Basic Microbiology and Infection Control for Midwives

Elisabeth Presterl
Magda Diab-El Schahawi
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ISBN 978-3-030-02025-5 ISBN 978-3-030-02026-2 (eBook)
https://doi.org/10.1007/978-3-030-02026-2

Library of Congress Control Number: 2018964062

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

According to the 2017 Revision of the World Population Prospects published by the UN Department of Economic and Social Affairs, every year there are about 139 million births worldwide, and the WHO estimates that about 830 women die from pregnancy- or childbirth-related complications every day. Of these, 99% occur in developing countries. Infections are one of the major complications that account for these maternal deaths. The access to quality healthcare before, during, and after childbirth is a key to save the lives of women and their newborn babies. Midwives are frontline providers of care for pregnant women. They are in a powerful position to significantly contribute and increase the health of future mothers and their babies among other things by reducing the burden of infectious diseases. The principles of infection prevention and control are essential for all healthcare settings. Understanding the fundamental processes behind infection transmission is the basis for setting appropriate actions which are intended to protect the health of patients as well as healthcare workers. This book focuses on "hygiene and microbiology for midwives" in high- and middle-income countries and is meant to enhance the knowledge and role of midwives regarding infections and infectious diseases, their transmission routes, and finally their prevention and control. A chapter dedicated to midwifery in low-income countries will briefly summarize relevant international literature and WHO documents.

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Foreword I

Infections play a major role in the morbidity and even mortality in obstetrics. Knowledge about existing guidelines is an important prerequisite for quality assurance; therefore, publications about these topics are of utmost importance. I congratulate the authors for this extensive overview to address the midwives. Midwife-led care for physiologic deliveries will become more important in the future based on excellent data demonstrating good quality care and high patient satisfaction. The present textbook should be of integral part of midwives' education in the future.

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Foreword II

Ignaz Philipp Semmelweis was the first doctor to identify the mode of transmission of puerperal fever (sepsis) in the General Hospital in Vienna 170 years ago. He recognized the difference in maternal mortality in two clinical departments. One department only employed midwives and students in midwifery; the other was also staffed by obstetricians and medical students who conducted autopsies. His introduction of washing hands with chlorinated lime solution was a highly effective and preventive measure which reduced maternal mortality substantially. Knowing about this history is important for midwives and doctors alike. The knowledge of hygiene and microbiology as is presented in this textbook is therefore vital in the contemporary as well as future education of midwives. I wish to thank the authors for their excellent task in compiling this essential work!

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History

The word hygiene originates from the Greek, ὑγιεινή [τέχνη] (hygieine téchne), meaning "healthy art." Hygeia is the name of the Greek goddess of health. Hygiea is the daughter of the god and physician Asclepius, who is a son of the god of medicine Apollo. In the Roman Empire, the knowledge of hygiene was well developed. Already at that time, the Roman physician Marcus Terentius Varro knew that diseases are caused by microorganisms. It was known that quarantine (isolation) could prevent the spread of infectious diseases. In Christian Europe in 1670, Antoni van Leeuwenhoek discovered the first "micro-creatures" seen using his self-built microscope. He saw in human secretions (saliva, dental plaque) "little animals" (microorganisms).

One of the pioneers of hygiene in Central Europe/Austria was Gerard van Swieten (1700–1772), who was the personal physician of Maria Theresia and founded the older Vienna School of Medicine. His successor Johann Peter Frank (1745–1821) was a professor at the Vienna General Hospital, Vienna, and founded the so-called public hygiene, today called public health (Public Health). He introduced strict guidelines for the protection of the population against infectious diseases. Further extensions of this institution are public health departments and regulatory reporting for infections that have the protection of the public against epidemics goal.

Ignaz Semmelweis (1818–1865) was an assistant doctor at the University Hospital in Vienna. As such, he made the observation that substances are transmitted to other people through contact with corpses, which can cause serious diseases (sepsis). He witnessed the death of his friend Jacob Kolletschka following an injury during autopsy of a septic corpse. Due to the similar clinical picture of the sepsis seen in women with puerperal fever and the sepsis of his friend, he concluded that there may be same cause and that there may be a transfer of infection via the hands of doctors and students working on postmortems of corpses and then going to the ward and treating pregnant women. He therefore called for hand hygiene prior to any examination of patients.

He performed the first epidemiological study comparing the mortality rates of two obstetric wards. At the Vienna University Hospital, there were two obstetric wards for the care of pregnant women. In one the care was in the hands of midwives and student midwives; the other was run by medical doctors, medical students, and midwives. In a meticulous investigation, he showed that the mortality rate at the

medical ward was much higher than the mortality rate at the ward with the midwives. Then he performed the first intervention study. The medical students and medical doctors had to disinfect their hands with chlorinated lime solution before contact with the postnatal women. It really came to a sharp drop in the death rate, which was finally identical on both wards. Nevertheless, there was considerable controversy, so Semmelweis finally had to leave Vienna. He received a professorship in Budapest. The mortality rate increased again.

Quite late in his life, he summed up his scientific findings in the scientific essay "The Etiology, the Concept and the Prophylaxis of Puerperal Fever." Semmelweis died eventually after a serious illness in Oberdöbling near Vienna.

The great period of medical microbiology came in the nineteenth century. Louis Pasteur (1822–1895) and Robert Koch (1843–1910) are considered to be the founders of clinical microbiology. Microbiology is the science of microorganisms including bacteria, fungi, and viruses. Louis Pasteur was the first to detect bacteria using the microscope and culturing them. He developed methods of clinical microbiology for the diagnosis of infectious diseases. Robert Koch discovered the pathogen of tuberculosis, *Mycobacterium tuberculosis*. He also established the so-called Koch's postulates for the general definition of a pathogen. Paul Ehrlich (1854–1915) was the founder of anti-infective therapy. He discovered and developed the drug Salvarsan. Salvarsan was used for the treatment of syphilis. Ilya Metchnikoff (1845–1916) developed basic microbiology and immunology. Immunology is the science of the immune system and its reaction to infection but increasingly to many other triggers. Metchnikoff also set milestones for the diagnosis and therapy of infectious diseases.

Infection Prevention in Hospital: Tasks of Hospital Hygiene

Infection prevention and control (IPC) in hospitals aims to streamline processes and care actions with respect to avoid the transmission and/or spread of infections and/or microorganisms. Measures include the advice of medical personnel and the involvement of the management of hospitals to implement the advice given, the choice of adequate technology and medical devices for use in patients, and the establishment of standards and guidelines. Additionally, the infection prevention and control team is consulted when building or rebuilding hospitals or parts of it.

In hospitals, specialist IPC advice is given by the IPC team. The IPC team consists of IPC nurses, IPC doctors, sometimes other IPC professionals, supporting assistants, epidemiologists, scientists, etc. IPC nurses, IPC doctors, and IPC professionals have special training in infection prevention and control. The IPC team creates the so-called IPC plan of the hospital. This plan includes IPC guidelines, disinfection and sterilization rules, surveillance (epidemiology) of healthcare-associated infection, etc. In some European countries, including Austria, IPC is legally endorsed.

Other tasks of the IPC team are surveillance and epidemiology of healthcare-associated infections (HAI) and detection of infectious outbreaks and transmission of pathogens.

Frequency and descriptive statistics on the antibiotic susceptibility of the most common pathogens in the hospital are usually supplied by the microbiological laboratory. These together with national and international guidance are the basis for the antibiotic policy within a healthcare institution. Additionally, these data give insight for the spectrum of pathogens, the change of susceptibility pattern, and also the mechanisms of antibiotic resistance.

In Austria hygiene and infection control are endorsed in three laws: the Act on Healthcare Institution, the Act on Physicians, the Act on Nursing, and indirectly the Act on Midwifery – "Midwives have to practice their profession conscientiously without distinction of person. The welfare and health of pregnant women, women giving birth, new mothers, newborns, mothers and infants have to be treated on the basis of statutory provisions and in accordance with the technical and scientific knowledge and experience…."

Contents

General Definitions

1

Elisabeth Presterl, Magda Diab-El Schahawi,
Luigi Segagni Lusignani, Helga Paula, and Jacqui S. Reilly

In the German-speaking parts of the world, hygiene is the science of the preservation of health and prevention of disease. According to the more up-to-date definition, hygiene comprises all measures for prevention and control of infections.

The World Health Organization (WHO) definition of health (1946) is: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".

In other parts of the world, hygiene mainly focuses on cleaning, disinfection and sterilization. All other parts are summarized under "infection prevention and control".

Infection Prevention and Control or Hygiene Comprises the Following:

- Any measures to combat and destruct pathogenic microorganisms, e.g. disinfection, sterilization, antimicrobial therapy, etc.
- Protection against and prevention of infections by laws and regulations in hospitals, the public health system, enforcing quality in the medical environment and vaccinations.
- Communication and networking to disseminate knowledge and information to protect against infection.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_1

- Teaching, educating and training of all people working in the health-care systems and beyond.
- *Epidemiology*: Description of the incidence, distribution and control of a disease in a population including the detection of the source and cause of epidemics of infectious diseases. Epidemiology is the study of the occurrence of diseases, their course and their distribution in a population. Epidemiological descriptive numbers to measure the burden of (infectious) causes of disease are mortality, morbidity, incidence and prevalence of a disease (see Chap. 24 on epidemiology).

Infections and Infectious Doctrine

2

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2.1 Definitions

Infection

Infection is defined as the invasion and propagation of a pathogen in an organism and the (immune) reaction of the organism to the pathogen.

Any microorganisms, e.g. bacteria, viruses, fungi, etc., causing infection are referred to as pathogens. Microorganisms that cause no disease in healthy persons but cause disease in immunocompromised or otherwise severely ill patients are called "opportunistic pathogens". In contrast all other pathogens are obligatory pathogens. To cause infection, a pathogen must penetrate into the body (invasion). The pathogen must multiply, and the host organism must show an immune response, e.g. fever.

The immune response may be generalized, e.g. sepsis with fever, low blood pressure and a pulse more than 100 beats/min. The local immune response depends on the site of infection, e.g. cough for lung infection or diarrhoea for bowel infection. The most common skin infection and infections of a surgical site present most commonly with redness, swelling, pus, warmth, pain and impaired function. For acquisition of an infection, a so-called chain of infection is common. The knowledge about this "chain of infection" is pivotal for infection prevention.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_2

The chain of infection is the basic model for the transmission of pathogens. There is the source of infection and then the propagation (transmission) by either direct or indirect contact with vehicles, vectors or items to the target of infection (usually the patient).

Horizontal transmission of infection means that a pathogen is transmitted from host/source to a host of the same generation. Vertical transmission of infection means that a pathogen is transmitted from one host/source to its descendants.

Examples for vertical transmission include:

- Prenatal or transplacental infection when a pathogen is transmitted via the placenta to the embryo or foetus before birth (in utero)
- Perinatal infection when the transmission of a pathogen occurs during childbirth
- Postnatal infection when the transmission of a pathogen occurs after birth, e.g. through breast milk or vaginal secretions

Common sources of infection are persons (patients, staff, visitors), animals (insect vectors, but also pets) or inanimate objects or materials (surfaces in the environment of the patient, liquids, instruments, old disinfectants, etc.). Most common sources of infection in the hospital are unclean hands of the healthcare staff, clothing (especially abdominal/stomach area, sleeves), urinary or vascular catheters, instruments, body bowls, dust and particles in the air and near and even distant surfaces in the patient environment.

2.2 Risks of Infection for Healthcare Personnel

Sources of infection are infectious patients, patient material (blood, secretions, stools, urine, tissue, etc.), contaminated objects and surfaces and medical waste. The most common occupational pathogens for the healthcare personnel are hepatitis B virus, hepatitis C virus and HIV in countries with high prevalence (see Chap. 15—Blood-Borne Viruses: HIV, Hepatitis B, and Hepatitis C).

The risk of infection even exists when a person or a patient is only colonized with a pathogen without any symptoms or has very little symptoms.

2.3 Classification of Infections and Infectious Diseases

There are several classifications for infections:

(a) Pathogen-related classification, e.g. bacterial, viral and fungal infection.
(b) Organ related (lung, pneumonia; urinary tract, urinary tract infection; skin/tissue, abscess soft tissue infections; bowel, diarrhoea).
(c) Immune response: systemic or localized infection. In a localized infection, only one organ/body site/space is affected, e.g. pneumonia. Classic systemic infection is sepsis, e.g. puerperal sepsis with severe illness.

