5. Solomon GM, Weiss PM. Chemical contaminants in breast milk: Time trends and regional variability. Environ Health Perspect 2002;110:A339–47.
6. Bradman A, Barr DB, Henn BGC, Drumheller T, Curry C, Eskenazi B. Measurement of pesticides and other toxicants in amniotic fluid as a potential biomarker of prenatal exposure: a validation study. Environ Health Perspect 2003;111:1779–82.
7. Foster W, Chan S, Platt L, Hughes C. Detection of endocrine disrupting chemicals in samples of second trimester human amniotic fluid. J Clin Endocrinol Metab. 2000;85:2954–57.
8. Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Declining semen quality and increasing incidence of testicular cancer: is there a common cause? Environ Health Perspect 1995;103(Suppl7):137–9.
9. Colborn T, vom Saal FS, Soto AM. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ Health Perspect 1993;101: 378–84.
10. Sharpe RM, Skakkebaek NE. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? Lancet 1993;341:1392–5.
11. Oliva A, Spira A, Multigner L. Contribution of environmental factors to the risk of male infertility. Hum Reprod 2001;16:1768–76.
12. Strohmer H, Boldizsar A, Plockinger B, Feldner-Busztin M, Feichtinger W. Agricultural work and male infertility. Am J Ind Med 1993;24:587–92.
13. Swan SH, Kruse RL, Liu F, Barr DB, Drobnis EZ, Redmon JB, Wang C, Brazil C, Overstreet JW. Semen quality in relation to biomarkers of pesticide exposure. Environ Health Perspect 2003;111:1478–84.
14. Larsen SB, Joffe M, Bonde JP. Time-to-pregnancy and exposure to pesticides in Danish farmers. ASCLEPIOS Study Group. Occup Environ Med 1998;55:278–83.
15. Lerda D, Rizzi R. Study of reproductive function in persons occupationally exposed to 2,4-dichlorophenoxyacetic acid (2,4-D). Mutation Research 1991; 262:47–50.
16. Tielemans E, van Kooij R, te Velde E, Burdorf A, Heederik D. Pesticide exposure and decreased fertilization rates in vitro. The Lancet 1999;354:484–85.
17. Recio R, Robbins WA, Borja-Aburto V, Moran-Martinez J, Froines JR, Hernandez RM, Cebrian ME. Organophosphorous pesticide exposure increases the frequency of sperm sex-null aneuploidy. Environ Health Perspect 2001;109: 1237–40.
18. Sanchez-Pena LC, Reyes BE, Lopez-Carrillo L, Recio R, Moran-Martinez J, Cebrian ME, Quintanilla-Vega B. Organophosphorous pesticide exposure alters sperm chromatin structure in Mexican agricultural workers. Toxicol Appl Pharm 2004;196:108–13.
19. de Cock J, Westveer K, Heederik D, te Velde E, van Kooij R. Time-to-pregnancy and occupational exposure to pesticides in fruit growers in The Netherlands. Occup Environ Med 1994;51:693–99.
20. Petrelli G, Figa-Talamanca I. Reduction in fertility in male greenhouse workers exposed to pesticides. Eur J Epidemiol 2001;17:675–7.
21. Sallmen M, Liesivuori J, Taskinen H, Lindbohm ML, Anttila A, Aalto L, Hemminki K. Time-to-pregnancy among the wives of Finnish greenhouse workers. Scand J Work Environ Health 2003;29:85–93.

22. Thonneau P, Abell A, Larsen SB, Bonde JP, Joffe M, Clavert A, Ducot B, Multigner L, Danscher G. Effects of pesticides on time-to-pregnancy. Am J Epidemiol 1999;150:157–63.
23. Abell A, Juul S, Bonde JP. Time-to-pregnancy among female greenhouse workers. Scand J Work Environ Health 2000;26:131–6.
24. Greenlee AR, Arbuckle TE, Chyou PH. Risk factors for female infertility in an agricultural region. Epidemiology 2003;14:429–36.
25. Fuortes L, Clark MK, Kirchner HL, Smith EM. Association between female infertility and agricultural work history. Am J Ind Med 1997;31:445–51.
26. Goldsmith JR. Dibromochloropropane: epidemiological findings and current questions. Ann N Y Acad Sci 1997;837:300–6.
27. Korrick SA, Chen C, Damokosh AI, Ni J, Liu X, Cho SI, Altshul L, Ryan L, Xu X. Association of DDT with spontaneous abortion: a case-control study. Ann Epidemiol 2001;11:491–6.
28. Savitz DA, Arbuckle T, Kaczor D, Curtis KM. Male pesticide exposure and pregnancy outcome. Am J Epidemiol 1997;146:1025–36.
29. Crisostomo L, Molina VV. Pregnancy outcomes among farming households of Nueva Ecija with conventional pesticide use versus integrated pest management. Int J Occup Environ Health 2002;8:232–42.
30. Restrepo M, Munoz N, Day NE, Parra JE, de Romero L, Nguyen-Dinh X. Prevalence of adverse reproductive outcomes in a population occupationally exposed to pesticides in Colombia. Scand J Work Environ Health 1990;16: 232–38.
31. Nurminen T. Maternal pesticide exposure and pregnancy outcome. J Occup Environ Med 1995;37:935–40.
32. Gold EB, Tomich E. Occupational hazards to fertility and pregnancy outcome. In: Gold EB, Lasley BL, Schenker MB (eds.), Occupational Medicine, State of the Art Reviews. Reproductive Hazards 1994;9:435–69.
33. Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, Furlong CE, Holland NT. Association of *in utero* organophosphate pesticide exposure and fetal growth and length of gestaion in an agricultural population. Environ Health Perspect 2004;112:1116–24.
34. Munger R, Isacson P, Hu S, Burns T, Hanson J, Lynch CF, Cherryholmes K, Van Dorpe P, Hausler W. Intrauterine growth retardation in Iowa communities with herbicide-contaminated drinking water supplies. Environ Health Perspect 1997;105:308–14.
35. Kristensen P, Irgens LM, Andersen A, Bye AS, Sundheim L. Birth defects among offspring of Norwegian farmers, 1967–1991. Epidemiology 1997;8:537–44.
36. Engel LS, O'Meara ES, Schwartz SM. Maternal occupation in agriculture and risk of limb defects in Washington State, 1980–1993. Scand J Work Environ Health 2000;26:193–8.
37. Blatter BM, Roeleveld N, Bermejo E, Martinez-Frias ML, Siffel C, Czeizel AE. Spina bifida and parental occupation: results from three malformation monitoring programs in Europe. Eur J Epidemiol 2000;16:343–51.
38. Garcia AM. Occupational exposure to pesticides and congenital malformations: a review of mechanisms, methods, and results. Am J Ind Med 1998;33:232–40.
39. Nurminen T, Rantala K, Kurppa K, Holmberg PC. Agricultural work during pregnancy and selected structural malformations in Finland. Epidemiology 1995;6:23–30.