(d) Epidemiological classification.
(e) Vector-borne infectious disease classification: vectors are, for example, insects (ticks, malaria mosquitos, etc.) that transmit the agents of infection (malaria parasites) to a susceptible host (human, animals).
(f) Behaviour-related infectious diseases, e.g. sexually transmitted diseases when omitting any precaution.
(g) Classification according to the clinical course. These are divided into acute (occurring suddenly), subacute (slowly occurring over weeks), chronic (duration 3 months) and recurrent (still healthy intervals repeatedly sweeping) infections.
(h) Classification according to the immune status of the host, e.g. infections in immunocompromised patients (e.g. after transplantation, cancer patients, leukaemia patients, rheumatic patients) that have often obscure symptomatology different to that in patients with normal immunity. These patients should be cared for in specialized centres and undergo advanced microbiological diagnostics including cultures and serology.
(i) Classification according to the origin of the pathogen: exogenous infection is the transmission of the disease through pathogens from the environment. Endogenous infection is an infection of the human body's own flora.

The most common infections in humans are infections of the upper respiratory tract (common cold: rhinitis, cough, otitis media, sinusitis). These can occur up to ten times/person/year. Nearly all of these infections are caused by viruses. Diarrhoeal diseases are in second place and occur one-two times/person/year. Also these diarrhoeal diseases are also commonly of viral origin (e.g. *Norovirus*) and rarely caused by bacteria. Skin infections (folliculitis, boils, impetigo) are in third place, followed by urinary tract infections in women. Skin infections are mostly due to bacteria (e.g. *Staphylococcus aureus*) and controlled by local disinfectant treatment and strict hygiene (handwashing). Up to 70% of all women have at least one UTI in their lifetime.

2.4 The Basics of Clinical Diagnosis

The causative agents of infectious diseases are microorganisms: bacteria, viruses, fungi, protozoa (single-celled organisms), worms and insects (see Chap. 18—Parasites and Parasitic Diseases).

The goal in the treatment of infectious diseases and infections is a rapid diagnosis and pathogen identification followed by immediate antimicrobial therapy.

The common procedure to admit a sick patient must include the accurate medical history and a clinical examination and taking blood pressure, pulse and temperature for fever. For diagnosis of infection, microbiological testing must be done: sample material is taken from the site of infection, e.g. blood cultures to detect bacteraemia, urine culture for urinary tract infections, chest X-Ray for pneumonia (note: only for particular indications in pregnant women), stool cultures for diarrhoea, wound swabs, etc. Biochemical blood tests, e.g. the increased numbers of leukocytes or the elevated C-reactive protein, may indicate infection.

2.5 Clinical Syndromes of Infection

Sepsis/Septicaemia/Bacteraemia

Sepsis is a systemic reaction triggered by infection that affects the entire body. Commonly this syndrome is blood poisoning. A typical example of a sepsis is puerperal fever. Typical symptoms of a systemic infection are fever, chills, low blood pressure, rapid pulse (tachycardia) and rapid breathing (tachypnoea). The most serious condition of sepsis is septic shock. Sepsis may have a primary or secondary focus site and associated symptoms. Local symptoms of skin, tissue or wound infections and abscesses are redness, warmth, swelling, heat, pain and impaired function. Organ-specific signs of infection depend on the affected organ as cough in pneumonia or headache in meningitis. Sepsis is a most serious type of infection. Therefore, it is pivotal to recognize sepsis in a patient as soon as possible. Based on several studies, there are definitions of sepsis particularly for emergency and intensive care medicine. Because of the high fatality of sepsis, the World Health Organization (WHO) has launched an entire programme on sepsis involving several many different institutions (http://www.who.int/sepsis/en/).

Laboratory testing (full blood count) reveals an increase of the white blood cells (leucocytosis) is found typically as well as the increase in C-reactive protein. In addition, the detection of bacteria or fungi in the microbiological results of the patient samples (e.g. blood, urine, bronchial secretions, stool, smears, aspirates) confirms the diagnosis of infection.

Fever is defined as a body temperature >38 °C. Temperatures below 38.2 °C are referred to as elevated body temperature. Nevertheless, an infection is not necessarily associated with fever. Old patients, patients who have swallowed antipyretic or analgesic tablets, may have a normal temperature despite serious signs of infection. However, note other causes of fever except infections are other inflammatory diseases, e.g. rheumatism, malignant tumours, postoperative fever, trauma and idiopathic hyperthermia.

Symptoms of sepsis include fever (38.2 °C), hypotension, tachycardia (heart rate over 100 beats/min), tachypnoea (respiratory rate 20/min), confusion, nausea, vomiting, coughing, fatigue, confusion, weakness and frailty. Septic shock can result in organ failure and coma. The detection of bacteria in the blood in the blood culture is called bacteraemia or septicaemia. Other signs of sepsis are changes in the blood count (leucocytosis above 10 G/L, thrombocytopenia <100 G/L).

The most frequent pathogens of sepsis are *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Enterobacter* species, beta-haemolytic streptococci group A or group B, *Enterococcus faecalis*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*, and the fungus *Candida albicans*, *E. coli*, *K. pneumoniae* and *Enterobacter* sp. are referred to as "enterobacteria" because they are most frequently found in faeces.

Puerperal fever has the clinical signs and symptoms of sepsis. Puerperal fever occurs immediately to a few days after delivery. Pathogens are beta-haemolytic streptococci of groups A and B, respectively, enterobacteria and the so-called anaerobic bacteria. Early identification and management of this are critical to the outcome. The patient must be necessarily taken to the hospital immediately.

Urinary Tract Infection

Urinary tract infection is the most common infection during pregnancy. In young, non-pregnant women, the urinary tract infection is considered to be as uncomplicated. Uncomplicated urinary tract infection requires only 3 days of treatment. Urinary tract infections in pregnancy are complicated because of the anatomical changes of the body during pregnancy. Any urinary tract infections in men, in patients with kidney stones, in immunocompromised patients and in patients with indwelling urinary catheters are complicated infections requiring accurate diagnosis and prolonged treatment.

The symptoms of lower urinary tract infection (infection of the bladder, cystitis) include burning (alguria), frequent voiding, blood in urine (haematuria), cloudy urine (proteinuria), pain and fever.

The symptoms of upper urinary tract infection (infection of the kidney, pyelonephritis) include the symptoms of lower urinary tract infection plus high fever, flank pain and pain. Pyelonephritis may be accompanied by the signs and symptoms of sepsis.

Most common pathogens of urinary tract infection are enterobacteria (*Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*), *Staphylococcus saprophyticus*, *Enterococcus faecalis* and group B beta-haemolytic streptococci.

Diagnostics of urinary tract infection are the chemical urine analysis for leukocytes, protein, nitrite (produced by some bacteria) and blood. For pathogen identification urine culture (midstream urine) should be done. Urine culture is recommended after at least two urinary tract infections within a short period or treatment failure.

The treatment of urinary tract infection in pregnant women is limited to antibiotics that are safe for pregnant women. However, the resistance to these antibiotics may be up to 50%. For intravenous therapy for pyelonephritis with sepsis, there are still beta-lactam antibiotics available. Thus, urine culture is mandatory in pregnant women with urinary tract infections. In non-pregnant women, quinolones (ciprofloxacin, levofloxacin), trimethoprim or fosfomycin trometamol can be used.

Vaginal Infection, Vaginosis and Vaginitis

Symptoms of vaginal infection (vaginitis, colpitis) include vaginal discharge, pain during intercourse, itching and redness. During pregnancy and particularly after intake of antibiotics, fungal infections of the vagina and external genitalia frequently occur. Signs and symptoms include burning and itching, redness and typical white friable discharge. Local antifungal cream or vaginal troches are the therapy of choice (see Chap. 17—Medical Mycology and Fungal Infections).

Other frequently occurring vaginal infections are trichomoniasis and bacterial vaginosis. Trichomoniasis is vaginal infection caused by the protozoon *Trichomonas vaginalis*. It is typically associated with foul-smelling discoloured discharge. The diagnosis is rapidly done by direct microscopy of the vaginal smear showing slowly moving *Trichomonas vaginalis* cells. During pregnancy, topical therapy is recommended.

Bacterial vaginosis is caused by *Gardnerella vaginalis*, a small Gram-labile rod (staining red and blue) sticking in dense numbers on squamous cells of the vagina epithelium (so-called clue cells).

Infections of the Skin, Soft Tissue and Wounds

Frequent skin infections are erysipelas, boils and abscesses. Symptoms include swelling, redness, pain, warmth, loss of function and pus.

Erysipelas is caused by beta-haemolytic group A streptococci. Erysipelas presents as a typical sharply demarcated redness. Entry points may be minor injuries. Pre-existent damage of the lymph drainage of the skin may lead to the occurrence of recurrent erysipelas. Occasionally, other beta-haemolytic streptococci of group B, C and G may cause cellulitis.

Boils are abscesses of the hair follicles. Wound infections occur after injuries but also after surgery (surgical site infections). Surgical site infections are considered as healthcare-associated infections (nosocomial infections). Common pathogens of boils, wound and surgical site infections are *Staphylococcus aureus*, beta-haemolytic streptococci group A and enterobacteria (e.g. *Escherichia coli*). Wound infections acquired in the hospital or after contact with long-term care patients may be caused by methicillin-resistant *Staphylococcus aureus* (MRSA). However, meanwhile MRSA may be even isolated in patients who had had no contact with healthcare (so-called community-acquired MRSA, CA-MRSA).

For microbiological sampling, the wound should be cleansed with sterile saline before sample collection. From boils and abscesses, pus can be aspirated with a sterile syringe.

A local wound cleansing with an antiseptic is necessary. For severe symptoms, systemic antibiotic treatment is necessary.

Respiratory Tract Infections: Infections of the Respiratory Tract

Frequent respiratory tract infections are pharyngitis (sore throat, "sore throat"), sinusitis (sinusitis), middle ear infection (otitis media), tonsillitis (tonsillitis) and bronchitis. Classic symptoms are cough and pain in the affected area. Bacterial tonsillitis is generally caused by beta-haemolytic streptococci group A with flaming redness of the tonsils. Scarlet fever may be a toxic complication of the infection with beta-haemolytic streptococci group A.

The pneumonia is the most severe form of respiratory tract infection. Pneumonia is an inflammation of the lung tissue with a high fever, painful breathing and coughing. In pneumonia purulent sputum is rare. Excessive purulent sputum is usually a sign of bronchitis. The majority of respiratory tract infections are of viral origin. Thus, antibiotic therapy has to restrict to bacterial infection because it is effective against viral infection.

The clinical examination of pneumonia includes auscultation (listening to breathing) with the stethoscope and chest X-Ray (care: only in strictly limited indications in pregnant women!). Microbiological samples include blood cultures (in pneumonia), sputum and serological tests (e.g. for *Mycoplasma pneumoniae*).

Common causative agents of pneumonia are *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae* and *Klebsiella pneumoniae*.

Diarrheal Diseases: Infections of the Gastrointestinal Tract

Infectious diarrhoea is defined as more than three unformed stools per day, evidence of a pathogen and at least one symptom such as fever, nausea, vomiting and abdominal pain. Duration of acute diarrhoea is less than 14 days, and duration of persistent diarrhoea is more than 14 days. Usually there is a diarrheal episode per person per year.

The most common bacterial pathogens of diarrhoea are *Salmonella* species, *Campylobacter* species (only in travellers to hygienically questionable areas, travel history), *Clostridium difficile*, *Yersinia enterocolitica* (children, pregnant women), *Escherichia coli* (enterohemorrhagic *Escherichia coli* EHEC – children) and *Vibrio cholerae* (tropical disease, travel history).

In most developed countries, the following pathogens cause notifiable diseases. Any cases have to be reported to the public health authorities, e.g. *Salmonella*, *Campylobacter*, Shigella, *Yersinia enterocolitica*, *Escherichia coli* EHEC, *Vibrio cholerae* and many more.

Microbiological diagnosis of bacterial diarrhoea is done by culture of stool (2 ml liquid stool to be sent to the microbiology laboratory in tightly closed vials). Most commonly only *Salmonella*, *Campylobacter* and Shigella are reported, for all other pathogens indicate a special request.

The treatment of choice for acute diarrhoea is oral rehydration. The oral hydration fluid according to the World Health Organization (WHO) can be self-prepared and consists of 1/2 teaspoon salt (3.5 gm), 1 teaspoon soda (2.5 gm $NaHCO_3$), 8 teaspoons of sugar (40 gm) and 250 ml orange juice (1.5 gm potassium chloride, KCl) diluted to 1 l with boiled and cooled water.

It is also commercially available products. In addition to oral rehydration and the observance of hygiene measures (handwashing, cleaning the toilet with normal toilet cleaners), Antibiotics are generally not indicated. They may only be necessary in critically ill infants with adequate rehydration, in the very old persons, in immunosuppressed patients and in patients with sepsis (typhoid fever) or bacterial dysentery due to *Shigella dysenteriae*.

Clostridium Difficile Infection (CDI) CDI is a special entity in patients with frequent contacts with healthcare institutions. General risk factors include intake of antibiotics or cytotoxic chemotherapy, age more than 65 years and kidney disease. Small children until the age of 2 years are usually asymptomatic carriers without illness. Thus, thorough handwashing and cleaning of the surrounding surfaces are essential after changing diapers or handling stool or stool-contaminated items.

Clostridium difficile-associated colitis has different clinical pictures; it primarily affects the large intestine. The symptoms range from watery stools to severe colitis with bloody mucous stools and sepsis due to intestinal perforation and ileus. Sometimes CDI may be relapsing, most often in elderly and very ill patients.

Hygienic measures include the washing of hands and adequate cleaning of the patient's environment with sporicidal disinfectants. Measures to avoid transmission

are strict hand hygiene of clinical staff, patients and visitors, a private toilet, protective clothing for the staff (e.g. apron or gown, gloves, mask, cap, even goggles depending on the risk of contamination and local hygiene standards) and isolation in single room during the duration of diarrhoea.

Listeriosis Listeriosis is a bacterial infection caused by *Listeria monocytogenes* that is generally acquired through intake of contaminated food. *Listeria monocytogenes* can normally found in the excretions and in the gastrointestinal tract of animals. Food at risk to be contaminated by *Listeria* include raw meat, smoked fish (salmon), raw milk, raw milk cheese and other contaminated foods.

Most commonly listeriosis can manifest as diarrhoea but as sepsis or abscesses in elderly or immunocompromised patients.

Pregnant women may acquire listeriosis via contaminated food, be asymptomatic or have just an episode of diarrhoea. But, infection of *Listeria* leads to a placentitis (febris infantiseptica) and abortion. To diagnose human listeriosis, *Listeria monocytogenes* can be detected in stool, blood or aspirates of abscesses.

The symptoms are fever, signs and symptoms of sepsis, weakness, diarrhoea, headache and delirium. Brain abscesses may cause seizures. Pregnant women may have premature labour and miscarriage.

Listeriosis in pregnant women and their offsprings may occur as a pre- and perinatal infection. The early-onset type may have common cold-like symptoms or fever of the pregnant women. Depending on the gestational age of the child, there may be septic abortion in first months of pregnancy or septic preterm birth in the second half of pregnancy. Premature babies are severely ill and show the signs and symptoms of sepsis, livid skin, microgranulomata, hepatosplenomegaly and respiratory insufficiency.

The delayed type is the so-called infant listeriosis. This is a perinatal infection through the contaminated birth canal of pregnant women. The infants develop signs and symptoms of meningitis from the second to fifth week after birth. The diagnosis is made by culture of the vaginal smear or a stool sample to prove the colonization of the mother or by blood cultures of the mother when she has systemic symptoms like fever, headache and fatigue. In the diseased infant blood cultures, culture of cerebrospinal fluid and/or stool cultures or rectal swabs are diagnostic.

2.6 Infections During Pregnancy

Pregnant women are particularly at risk for certain infections. Either the infection affects the pregnant woman only or it affects the foetus or the newborn with severe sequelae. Infection occurs either via the bloodstream and the placenta or during birth.

The most important infections impairing the child include the following:

- Viral infections
  - Rubella
  - Human immunodeficiency virus (HIV) infection

  - Parvovirus B19 infection ("fifth disease")
  - Varicella (chickenpox)
  - Cytomegaly (cytomegalovirus CMV)
  - Herpes simplex infection
  - Hepatitis B
  - Lymphocytic choriomeningitis
- Bacterial infections
  - Syphilis
  - Listeriosis
  - Gonorrhoea
  - Sepsis and meningitis of the newborn by beta-haemolytic streptococci group B
  - Chlamydia infection
  - Tuberculosis
  - Sepsis and meningitis of the mother and newborn by *Escherichia coli*, *Staphylococcus aureus* and anaerobes
- Parasitic infections
  - Toxoplasmosis
  - Malaria

Infection during pregnancy may result in malformations, defects and developmental disorders of unborn child. Infection during the first 3 months may cause embryopathy because of impaired organogenesis. Later infection is referred to as fetopathy. The main causes of these prenatal infections and their respective pathogens are syphilis (*Treponema pallidum*), listeriosis (*Listeria monocytogenes*), toxoplasmosis (*Toxoplasma gondii*), rubella (*Rubella virus*), cytomegaly (CMV), varicella (varicella zoster virus), HIV infection (HIV), lymphocytic choriomeningitis (lymphocytic choriomeningitis virus) and parvovirus B19 infection (parvovirus B19).

Perinatal infections occur during, shortly before or shortly after birth. Common infections and their respective pathogens are sepsis or meningitis due to *Listeria monocytogenes*, sepsis or meningitis due to beta-haemolytic streptococci group B (*Streptococcus agalactiae*), sepsis or meningitis due to *Escherichia coli*, eye infection or sepsis due to *Neisseria gonorrhoeae*, eye infection due to *Chlamydia trachomatis*, hepatitis B, primary genital herpes simplex and primary varicella.

To control these infections, many countries worldwide have a special monitoring programme for pregnant women. In Austria, this is the "mother-child pass" which is similar to the Torch programme in the United States. The following examinations for infections are carried out until the end of the 16th week of pregnancy: blood tests for syphilis, toxoplasmosis, rubella and HIV. In the pregnancy weeks 25–28, hepatitis B serology is performed. If there is any clue for these infections, appropriate further tests and treatment are initiated and carried out.

The most common infections in pregnant women are urinary tract infections and diarrhoea due to common intestinal pathogens *Salmonella* or *Campylobacter*. Tuberculosis is a rare disease in the developed countries but frequent in countries with poverty and uncontrolled HIV infections.

Pregnant women have therefore to take care of special rules to avoid the risk of infection for listeria or other diarrhoeal pathogens.

The following food is at risk for contamination of *Listeria* and should not be eaten during pregnancy:

- Raw or incompletely cooked meat, raw meat spread/pate ("mettwurst") and raw sausages
- Raw milk or raw milk products, fresh raw/unpasteurised cheese
- Cold smoked fish (salmon)
- Raw fish (sushi)
- Raw shellfish
- Raw eggs

Meat should be thoroughly cooked. Hand and kitchen hygiene has to be obeyed. Handle raw meat properly; separate kitchen items for handling meat and food to be eaten raw. Wash kitchen utensils properly. Observe cleanliness.

Pregnant women should perform adequate hand hygiene before preparing food and eating; avoid any raw food, and obey kitchen and food hygiene according to guidelines by the health authorities; get vaccinated best before pregnancy, particularly for rubella, measles, mumps and varicella; be cautious to get in contact with sick people; and avoid unnecessary long-distance travel to tropical countries.

2.7 Healthcare-Associated Infections (HAI, Also Called Nosocomial Infections)

HAI are serious complications of medical treatment and support, e.g. surgical site infections, catheter-related infections and ventilator-associated pneumonia. More than 70% of these infections are caused by endogenous flora of the patient himself. However, 25–30% of HAI may be caused by transmission in the hospital, e.g. from the contaminated surfaces or contaminated hands of the personnel. HAI occur in 3–15% of the patients: high-risk areas are intensive care unit because the severely ill patients with major life-supporting measures are particularly at risk. HAI may lead to increased mortality, length of stay and the cost of healthcare.

Multidrug-resistant microorganisms (MDRO) are emerging in hospitals. These bacteria host multiple genes in their genome that code for resistance factors against antibiotics commonly used for treatment of infections. These multiresistant microorganisms are pathogens of HAI, which cannot be treated by standard antibiotics any longer. More generally, the presence of multiresistance genes in MDRO is also referred to as "antimicrobial resistance" (AMR).

The most multiresistant pathogens of HAI include methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase (ESBL)-producing enterobacteria, multiresistant *Pseudomonas aeruginosa*, multiresistant *Acinetobacter baumannii* complex and vancomycin-resistant enterococcus (VRE).

The most common HAI are urinary tract infections (up to 35%), postoperative wound infections (up to 25%), infections of the lower respiratory tract (up to 20%), skin and tissue infections (up to 10%), sepsis and bacteraemia (up to 5%) and others (up to 15%). Clostridium difficile infection (CDI) may be up to 20% in certain institutions. The mortality of HAI is up to 8%. Therefore, it is important to know the epidemiology of HAI to protect the patients. There is little about HAI and pregnant women because nearly all pregnant women are cared for in an outpatient setting or by midwives. However, there is data on the surgical site infection after caesarean section: the Annual Report on Surgical Site Infection in Europe published by the European Centre for Disease Prevention and Control reports an infection rate of 1.9 [0.5–5.2] percent in a population of nearly 100,000 caesarean sections in 2016. Surveillance of surgical site infections after caesarean section is an important tool for patient's safety and quality of care (https://ecdc.europa.eu/en/home).

HAI are defined as any type of infection that occurs by definition 48 h after admittance or on readmission following previous hospitalization. The average day of onset ranges from 8 to 21 days after admission.

Risk factors for HAI include the following: immunodeficiency, breach natural barriers (skin lesions, surgical wounds, site of entry of catheters), colonization by multiresistant microorganisms, serious underlying illness, advanced age, malnutrition, alcoholism, smoking and chronic respiratory diseases, diabetes mellitus, acute surgery, serious injuries and burns, invasive therapeutic procedures such as endotracheal or nasal intubation, mechanical ventilation, peripheral or central vascular catheters, extracorporeal renal replacement therapy (dialysis), indwelling drainages, gavage, tracheostomy and urinary catheters, blood transfusions, other infections and antimicrobial therapy, immunosuppressive therapy, bed rest and parenteral nutrition.

Examples of Healthcare-Associated Infections

Urinary tract infection: Urinary catheters allow the ascension and adherence of microorganisms (catheter-associated urinary tract infection). Most frequent pathogens: *Escherichia coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Enterobacter cloacae*, *Candida* spp., etc.

Surgical site infection (*SSI*): Infection after operation such as caesarean section. Bacterial spectrum depending on the site of surgery performed: *Staphylococcus aureus* (in surgery of soft tissues, bone and joint, cardiothoracic), *Escherichia coli* and other gram-negative bacteria after intra-abdominal surgery.

Pneumonia: Micro- and/or macroaspiration; intubation leads to the suppression of local defence mechanisms (cough, mucociliary clearance); the risk of pneumonia is particularly high risk with a long duration of mechanical ventilation (VAP, ventilator-associated pneumonia).

Catheter-associated infections and bacteraemia: Intravascular catheters (central venous catheters, peripheral catheters, arterial catheter). The most common pathogens are *Staphylococcus aureus*, coagulase-negative staphylococci, enterococci, *Escherichia coli*, *Klebsiella* species, other enterobacteria, *Pseudomonas* species and *Candida* (yeast). All microorganisms may produce the so-called biofilms on foreign

material bodies (e.g. on the surface of central venous catheters or orthopaedic prostheses) and enable themselves to be protected from the immune system and/or antimicrobial therapy.

To prevent HAI infection, control is pivotal as well as other clinical measures: patients should be mobilized as soon as possible, and indwelling vascular catheters (peripheral and central venous catheters) and urinary catheter should be avoided or removed as soon as possible. Unnecessary antibiotic therapy or therapy with broad-spectrum antibiotics should be avoided. It is pivotal to check daily if any measure, treatment or supporting invasive device is needed.