40. Garcia AM, Benavides FG, Fletcher T, Orts E. Paternal exposure to pesticides and congenital malformations. Scand J Work Environ Health 1998;24:473–80.
41. Garcia AM, Fletcher T, Benavides FG, Orts E. Parental agricultural work and selected congenital malformations. Am J Epidemiol 1999;149:64–74.
42. Efird JT, Holly EA, Preston-Martin S, Mueller BA, Lubin F, Filippini G, Peris-Bonet R, McCredie M, Cordier S, Arslan A, Bracci PM. Farm-related exposures and childhood brain tumours in seven countries: results from the SEARCH International Brain Tumour Study. Paediatr Perinat Epidemiol 2003;17:201–11.
43. Holly EA, Bracci PM, Mueller BA, Preston-Martin S. Farm and animal exposures and pediatric brain tumors: results from the United States West Coast Childhood Brain Tumor Study. Cancer Epidemiol Biomarkers Prev 1998;7: 797–802.
44. Kristensen P, Andersen A, Irgens LM, Bye AS, Sundheim L. Cancer in offspring of parents engaged in agricultural activities in Norway: incidence and risk factors in the farm environment. Int J Cancer 1996;65:39–50.
45. Zahm SH, Ward MH. Pesticides and childhood cancer. Environ Health Perspect 1998;106:893–908.
46. Daniels JL, Olshan AF, Savitz DA. Pesticides and childhood cancers. Environ Health Perspect 1997;105:1068–77.
47. Meinert R, Kaatsch P, Kaletsch U, Krummenauer F, Miesner A, Michaelis J. Childhood leukaemia and exposure to pesticides: results of a case-control study in northern Germany. Eur J Cancer 1996;32A:1943.
48. Rodvall Y, Dich J, Wiklund K. Cancer risk in offspring of male pesticide applicators in agriculture in Sweden. Occup Environ Med 2003;60:798–801.
49. Kristensen P, Andersen A, Irgens LM, Bye AS, Vagstad N. Testicular cancer and parental use of fertilizers in agriculture. Cancer Epidemiol Biomarkers Prev 1996;5:3–9.
50. Fear NT, Roman E, Reeves G, Pannett B. Childhood cancer and paternal employment in agriculture: the role of pesticides. Br J Cancer 1998;77:825–9.
51. Goldenberg RL, Thompson C. The infectious origins of stillbirth. Am J Obstet Gynecol 2003;189:861–73.
52. Tenter AM, Heckeroth AR, Weiss LM. Toxoplasma gondii: from animals to humans. Int J Parasitol 2000;30:1217–58.
53. Maurin M, Raoult D. Q fever. Clin Microbiol Rev 1999;12:518–53.
54. Raoult D, Fenollar F, Stein A. Q fever during pregnancy: diagnosis, treatment, and follow-up. Arch Intern Med 2002;162:701–4.
55. Jorgensen DM. Gestational psittacosis in a Montana sheep rancher. Emerg Infect Dis 1997;3:191–4.
56. Flanagan PG, Westmoreland D, Stallard N, Stokes IM, Evans J. Ovine Chlamydiosis in pregnancy. Br J Obstet Gynaecol 1996;103:382–5.
57. Giannacopoulos I, Eliopoulou MI, Ziambaras T, Papanastasiou DA. Transplacentally transmitted congenital brucellosis due to *Brucella abortus*. J Infect 2002;45:209–10.
58. Chedraui PA, San Miguel G. A case of leptospirosis and pregnancy. Arch Gynecol Obstet 2003;269:53–4.
59. McKinney WP, Volkert P, Kaufman J. Fatal swine influenza pneumonia during late pregnancy. Arch Intern Med 1990;150:213–5.
60. Interim guidelines for the evaluation of infants born to mothers infected with West Nile virus during pregnancy. MMWR Morb Mortal Wkly Rep 2004; 53:154–7.

61. Paul M. Occupational and Environmental Reproductive Hazards. Baltimore: Williams and Wilkins,1993.
62. Nurminen T. Female noise exposure, shift work, and reproduction. J Occup Environ Med 1995;37:945–50.
63. Hatch M, Ji BT, Shu XO, Susser M. Do standing, lifting, climbing, or long hours of work during pregnancy have an effect on fetal growth? Epidemiology 1997;8:530–6.
64. Engberg L. Women and Agricultural Work. Occupational Medicine. State of the Art Reviews 1993;8:869–82.

Index