Infection Control in High-, Middle- and Low-Income Countries

Infection control is as much a public health issue as it is a question of safety for patients and personnel. This also includes general health and nutritional status of the public and their living conditions (housing, sanitation, water quality). These parameters affect the prevalence of infectious disease in a community, which in turn has an impact on the level of infection among persons requiring medical attention in a healthcare facility. Thus, setting infection control policies and creating appropriate protocols for infection control in a healthcare facility are requisites for managing the infectious disease burden in any healthcare setting. Although this principle applies to every healthcare facility worldwide, there are marked differences between practical execution of infection control techniques between developing and developed countries.

Developed countries: The framework of infection control in developed countries operates on an economically very different level. Due to the higher availability of resources, the infrastructure of infection control in high-income countries comprises a wide range of tools and skills. Most importantly, access to ongoing education in this field is a valuable resource for healthcare professionals. The World Health Organization (WHO) has compiled a comprehensive manual ("Infections and infectious diseases – A manual for nurses and midwives in the WHO European Region") on this subject specifically geared towards nurses and midwives, with the intent of developing the knowledge, skills and attitudes regarding infectious diseases and their prevention and control. This manual should be interpreted as a basic learning tool for understanding the fundamental principles of modern infection control.

Developing countries: There is no question that midwifery care has an indispensable contribution to public health in low-income countries. Poor quality of maternal and newborn care is a major factor in mortality among the respective cohorts, and it contributes to acute and chronic clinical as well as psychological morbidity. The lack of coverage of basic human needs such as clean water and suitable shelter in developing countries constitutes a major problem for pregnant women; access to any form of standardized healthcare is considered a luxury for many. The poor infrastructure of healthcare facilities in many developing countries may actually raise infection rates. Budgetary reasons and the lack of knowledge in basic infection control represent common contributing factors, but not exclusively so.

Standard hygiene measures include hand hygiene, asepsis and decontamination. Handwashing is the single most important precaution against infection transmission. Ensuring that healthcare workers are adequately trained and educated in the basic principles of good hand hygiene goes a long way in infectious disease prevention even in rudimentary conditions. Proper handwashing along with the use of an alcoholic hand rub can limit both cross infection of microorganisms and contamination of blood-borne pathogens.

Asepsis includes decontamination of the skin and mucous membranes at the site of a procedure and is thus of vital importance especially during invasive procedures. This also includes practising aseptic techniques among healthcare workers to prevent microorganisms from reaching vulnerable sites. Preparing sites for intravenous cannulation or surgical incision requires effective application of appropriate antiseptics. Most common antiseptics include alcohol, chlorhexidine, iodophor and triclosan.

In 2017, the World Health Organization (WHO) has launched a Maternal Health programme which focuses on the health of women during pregnancy, childbirth and postpartum period. It addresses maternity-related topics such as the major causes of maternal morbidity and mortality, unsafe abortion, postpartum depression, etc. The programme also provides frequently updated guidelines and current standards for sexual, reproductive, maternal, newborn, child and adolescent health programmes as part of the maternal health campaign. More information can be accessed at http://www.who.int/maternal-health.

Suggested Reading

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Hand Hygiene

3

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3.1 Introduction and Definition

Healthcare-associated infections (HAI) are the most common complication of medical care. Healthcare-associated infections are infections that are acquired in the hospital ("nosos", illness; "komein", maintain). It has long been recognized that these infections are not limited to hospitals but can occur in all healthcare settings, both as a result of repeated treatments for the chronically ill in outpatient and inpatient care and long-term care facilities and rehabilitation centres. In the Anglo-American area, it has been ignored by "health-care associated infections" (HCAI, HAI) so to speak.

HAI have several risk factors: patient-related factors, e.g. severe underlying disease, and treatment-specific factors, e.g. duration of surgery, medical device use and hygiene deficiencies as lack of hand hygiene (see Fig. 3.1).

Ignaz Semmelweis, gynaecologist and obstetrician at the General Hospital of Vienna, was the pioneer of hand hygiene. Long before the discovery of bacteria, Semmelweis recognized in 1846 the transmission of infectious material as the cause of infection. Specifically, it was the transmission of the pathogens of childbed fever, apparently by students and doctors who came from the autopsy room and examined

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_3

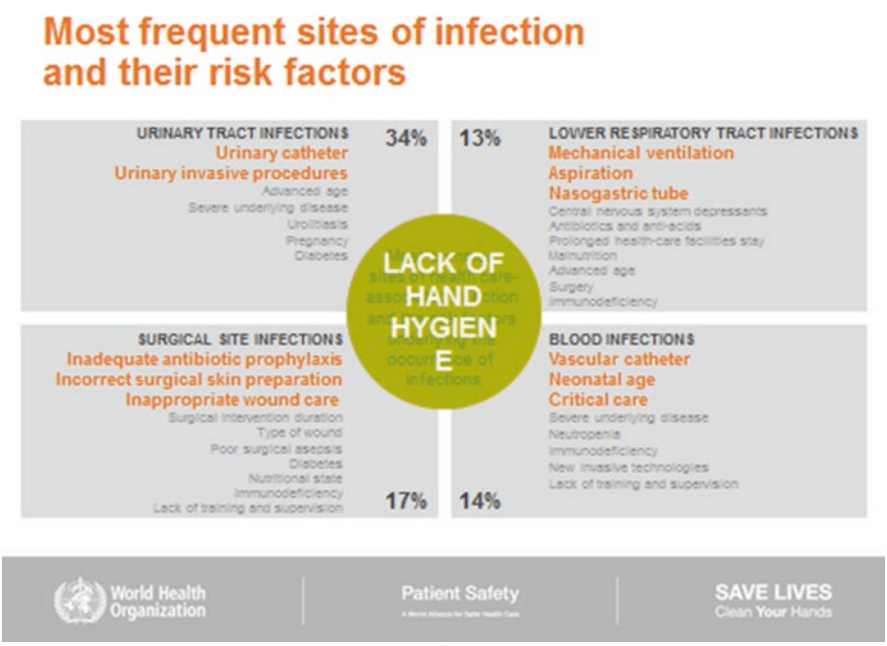


Fig. 3.1 Most common healthcare-associated infections and related risk factors (Source: WHO Patient Safety: Education Session for Trainers, Observers and Health-Care Workers, Clean Care is Safe Care)

pregnant women. In order to stop the transmission of infection by hand, Semmelweis introduced as an intervention the hand disinfection with chlorinated lime. "The need to disinfect the hand will therefore always remain …". The infection rate dropped from 11.4% (1846) to 1.27% (1848).

This first hygienic intervention was followed by the great age of antisepsis (disinfection and sterilization) of surgical instruments and environment, which forms the basis of modern medicine not only in the surgical and intensive care sectors. Semmelweis had already noticed that "… not just the examining finger, but all objects that came in touch are contaminated …; these objects must be disinfected or changed; this includes instruments, bedding, sponges, bowls, etc..".

Through the discovery and use of antimicrobials, infections were further contained in hospital settings.

Already in the 1950s and 1960s of the twentieth century, antibiotic-resistant bacteria, e.g. penicillin-resistant streptococcus pneumoniae, beta-lactamase-producing *Neisseria gonorrhoeae* and sulphonamide-resistant *Neisseria meningitidis*, developed in the 1990s; the prevalence of methicillin-resistant *Staphylococcus aureus* infections around the world made hygiene and made both detection and prevention of nosocomial infections a major issue in healthcare.

Colonized patients can easily become the source of outbreaks, especially when hygiene is not a top priority. The treatment of multiresistant pathogen infections is more difficult because fewer antibiotics are available for treatment.

The European Commission decided in 1999 to implement the detection of both nosocomial infections and antimicrobial resistance (Commission Decision 2000/96/EC). HAI surveillance networks have been established in both Europe and the United States. Nevertheless, the capture of HAI is complex. HAI surveillance and correct interpretation of the results require the use of standardized criteria as well as the availability of microbiological diagnostics and expertise.

Infections with or without symptoms and microbiological findings can affect any organ and any body site.

3.2 Most Common Healthcare-Associated Infections and Current Data

The European Centres for Disease Control (ECDC) estimates that in 1 day, about 80,000 patients in European hospital have at least 1 HAI. In other terms, 1 in every 18 patients in Europe suffers from a healthcare-associated infection. The basis for these figures was the 2011–2012 European-wide point prevalence study of the ECDC. The prevalence of all healthcare-associated infections in the investigated patient population was 6% (country range, 2.3–10.8%). That is, of a total of 273,753 enrolled patients, around 15,000 healthcare-associated infections were detected. The most common infections were pneumonia and other respiratory infections (23.5%), postoperative wound infections (19.6%), urinary tract infections (19%), sepsis (10.7%) and gastrointestinal infections, including *Clostridium difficile* infections (7.7%). In this study, also hospital's structural and hygienic aspects were taken into account: the median single-room rate was 9.9% of all patient rooms in the participating hospitals, with higher rate in France (>50%) and lower rate in Southeastern Europe (<5%). The average consumption of alcohol-based hand rub was 18.7 L/1000 patient days and was significantly lower in primary care hospitals compared to central hospitals (1). It is sobering that there were no IPC specialists in 118 participating hospitals from 12 countries. Great Britain and Scotland were the best equipped countries with 2114 full-time IPC specialists looking after 250 beds. This high IPC number in the United Kingdom (UK) and Scotland bore fruit: the MRSA rate was reduced from almost 50% in the previous years to less than 10% in 2012.

The WHO has published a systematic literature review of the worldwide extent of healthcare-associated infections, with an infection rate of 7.6% in high-income countries compared to 10.1% in low-income countries. The highest rates of infection are in ICU patients (according to WHO, 30%; according to ECDC prevalence studies, 19.5%) that have several risk factors including the presence of invasive device such as urinary and vascular catheters and artificial respiration (see also Fig. 3.1).

3.3 Measures for the Prevention of Healthcare-Associated Infections

According to many experts, humanity is well on its way to losing the effects of antibiotics. Without effective antibiotics, many infectious diseases will be deadly again in the future. From this point of view, the importance of preventing the transmission of infections and their pathogens must be constantly recalled. Depending on the route of transmission, different measures to prevent transmission of infection are necessary, e.g. hand hygiene, spatial separation between infectious and noninfectious patients and adequate preparation of medical devices and all objects with which patients come into contact.

3.4 Hand Hygiene

Hand hygiene includes both hands rubbing with alcohol-based solution, handwashing, and asepsis. While alcohol-based hand rub disinfection between the patient contacts and before all aseptic activities is necessary, only with visible pollution the hands also have to be washed. The often cited handwashing is therefore not the central hygiene measure in medical professions, and alcohol-based disinfection with high-quality hand agent is much less stressful than constant handwashing.

3.5 Clean Care Is Safer Care

In October 2005, WHO launched the "Clean Care is Safer Care" action under the Global Patient Safety Challenge (GSCP) to reduce the rate of healthcare-associated infections worldwide (http://www.who.int/gpsc/5may/en/). Key activity of "Clean Care is Safer Care" is the positioning of hand hygiene: hand hygiene is simple and effective. There is clear evidence in the literature that hand rub with an alcoholic hand sanitizer significantly reduces the incidence of NI.

Hands and gloves can be contaminated with bacteria, e.g. Gram-negative pathogens, *Staphylococcus aureus*, *Enterococci* and *Clostridium difficile* are contaminated after contact with infected or colonized patients, contact with patient environment or contact with objects. Microorganisms can survive on hands and gloves but also on all other surfaces for up to 60 minutes or longer, and thus they can easily be transmitted in the absence of hygiene measures. Without hand hygiene, contamination of the hands and gloves adds up to ongoing patient contact, increasing the odds of transmitted microorganisms on the hands and gloves. Outbreaks of healthcare-associated infections with multiresistant pathogens such as *Serratia marcescens*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* due to poor hand hygiene have been reported repeatedly in intensive care units, cardiac surgery departments and neonatal intensive care units. In the investigation of an outbreak with carbapenem-resistant *Acinetobacter baumannii*, the pathogens are often detected in patients, as well as on surfaces and

objects and on the hands of healthcare staff. Carbapenem-resistant pathogens are nowadays no longer treatable with standard antibiotics. Transmission and dissemination of carbapenem-resistant pathogens require a variety of measures, including hand hygiene, patient isolation, root cause analysis, intensified diagnostics and typing, staff training and antibiotic stewardship programmes. Hand hygiene can strongly protect patients and healthcare workers against transmission and hospital outbreaks.

Moments for Hand Hygiene (WHO) The 5 moments for hand hygiene to ensure maximum protection against transmission of the hospital microorganisms are:

- Before patient contact
- Before an aseptic task (i.e. bandage change, infusion, etc.)
- After body fluid exposure risk (after glove removal)
- After patient contact
- After contact with patient surroundings

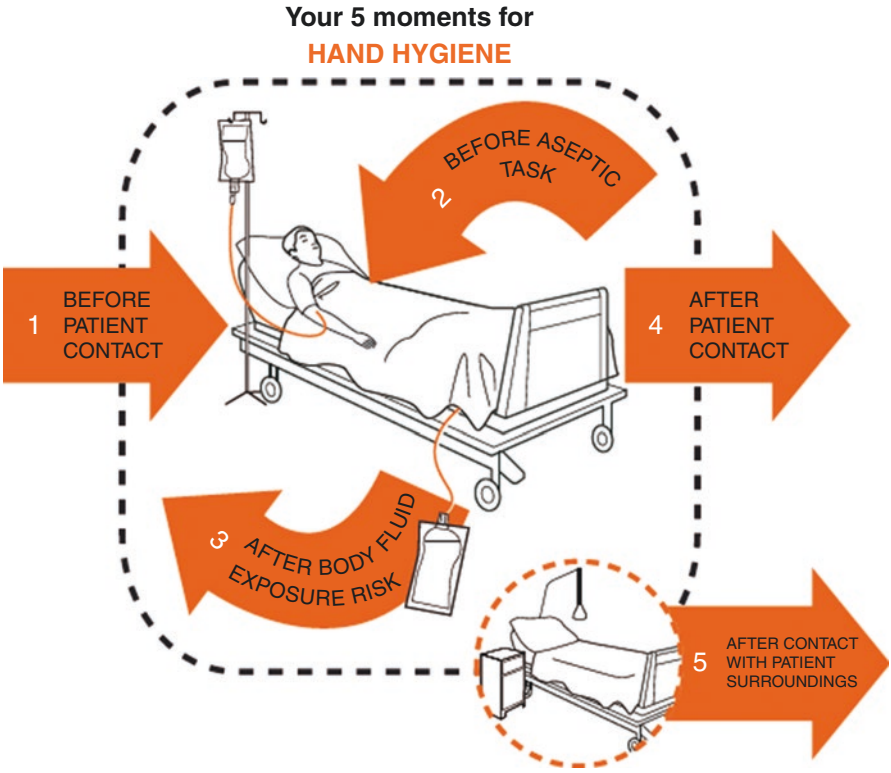
The patient's surrounding includes all surfaces that the patient can colonize with his or her hands but also through sneezing and coughing with "his or her" bacteria. Usually, it represents the radius of 1–1.5 mt. around the patient.

Hand hygiene campaigns and continuous training can increase hand hygiene compliance. It is important that dispensers with alcoholic hand agents are easily accessible and available. In addition, portable bottles with alcohol-based hand rub represent a valid alternative for hand hygiene when the dispenser is not available (Fig. 3.2).

Scarce education, poor training, adherence to past wrong behaviours and poor role models are just few of the reasons for the low levels of hand hygiene compliance. Other reasons include lack of time, lack of staff, no easily reachable hand dispenser, concern on skin damage, no understanding of pathways of pathogens and wearing of gloves. Training on hand hygiene and healthcare-associated infections can strongly improve the hand hygiene compliance. However, imprinted behaviours are slow to change.

Physicians have a special responsibility as role models. There is clear evidence that the role model function is very important and sustainably supports hand hygiene programmes. Eliminating the role model, the hand hygiene rate can drop from 50% to 5%. However, a strong role model requires the willingness of the entire medical team (doctors, carers, medical assistants and all other professionals involved in patient care) to perform hand hygiene at the 5 moments. In addition, hand sanitizer must be steadily available. Recalling and helping each other are part of a good medical practice beyond health professional boundaries. The final common goal is the well-being of the patient.

Efforts to improve hand hygiene have been proven to reduce infection rates and improve patient care. The compliance to perform antiseptic hand rub on the "5 moments" as well as in the correct rubbing technique can best be determined by a structured observation according to WHO ("WHO Observation Sheet") and



1	BEFORE PATIENT CONTACT	WHEN? Clean your hands before touching a patients when approaching him or her WHY? To protect the patient against harmful germs carried on your hands
2	BEFORE AN ASEPTIC TASK	WHEN? Clean your hands immediately before any aseptic task WHY? To protect the patient against harmful germs, including the patient's own germs, entering his or her body
3	AFTER BODY FLUID EXPOSURE RISK	WHEN? Clean your hands immediately anfer an exposure risk to body fluids (and after glove removal) WHY? To protect yourself and the health-care environment from harmful patient germs
4	AFTER PATIENT CONTACT	WHEN? Clean your hands immediately anfer an exposure risk to body fluids (and after glove removal) WHY? To protect yourself and the health-care environment from harmful patient germs
5	AFTER CONTACT WITH PATIENT SURROUNDINGS	WHEN? Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving - even without touching the patient WHY? To protect yourself and the health-care environment from harmful patient germs

Fig. 3.2 The "5 moments of hand hygiene" (WHO, Clean Care is Safer Care)

indirectly by the consumption of alcohol-based hand rub solution. Hand hygiene training, "advertising campaigns" with posters and other "promotional material", direct observations and feedback of the results result in a significant improvement in hand hygiene compliance. These hand hygiene campaigns are carried worldwide with a special focus on the 5th of May, the WHO day of hand hygiene, annually.

The impact of improved hand hygiene behaviour on the rate of healthcare-associated infections has been proven in numerous studies: Prof. Didier Pittet and his hygiene team increased hand hygiene compliance at Geneva University Hospital through a dedicated hand hygiene campaign during the 1990s and were able to reduce the HAI rates within 10 months by 42%. Continuing action on hand hygiene has made success sustainable over years. Further studies in the United States, the United Kingdom and Australia confirmed these results. By consistently performing alcohol-based hand rub before patient contact, aseptic activities, contact with patient material, patient contact and touching the patient environment (5 moments of hand hygiene), postoperative wound infections in orthopaedic facilities could be significantly reduced from 8.2% to 5.3% and by 54% in a neurosurgical units. Similarly, the literature shows that the transmission of rotavirus infections can be significantly reduced.

3.6 Further Protective Measures Against the Transmission of Multidrug-Resistant Microorganisms

With regard to the isolation of patients with multidrug-resistant pathogens in hospitals, a distinction has to be made between patients in whom contact transmission is to be prevented and those in whom an aerogenic transmission of the infectious agents is possible. In these particular cases, e.g. massive colonization or infection of the respiratory tract, large wound areas colonized with multidrug-resistant pathogens, scaly skin disease colonized with multidrug-resistant pathogens or in activities with the possibility of aerosol formation, the microorganisms are also released into the ambient air and spread. These patients ("spreaders") must be strictly isolated in single rooms, and the caregivers must wear complete protective clothing in the isolation room.

3.7 Procedures and Techniques of Hand Hygiene

Hand hygiene includes handwashing as well as hand rubbing with alcohol-based solutions. An important aspect of this topic, however, is also the asepsis, or "non-contamination", technique, which means that hands should not be contaminated whenever possible.

Alcohol-based hand rub:

- Hand rub is much more efficient in microorganism removal than handwashing.
- The hand rub should eliminate transient microorganisms.
- Surgical hand rubs aim to eliminate transient and resident microorganisms. It is part of the surgical hand preparation and applies to all surgical procedures.

Alcohol-based hand rub solution has a germicidal effect and prevents the spread and transmission of microorganisms, in contrast to handwashing, in which the pathogens are only mechanically rinsed off. In order to reduce the risk of transmission of infection, hands are thus disinfected. The optimal location of the dispenser facilitates and supports regular use.

Execution technique:

- Take a portion (about 3 mL) of a hand sanitizer from a dispenser, and rub into the dry hands.
- Rubbing technique (see Fig. 3.3). The extracted portion of hand rub dispenser must be rubbed until the alcohol has evaporated (at least 30 s). Finally no hand drying with towel!

Fig. 3.3 Antiseptic hand rub technique (WHO)

To avoid the spread of *Clostridium difficile* infections, handwashing has to be performed to rinse the spores, and, after drying with a disposable paper towel, hand rub with alcohol solution is recommended.

3.8 Selection of the Hand Dispenser

Choosing a suitable hand dispenser is very important to obtain optimal hand hygiene compliance. Almost all commercial preparations in Europe are alcohol-based (n-propanol, isopropanol and ethanol in different combinations/concentrations). They are bactericidal, fungicidal and (limited) virucidal, but not sporicidal. Therefore, when combating bacterial spores, it is advisable to wash hands thoroughly before or after antiseptic hand rub to mechanically remove the bacterial spores with water and soap. Since a purely alcoholic disinfectant can lead to skin damage through its strong drying effect and frequent use, alcohol-based hand rub preparations contain moisturizing and skin-care additives. A distinction is made between liquid- and gel-based alcohol-based preparations. Comparative studies between liquid- and gel-based alcohol-based hand disinfectants have shown that the bactericidal activity of some alcoholic gels is significantly lower than that of liquid preparations possibly because of their longer exposure time. In any case, the alcohol-based hand rub products should be approved by a recognized experts' commission. Only products that are mentioned in such hygiene commissions meet the verified efficacy criteria, such as:

- Rapid action (short exposure time)
- Broad spectrum of action
- Low inactivation by blood and proteins
- Good tolerability and low risk of allergic reactions

3.9 Compatibility of Hand Sanitizers and Gloves

By incorporating moisturizing and nourishing substances, alcoholic disinfectants are well tolerated if they are used properly, i.e. not on wet and irritated skin. Healthy intact skin incompatibility is very rare.

Wearing gloves in clinical practice does not replace alcohol-based hand rub. Wearing gloves may lead to sweating, damage and maceration of the skin. Gloves must be worn if body fluids or other contaminated materials are present. Gloves need to be changed every time the healthcare workers move to another patient because also gloves can transmit microorganisms. Depending on the quality of the gloves, prolonged wear can lead to micropore and microorganism permeability. After glove removal, hand disinfection must been done.

3.10 Asepsis ("Non-contamination")

3.10.1 "No-Finger" Technique

This includes the use of instruments (tweezers, probe, etc.) instead of hands and fingers or of the elbow or forearm instead of hands by dispensers or wash taps.

3.10.2 Disposable Gloves

Gloves are divided into three categories: sterile and non-sterile examination gloves, sterile surgical gloves and protective gloves for the administration of chemotherapy. Examination gloves and protective gloves are mainly used for self-protection. Contaminated gloves, as well as hands and other contaminated items, can transmit pathogens. Therefore, all gloves must always be removed after unclean operations, avoiding cross-contamination.

Non-sterile disposable gloves should always be used when handling body fluids or when there is a risk of contamination during an activity. Disposable gloves must always be removed after unclean activities. Wearing gloves for a long time damages the skin due to moisture accumulation.

Gloves are not universal protection. A wrong gloves' removal may contaminate the hands and surrounding skin area. Therefore, the hands must always be disinfected after removing the gloves.

3.11 Handwashing and Drying

Washing hands with soap and water is mainly used for the mechanical removal of dirt and for a smaller proportion of loosely adhering bacteria. When combating bacterial spores, it is also important to wash hands thoroughly before and after alcohol-based hand rub to mechanically rinse the alcohol-resistant bacterial spores.

Please note the following:

- The right washing of the hands at the right time is a central hygiene measure.
- Handwashing does not cause a microorganism's reduction as an effective antiseptic alcohol-based hand rub.
- When washing, microbes that are capable of reproduction can be spread into the environment.
- When drying hands, a hand's contamination with microorganisms is possible.
- Do not touch the liquid soap dispenser with soiled fingers (see non-contamination techniques).

- Thoroughly wash and rinse hands, especially cleaning the fingertips and nailfolds as well as the spaces between the fingers.
- Dry hands with a clean (disposable) paper towel. Disposable towels have to be disposed of correctly.

3.12 Skin Care

An intact and healthy skin is the prerequisite for good hygiene; therefore, skin protection and skin care play an important role. Many hand disinfectants already contain skin care substances.

- Do not set water too hot.
- Use brushes only to clean visible dirt beneath the fingernails.
- Rinse soap residues as well as you can.
- Perform the final rinse with cold water.
- Use protective gloves when working with aggressive substances (such as earth, cement).
- Do not use disposable gloves with alcohol-wet hands.
- Use fatty hand cream (especially overnight).

3.13 Conclusions

Hand hygiene is the fastest and most effective way to protect patients from transmission of infectious agents and infections. The 5 moments of hand hygiene are *before* patient contact, *before* an aseptic task, *after* body fluid exposure risk, *after* patient contact and *after* contact with patient surroundings. The common goal of hand hygiene is the well-being of the patient.

Further Reading

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Medical Instruments and Devices

4

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4.1 Basics: Medical Devices, Reprocessing and Validated Procedures

Medical instruments and devices (MDs) are medical products intended for human use by the manufacturer. These include implants, products for injection, infusion, transfusion and dialysis, software, catheters, pacemakers, dental instruments, dressings, vision aids, x-ray equipment, condoms, walking aids, prosthesis, etc.

Unlike drugs that act pharmacologically, immunologically or metabolically, the intended main effect of medical devices is primarily achieved by physical means. They must therefore have no pharmacological effect or intervene in immunological processes or the metabolism of humans. As a rough rule of thumb, the following can be distinguished:

- Medicines have a chemical/biochemical effect.
- Medical devices have a physical effect.

Pathogen-contaminated MDs can be the source of human infections. If it is a reusable MD, measures must be taken before application to the next patient so that pathogens cannot be transmitted. The general term reprocessing usually includes

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_4

cleaning, disinfection and sterilization. In order to place MD in a microorganism-free or sterile condition after use, its preparation must be selected as intended and carried out with validated procedures.

Validated Procedures Since sterility is not immediately apparent after reprocessing, reprocessing procedures must be performed in a manner that ensures the traceability of these procedures and do not jeopardize the safety of patients, users or third parties.

The chain of all necessary treatment processes must be optimized and designed so that weaknesses in one of the individual steps can be demonstrated and the overall success of the treatment is not endangered.

The preparation usually comprises the following individual steps:

- Proper preparation—precleaning, disassembly of the medical device if necessary and preparation for transport
- Cleaning/disinfection, rinsing and drying
- Check for cleanliness and integrity (e.g. material damage, corrosion) and visual inspection
- Care and repair
- Functional testing
- Packing and sterilization if required
- Reprocessing ends with documented release of the MD for reuse

When reprocessing, *mechanical processes are to be preferred over manual processes* because they can be validated, and the cleaning result can therefore be traced. For reasons of internal organization and the required quality management, all steps of the reprocessing of MD must be regulated and documented. Manual cleaning and disinfection procedures must also be carried out according to documented work instructions, using resources and methods agreed with the MD. In addition, mechanical and manual reprocessing processes may only be carried out by trained specialist personnel entrusted with this task.

4.2 Risk Classification for Medical Devices

One of the most important measures for the proper execution of the treatment is the risk assessment of the reprocessed MDs. The classification into risk classes is based on the necessary reprocessing procedure. The operator is responsible for the correct classification of the MD and the determination of the treatment methods, taking into account the information provided by the product manufacturer. The level of terminal reprocessing required by medical devices is based on the classification system

developed by Spaulding in 1970. It classifies medical devices (MDs) into three categories, based on the client/patient/resident's risk of infection due to contact with various types of devices. The correct reprocessing procedure should minimize the risk of residues from previous applications (e.g. blood, secretions, blood or body components) or changes in material properties (e.g. embrittlement, accelerated wear of materials, changes in surface properties).

Spaulding classification according to risk levels categorized medical devices into (1) *noncritical* MDs which come in contact with intact skin; (2) *semi-critical* MDs which come in contact with mucous membrane, wounds or non-intact skin; or (3) *critical* MDs which come in contact with blood, blood products, primarily sterile tissue or in MDs which penetrate the skin or mucous membranes and come into contact with the human blood system, tissue or organs.

Semi-critical items with the potential for contact with open lesions, or irritated mucous membranes, are treated as critical items.

Medical products can be also classified according to the type of reprocessing. Medical devices for which the effectiveness of cleaning is not directly assessable by inspection (i.e. by small/long lumens, more complex/difficult to access and therefore poorly clean surfaces) have increased demands on their preprocessing. This includes those products whose number of treatments or applications is limited by the manufacturer to a certain number. Within the critical medical devices, it is important to make a distinction between thermolabile and thermostable products:

- Thermostable: steam sterilizable at 134 °C
- Thermolabile: not steam sterilizable

The particularly high demands on the preprocessing of thermolabile MDs result from the fact that with these products steam sterilization is not possible; therefore a low-temperature chemical sterilization procedure is needed. If MDs have additionally small lumens, cavities or rough/grooved surfaces, these represent extra reprocessing difficulties to be considered. If reprocessing of these products cannot be performed by validated processes or reprocessing is not effectively possible due to the previously mentioned reasons, reprocessing is waived, and these MDs are classified as disposable products to minimize risk.

4.3 Cleaning and Disinfecting Agents

The disinfectants used for treatment must be listed in an expertise directory of tested and approved disinfectants. To be listed in this directory, the manufacturer of a substance must present certificates of disinfecting effectiveness of the disinfectant that he wants to be listed. The effectiveness tests are carried out by registered and certified microbiological laboratories and are documented in certificates of effectiveness.

4.3.1 Disinfection Procedures

4.3.1.1 Physical Disinfection Procedures

Physical disinfection has good environmental compatibility and is safe to use. Physical disinfection is mostly used in the health-care environment and microbiological laboratories. There are three physical disinfection methods:

- Dry heat: microwave disinfection, burning and annealing
- Moist heat: low-pressure steam (105 °C) and dishwasher (80–95 °C)
- UV radiation (UV-C): air and water disinfection

Further details are described in Chap. 5.1.3.

4.3.1.2 Chemical Disinfection Procedures

The mechanism of action of chemical disinfectants is usually unspecific. It is explained in detail in Chap. 5.1.4.

4.3.1.3 Chemo-Thermal Disinfection Procedures

Chemo-thermal disinfection is the combination of chemical agents and heat in order to be able to lower the temperature when, for example, dealing with thermolabile products (e.g. automated endoscope washer disinfectors where disinfection is achieved at 50–65 °C with addition of disinfectant).

4.4 Task of Hospital Hygiene

Every medical device used in the hospital should have been tested for its reprocessability requirements and their realistic implementation. The manufacturer's information of an MD must be reasonable and feasible. They must also comply with modern standards in terms of safety (a technical test is carried out by technical departments). It is paramount to ensure patient safety from the technical as well as the hygienic side. If ambiguities arise in the preparation procedure recommended by the manufacturer, the manufacturer must be contacted directly. The hygienic evaluation of an MD is based on the following guidelines:

1. Is it a non-reprocessing disposable or reprocessable MD?
2. Are there any manufacturer information on intended use and treatment?
3. Is risk classification according to Spaulding classification (noncritical/semicritical/critical) available? (See Table 4.1.)
4. Can the MD be cleaned easily or is an increased effort necessary?
5. Has the manufacturer named cleaning and disinfection agents that have a credible claim regarding their antimicrobial efficacy?
6. Are disinfection and validated sterilization procedures mentioned, which can be carried out and organized in-house by means and devices in such a way that the success of these procedures is comprehensibly guaranteed and the safety and health of patients, users or third parties is not at risk?

Table 4.1 Spaulding's classification of medical devices

Classification	Definition	Medical device	Process special requirements
Noncritical	MDs that do not touch the client or touch only intact skin, but no mucous membranes	ECG electrodes, oximeters, environmental surfaces, shared wheelchairs in clinics, treatment surfaces, blood pressure cuffs, toys, stethoscopes and audiometers	Cleaning alone or cleaning followed by low-level disinfection
Semi-critical	Items that come into contact with non-intact skin or intact mucous membranes, but do not penetrate body surfaces	Anaesthesia equipment, tonometer, respiratory therapy equipment, reusable ear syringe nozzles, trans-rectal probes, and vaginal, nasal and rectal specula	Cleaning followed by high-level disinfection (bactericidal including mycobacteria, fungicidal and virucidal), sterilization is preferred
Critical	Items penetrating body tissues allowing for direct contact with the bloodstream or another sterile area of the body	Surgical and dental instruments, foot and nail equipment, biopsy instruments and MIC-Trocar	Cleaning followed by sterilization after every use

Suggested Reading

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Reprocessing: Cleansing, Disinfection, Sterilization

5

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5.1 Cleansing and Disinfection

Cleaning refers to the removal of all visible dirt or contamination of fomites or the environment. The most frequently used cleaning agents are detergents. Soap is not used for environmental cleaning anymore but the cleaning of hands and skin.

5.1.1 Definitions

Disinfection refers to the elimination of all potential pathogenic microbes. The number of microbes on a surface or an object is reduced so far that no infection can occur (reduction of 5 log steps, e.g. by a factor of 100.000 of the initial germ count). Disinfection with sporicidal disinfectants also kills bacterial spores. For a disinfection process, it is not required that all microbes are inactivated but that all pathogenic microorganisms are eliminated.

Therefore, the disinfection aims to break the chain of infection and prevent shedded pathogens to reach a new infection target (human, food, etc.). To achieve this, disinfection must always be carried out meticulously. A strict conformity what to disinfect, what pathogens must be eliminated and what are the conditions sensitivity, humidity, pollution and temperature has to be ensured.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_5

Disinfection is the selective reduction of the number of pathogens by physical or chemical inactivation, so that infection by these objects is not possible. Continuous disinfection of the healthcare environment prevents the spread of pathogens during the care and treatment of a patient. All surfaces and objects in the healthcare environment that are contaminated by infectious secretions shed by the patient should be disinfected. Final disinfection of surfaces and objects has to be carried out when there is a change of patients in the room.

5.1.2 Classification of Disinfection Procedures

Disinfection procedures are classified according to their intended practical use in healthcare according to the sensitivity of the pathogen:

- Group A—killing of vegetative forms of bacteria (including mycobacteria) and fungi
- Group B—inactivating viruses
- Group C—killing spores of *Bacillus anthracis*
- Group D—killing the spores of *Clostridium perfringens* and *Clostridium tetani*

Disinfection procedures are classified according to the method of disinfection:

• Physical disinfection procedures – Fire or heat – Water • Thermal disinfection procedures • Actinic disinfection procedures – Irradiation	• Chemical disinfection procedures – Alcohols – Phenols – Aldehydes – Halogens – Oxidants – Heavy metals

5.1.3 Physical Disinfection Procedures

5.1.3.1 Thermal Disinfection

In order to inactivate the pathogenic microorganisms, heat with sufficient temperature must be transferred to the germs. It should be noted that the microorganisms can be spared from the heat effect by protection in dirt particles (e.g. blood, pus, fats, soil) for even long periods and thus no disinfection is achieved.

For the disinfection of thermostable articles (e.g. objects which can withstand heat without being damaged), a thermal process should always preferred to chemical processes since they have a safer and measurable effect.

5.1.3.2 Disinfection Using Fire

Burning (Incineration)

Incineration is the safest method of disinfection provided that all objects to be disinfected are completely burned. Incineration is applicable to contaminated wound

dressings in a hospital, disposable articles and other disposable devices with blood residues, waste of a microbiological laboratory, etc.

Attention: incineration of products made of polyvinyl chloride produces hydrochloric acid!

Annealing
Disinfection of metal instruments, e.g. platinum loops as used in the microbiology laboratories. Scalpels are not annealed because they get truncated and thus useless.

Flaming
Flaming is limited to fomites or devices that are thermostable. Flaming is usually a process of short duration. It can be safely applied to metal instruments and objects that conduct heat well because due to their thermal conductivity, the maximum temperature is reached immediately to kill the germs. But due to the insecure conducting properties, it cannot be assured that once the required temperature is reached, it can kill the germs. Therefore flaming is regarded as an uncertain disinfection procedure.

5.1.3.3 Disinfection Using Boiling Water

Hot Water
Hot water with a temperature of 85–95 °C achieves disinfection. Exposure to hot water for 3 min disinfects the category groups A and B; exposure for 15 min disinfects the category groups A, B and C. Disinfection with hot water is performed in dishwashers, bedpan washer disinfectors and laundry disinfection (categories A, partly B).

Boiling
Boiling in water at temperatures of 99–100 °C achieves disinfection. At 3 min boiling water disinfects category groups A and B, at 15 minutes boiling the groups A, B and C.

Steam Disinfection
The heat in steam is greater than in hot water. Goods and objects to be disinfected must be loosely introduced into the steam disinfection device, so that the steam can penetrate equally well everywhere.

There are two steam disinfection methods:

- Steam flow method
  The air is displaced by saturated steam from the disinfection chamber. The flowing steam (depending on the air pressure) reaches a maximum of 100 °C. A time of 5 min is needed to kill the germs from the groups A and B; 15 min are needed to kill the group C. This method is used to disinfect medical waste.
- Fractionated vacuum process (VDV procedure)
  Removal of air is performed by repeated (fractionated) evacuation. Then there is the inflow of saturated steam. Disinfection temperatures are 75–105 °C. Then a drying step follows and evacuation of the vapour. Depending on the duration and temperature, microorganisms of groups A, B or C are killed.

5.1.3.4 Combined Chemo-thermal Disinfection

Additional chemical disinfectants are added to thermal disinfection (60°C for 10 min = Groups A and B). This is the method of choice for heat-unstable material (anaesthesia masks, tubing, endoscopes).

5.1.3.5 Actinic Disinfection

Radioactive rays (beta or gamma rays) and ultraviolet rays (UV rays) can be used for the inactivation of microorganisms by ionizing radiation. Ionizing radiation is mainly used in industrial and technical contexts. UV disinfection is commonly used for disinfecting air and water. There are some efforts to use UV disinfection for medical devices. The back draw is that UV rays do not penetrate solid materials and the so-called areas which are shadowed from the reach of UV rays may inhibit full disinfection.

5.1.4 Chemical Disinfection

Chemical disinfectants are usually complex formulations of active molecules. The mode of action of these active molecules is thought to be non-specific; chemical disinfectants dissolve viable parts of microorganisms or interfere with their metabolism. All chemical disinfectants need to come in contact with microorganisms in order to act.

5.1.4.1 Possible Pitfalls of Chemical Disinfection

When submerging medical instruments for disinfection purposes in a chemical disinfectant solution, it is very important to assure that all surfaces of the medical instruments come in contact with the chemical disinfectant (open scissors or clamps before submerging them), lumina might be inadequately filled with disinfectant solution (narrow tubes, needles, etc.), or they could be coated with lipids and therefore have an increased surface tension. It should also be noted that there may be considerable variation (in terms of pH, hardness, salinity, etc.) in the solutions surrounding the target microorganisms and the state in which the latter is present (e.g. isolated bacterium or bacterium included in complex biofilm).

Surfaces should be disinfected by wiping and scrubbing motions. This is very important in order to remove dirt particles that could otherwise “protect” bacteria from the disinfectant. Do not use spray disinfection, as the mechanical component of removing the dirt particles will be lost. And furthermore when spraying, you create disinfectant aerosols, which can then be inhaled by the healthcare workers and lead to medical impairment.

5.1.4.2 Most Important Chemical Disinfectant Groups

Alcohol

In the hospital setting, monovalent alcohols are mostly being used, especially:

- Ethanol
- Isopropanol
- n-Propanol

Alcohols are bactericidal rather than bacteriostatic against vegetative forms of bacteria; they also are tuberculocidal, fungicidal and virucidal, but they are not active against bacterial spores. Their bactericidal activity is based on the fact that alcohols dissolve the bacterial cell wall (but not those of bacterial spores); they can also act on enzymes and bacterial by-products. The activity of alcohols depends strongly on their concentration. When diluted below 50% concentration, alcohols lose their bactericidal activity; their optimum bactericidal concentration is between 60% and 90% solutions in water (volume/volume).

Alcohols are very fast-acting disinfectants; however they also evaporate rapidly, making extended exposure time difficult to achieve. It is therefore very important to keep the medical items continuously alcohol wet. Use ethanol 80 vol%, isopropanol 60–70 vol% or n-propanol 50–60 vol% for hand disinfection.

Alcohol is flammable and consequently cannot be used to disinfect large surfaces! It must be stored in a cool, well-ventilated area.

Main uses: Hand disinfection, instrument disinfection, disinfection of small surfaces (<1 m^2)

Aldehydes

Aldehydes are used for disinfection of medical devices and hospital surfaces. They are very reliable disinfectants and gentle regarding instrument longevity.

Formaldehyde is the main aldehyde used for disinfection purposes and is used principally as a water-based solution called formalin, which is 35–40% formaldehyde by weight.

Formaldehyde has an allergenic potential on the skin and is therefore not used for skin disinfection. It has a pungent odour and is a potential carcinogen which is why an employee exposure standard for formaldehyde has been set that limits an 8-h time-weighted average exposure at 0.6 mg/m^3 ambient air. It should be used for targeted purposes only.

Formaldehyde has good bactericidal activity, and in high concentrations with long exposure times, it shows tuberculocidal, fungicidal, virucidal and sporicidal activity.

For the disinfection of medical devices (e.g. surgical instruments), formaldehyde is used in its gaseous form (low-temperature steam formaldehyde sterilization): formaldehyde gas (5 g/m^3) in steam (requires high humidity at least 70% room humidity) for at least 6 h. Effective range: A and B

For surface disinfection and for laundry disinfection, formalin can be used. For laundry disinfection the laundry is being exposed for at least 5 h to 3% formalin.

Disadvantages of Aldehydes

Pungent odour, allergenic potential (employee exposure standard: 0.6 mg/m^3 air) and high "protein error" (i.e. the bactericidal activity of aldehydes is decreased in the presence of protein or soil, e.g. pus, blood serum, etc., due to the fact that the active compound is bound to protein and therefore not available in a sufficient concentration to act as a disinfectant)

A high "protein error" is found for aldehydes (depending on the compound), quaternary ammonium compounds and oxidants. Alcohols and phenols have a low

"protein error" (i.e. the presence of proteins does not interfere so much with their bactericidal activity).

Effective Range

- Bacteria
- Bacterial spores only when maintaining higher concentrations over longer exposure times at higher temperatures
- Many viruses (HBV only when using high concentrations and long exposure times at higher temperatures)
- Fungi (less reliable activity than for bacteria)

Usage

In its gaseous form: Disinfection of medical devices and instruments (special anaesthesia supplies, face masks, mattresses) using low-temperature formaldehyde and formaldehyde vapour (5 g/m^3) in steam (at least 70% room humidity) for at least 6 h. Effective range: A and B

Phenolics

The first phenol used by Joseph Lister in his pioneering work on antiseptic surgery was carbolic acid, which nowadays is obsolete. Phenolics are active against bacteria, fungi and some viruses but not against bacterial spores or HBV.

Phenolics are toxic and can be absorbed via the skin or be inhaled if spread on large surfaces. They can lead to liver damage with hyperbilirubinemia in premature infants and new-borns and should therefore not be used in these areas.

The indication for the use of phenolic disinfectants is therefore limited. One of their important advantages is their low "protein error" and therefore suitability to dissolve blood contaminations.

More important than phenol itself are phenolic derivate such as diphenylderivates. Diphenylderivates have a very narrow range, showing mostly bacteriostatic activity against gram-positive bacteria. Its most important representatives are chlorhexidine and octenidine, used for mucosal and skin decontamination for certain healthcare-associated gram-positive pathogens.

Halogens and Halogen-Releasing Agents

Chlorine-, iodine- and bromine-containing compounds are highly reactive as oxidizing agents; they show good bactericidal activity against bacteria, fungi and certain viruses (A, B, partially C). Chlorine is used in water, linen, and environmental surface disinfection in sanitary and kitchen areas.

Iodine shows good activity against bacteria and bacterial spores, but its virucidal effect is unreliable. Elemental iodine bound to high-molecular weight surface-active compounds is used as an antiseptic, e.g. as polyvinylpyrrolidone (PVP-Jod) for mucous membrane disinfection. PVP-iodine preparations should be avoided in neonates, in patients with thyroid disorders and during pregnancy, as iodine can be resorbed and lead to a systemic increase of iodine in the organism.

PVP-iodine-containing soaps are used for surgical handwashing, and their effect is increased, when alcohol is added.

Peroxygens and Other Forms of Oxygen

Oxidizing agents (oxidants) are substances that accept electrons liberated during oxidation. Oxidants are potent antimicrobial agents. They include substances such as ozone, potassium permanganate or hydrogen peroxide.

Oxidants are very effective antimicrobials showing potent bactericidal, fungicidal and virucidal activity. Due to their corrosiveness and therefore very restricted material compatibility, their use for instrument disinfection is limited to corrosion-resistant materials. They are mainly used for specified instruments such as ventilators and infusion pumps and also for surface disinfection.

Oxidants, e.g. perform 0.75%, are easy and safe to use for routine disinfection and sanitization purposes in the hospital. Some of their representatives come in a ready-to-use format, helping to avoid dosage errors.

Disadvantages: Oxidants have a high "protein error" and can therefore only be used on previously cleaned surfaces; they should under circumstances be used on blood or otherwise protein-contaminated surfaces. In such cases previous removal of blood contamination, e.g. with phenolics, must precede the use of oxidants.

Metals

Metals used for disinfection are often called "heavy" metals, a term used to qualify metallic elements with a greater specific density. The formally frequently used mercury compounds (Mercurochrome, Merfen) are nowadays obsolete. They are not used anymore due to their toxicity and comparably low disinfectant (only microbiostatic) activity.

5.1.4.3 Disadvantages of Chemical Disinfection

- Gaps in effectiveness (spores, HBV) and environmental contamination.
- Chemical disinfectants are concentration-, temperature- and pH-dependent.
- Decomposition and loss of activity.
- Protein error.
- Recontamination potential (if disinfected materials are flushed with water—against the instructions!)
- Residual chemicals in materials (e.g. in rubber parts).
- Material corrosion.
- Health effects on healthcare users.

5.1.5 Surface Disinfection

There are many surface disinfection products with varying active ingredients on the market. Depending on the active ingredient, certain factors such as "protein error" and microbicide activity have to be considered when choosing the correct disinfectant. In the presence of bodily fluids, e.g. there is—from a microbiological-hygienic

point of view—no alternative to aldehydes, particularly formaldehyde. (When using aldehydes the necessary precautions regarding employee safety have to be respected.) Chlorine- or iodine-based disinfectants are not recommended for surface disinfection, due to their high "protein error". Peroxides are equally not recommended, as they are inactivated through peroxidases present in blood and human bodily fluids. Alcohols in adequate concentration cannot be used on big surfaces due to their fast evaporation and their fire and explosion hazard, even though they would provide the correct microbicide effectiveness needed and show a low "protein error".

Aldehyde-free disinfectants can be used for routine periodical surface disinfection in non-medical areas where disinfection is deemed necessary for other than medical purposes, e.g. whenever the detergent activity is more important than the actual safe disinfectant activity. This kind of routine disinfection can only be done on previously clean surfaces, and cleaning utensils need to be clean themselves so as not to disseminate potential microorganisms.

Surfaces should always be disinfected by wiping and scrubbing motions in order to remove dirt particles, which could otherwise "protect" bacteria from the disinfectant.

Never apply surface disinfectants using spray disinfection, as the mechanical component of removing dirt particles will be lost. Furthermore when spraying disinfectants, you create disinfectant aerosols, which can then be inhaled by the healthcare workers and lead to medical impairment.

5.1.6 Routine Disinfection

We speak about routine disinfection if no contamination of the surface to be treated with blood, other bodily fluids or microbial cultures is to be expected. Under these circumstances all disinfectants listed as "surface disinfectants" in the expert register of the ÖGHMP/ASHMPM (Austrian Society for Hygiene, Microbiology and Preventive Medicine) can be used.

5.1.7 Disinfection of the Hospital Environment of a Known Infectious Patient

In such a case, aldehyde-based disinfectants listed as "surface disinfectants" in the expert register of the ÖGHMP/ASHMPM (Austrian Society for Hygiene, Microbiology and Preventive Medicine) should be used. Formaldehyde is the preferred choice if abundant protein residues are expected (e.g. blood, excretions and bodily fluids) on the surfaces or items to be disinfected.

Application: Remove the contamination using a disinfectant-soaked single-use cloth until no more residues can be seen. Then with a new single-use cloth, moisten the area with disinfectant, and adhere to the manufacturer's recommended exposure time. Finally discard the cloth avoiding any contamination.

5.1.8 How to Proceed in Case of Extended Contamination

(E.g. extended blood pool, spilled bacterial culture, etc.)

Step 1:	Absorb coarse dirt particles with an absorbent material (e.g. cellulose or similar) and dispose without contamination (garbage bag for medical waste). *Do consider*: Self-protection using gloves and single-use aprons. If liquids are discarded in garbage bags, always use sufficient absorbent materials to avoid spillage!
Step 2:	Spread the absorbent material onto the contaminated surface and carefully soak with disinfectant solution. Leave as it is for 1 hour, to ensure optimal working conditions for the disinfectant. Clearly delineate and secure the contaminated area for the entire time of disinfection.
Step 3:	Discard the soaked absorbent/covering material in the garbage bag. Finish off with a wipe surface disinfection.

Mycobacterium Tuberculosis Only use disinfectants with mycotuberculocide activity, and strictly follow manufacturer's recommendations regarding concentration and exposure times.

Rotavirus Infected patients usually massively shed rotaviruses with the stool and vomit and contaminate the environment. Therefore routine disinfection measures are not sufficient to eliminate this massive environmental contamination and interrupt the infectious chain. Additional barrier precautions such as gloves, nose-mouth mask and single-use aprons are needed (never touch surfaces with unprotected hands; try to avoid surface contamination). The use of virucidal disinfectants (hand—as well as surface disinfectants) is mandatory.

5.1.9 Disinfection of Medical Instruments

Disinfection of medical devices is important to avoid transmission of infectious diseases between patients but also to protect healthcare workers against potential infection risks. Furthermore it is important for the maintenance and preservation of the medical devices. Medical device reprocessing comprises different steps from the initial use until the renewed allocation.

Medical devices should be disposed of in a dry manner from the place of use until the reprocessing area.

Automated cleaning and thermal disinfection with validated processes allow for the best possible quality of reprocessing and safety not only for patients but also for the reprocessing personnel. Such reprocessing units are best organized in a centralized cost-effective setting. Disposal systems, chemical waste disposal, water quality and other process relevant factors need to be matched according to the available automated reprocessing system in use. Cleaning and disinfection parameters need

to be revaluated regularly (using physical, chemical or quantitative biological markers); additionally yearly revalidation is recommended. Manual cleaning and/or disinfection should only be used exceptionally, e.g. breakdown of automated reprocessing.

5.2 Sterilization

5.2.1 Definition

The process of sterilization consists of eliminating all viable organisms including bacterial spores from a surface or a product.

What Distinguishes Sterilization from Disinfection?
Sterilization is intended to eliminate all existing viable organisms, including bacterial spores.

5.2.2 Sterilization Procedures

Similar to the disinfection methods, we distinguish physical from chemical sterilization techniques:

I. Physical techniques:
   1. Moist heat (steam) sterilization
   2. High-temperature dry-heat sterilization
   3. High-energy ionizing radiation sterilization
II. Chemical sterilization techniques:
   1. Ethylene oxide (EO) sterilization
   2. Formaldehyde (FO) sterilization

Moist heat (stem) sterilization is still considered to be the gold standard of sterilization and should be applied whenever possible. Nevertheless medical diagnostics and treatment options are increasingly relying on technically complex and at the same time very delicate medical instruments which are often susceptible to heat, pressure and moisture. Such thermolabile medical devices cannot be sterilized at high temperatures. For each medical device, appropriate procedures for the disinfection and sterilization need therefore to be defined. There is currently no universal sterilization procedure.

5.2.2.1 Physical Sterilization Techniques

Moist Heat (Steam) Sterilization
Moist heat (steam) sterilization is currently the most reliable sterilization technique available. Through condensation of high-temperature steam on surfaces, the

liberated energy irreversibly damages microorganisms. Direct contact of the sterilant (high-temperature steam) with the MO throughout the whole exposure time is necessary for the sterilizing effect to occur. By increasing the pressure (pressure >1 bar) of the process exposure conditions, high-temperature saturated steam can be produced in order to generate sufficient microbicide energy within shorter time periods.

For steam sterilization the following cycles are widely used: 15 min sterilization at 121 °C (steam pressure 2 bar) or 3 min at 134 °C (steam pressure 3 bar).

Steam sterilization is performed in so-called autoclaves—steam sterilizers. They consist of chambers shaped depending on their application and capable of withstanding the required atmospheric pressures for sterilization. In order for steam to also be able to penetrate hollow lumens, efficient air removal from the autoclave chambers is essential.

Selected steps of the technical time schedule of a steam sterilization cycle inside an autoclave are as follows:

Preheating: Time needed for the inner chamber walls to reach a certain temperature. *Heating time*: Time from the beginning of heat supply inside the autoclave until a temperature of 120 °C is reached. *Temperature compensation time*: Time until the temperature of the goods to be sterilized has reached the expected steam temperature of, e.g. 121 °C or 134 °C. *Killing time*: Time needed to kill targeted microorganisms *Safety margin*: Additional time given on top of the killing period to ensure safe inactivation of MO	*Pressure relief*: Time necessary until readjustment of the pressure inside the autoclave to the environmental pressure *Drying time*: Time needed for the goods to be sterilized to dry within the autoclave *Operating time*: Time necessary for a full sterilization cycle

High-Temperature Dry-Heat Sterilization

High-temperature dry-heat sterilization (e.g. 180 °C for at least 30 min) consists of sterilization using hot dry air, comparable to the use of an oven.

Disadvantages of dry-heat sterilization:

- Slow heat transfer onto the goods to be sterilized.
- Higher temperatures and longer sterilization cycles are needed in comparison to other sterilization techniques.
- Heat is not evenly distributed within the chamber leading to heat stratification with certain areas of the load remaining cooler than others. Certain goods might therefore not be safely sterilized.
- Loading patterns of the goods have a big effect on the sterilization outcome; overloading can lead to uneven heat distribution with inadequate sterilization.

- No validation protocols for this sterilization technique are currently available.
- High-temperature dry-heat sterilization should not be used in the hospital setting!

5.2.2.2 Chemical Sterilization Techniques

Chemical sterilization techniques are low-temperature gas sterilization techniques using broad-spectrum antimicrobial/biocidal agents as chemical sterilant (e.g. ethylene oxide or formaldehyde) in a closed system. Only thermolabile medical devices not withstanding steam sterilization should be "gas sterilized".

Requirements necessary for safe sterilization (temperature, humidity, gas concentration, exposure time) need to be fulfilled for all external and internal surfaces of the goods to be sterilized.

For all sterilization goods, steam sterilization should be the first priority. Only if material incompatibility hinders steam sterilization, gas sterilization should be considered.

Formaldehyde Sterilization

Formaldehyde (FO) is used as a biocide in gaseous form and requires a highly humid environment for its biocidal activity. FO is used in a low-temperature steam mixture for sterilization purposes. This mixture is neither flammable nor explosive and is easily removed from the sterilized goods—i.e. rapid aeration over time—after the sterilization cycle, allowing for its rapid reuse after reprocessing.

Formaldehyde gas sterilization achieves microbicide activity at temperatures between 60 and 75 °C. (Neither saturated steam nor FO alone is sporicidal at these temperatures; it is the combination of both processes that ensure a sporicidal effect.)

Applications: This sterilization technique applies to thermo-sensitive medical devices that need to be sterilized and are compatible with FO, e.g. endoscope reprocessing, implant at sterilization, intubation catheters, special probes, etc.

FO is considered to be a hazardous substance. There still remains concern about the safe use of FO, which is toxic, mutagenic and carcinogenic. National regulations regarding safe FO use need to be complied with.

Ethylene Oxide Sterilization

Ethylene oxide (EO) is toxic at relatively low concentrations. Further EO is carcinogenic and considered a hazardous substance. Safety regulations apply.

Advantages of EO sterilization are its good material penetration abilities and the low sterilizing temperatures needed. On the other hand, to remove residual EO from the load, adequate aeration times (of up to 16 h) can be required, making EO sterilization inadequate for emergency sterilization or sterilization of goods with a high turnaround time.

5.2.3 Organization of Hospital Sterilization and Disinfection Units

Central Organization

All goods that need reprocessing (disinfection or sterilization) are transferred to a centralized reprocessing unit where contaminated goods are decontaminated

(validated automated washing, disinfection followed by packaging and various sterilizing techniques depending on material compatibility).

After successful reprocessing the sterilized goods are delivered back to the original sender and have to be stored according to current regulations until further use.

Decentral Organization
All necessary reprocessing steps are carried out on site in a decentral reprocessing unit.

5.2.4 Which Medical Devices Need to Be Sterile?

According to the "Spaulding's Classification of Medical Devices", all critical medical devices that enter sterile tissues, including the vascular system and wounds, need to be sterile.

5.2.5 Which Sterilization Technique Should You Use?

The sterilization technique to be used depends on the materials to be sterilized. Metallic items and instruments are often more thermoresistant and therefore compatible with steam sterilization. For thermo-sensitive goods (e.g. rubber or synthetic materials), low-temperature sterilization techniques might be more appropriate. Always consult manufacturer's instructions.

5.2.6 Important Prerequisites for Sterilization

The most important precondition for sterilization is a previous thorough cleaning process, followed by disinfection and inspection of the goods. Only clean, residue-free and maintained goods should be sterilized; otherwise goods may be altered or even damaged during the sterilization process.

Requirements for the Sterile Packaging
The sterile packaging material must not obstruct the sterilization process and must ensure sterility throughout the life cycle of the sterile goods. The sterile packaging must be easy to handle, i.e. removal of the sterilized goods must be possible without recontamination.

In accordance with currently valid standards, *the following sterile packaging's systems are recommended*:

- Rigid aluminium container
- Transparent paper-foil combination wraps
- Sterilization paper wrap

Sterile containers made of stainless steel are not recommended; they have a very low capacity for thermal absorption and are very heavy. The sterile packaging system used needs to be matched with the respective sterilization technique applied.

5.2.7 Sterilization of CJD (Prion)-Contaminated Medical Devices

Instruments used on patients suspected of having Creutzfeldt-Jakob disease (CJD) cannot be reused. Whenever possible, disposable single-use neurosurgical medical instruments should be employed. To minimize the possibility of use of neurosurgical instruments that have been potentially contaminated during procedures done on patients in whom CJD is later diagnosed, hospitals should consider using the sterilization guidelines for CJD outlined below for all neurosurgical instruments as prevention measure: steam sterilization at 134 °C with an exposure time of 18 minutes. If this is not possible, the conventional sterilization cycle at 134 °C with 3 min of exposure time needs to be preceded by a disinfection of the instruments with sodium hydroxide or 2.5% till 5% sodium hypochlorite solution for 24 h.

5.2.8 Sterilization Monitoring and Control and Documentation

The efficacy of the sterilization process cannot be confirmed by testing the final product. Therefore it is mandatory to routinely monitor, document and validate each aspect t of the sterilization process. Necessary requirements for documentation and process control are summarized in the DIN EN 17665 sterilization of healthcare products—moist heat—Part 1: requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 17665-1:2006):

- An automated, permanent recording of process parameters such as temperature, pressure and exposure time within the sterilizer for every sterilization load
- An (chemical) indicator system able to differentiate between sterilized and not sterilized loads
- Allocation of batch numbers
- Product (charge) release after confirmation that each aspect of the sterilization process has been complied with
- Monitoring and controlling using standard non-biological (chemical indicators or physical process control) indicators, always considering suboptimum sterilization conditions

Performance of sterilization systems is periodically validated according to current applicable standards. Frequency of revalidation depends on the technical operational safety of sterilizers, utilization frequencies and current applicable standards. Recurrent performance assessment of steam sterilizer systems should be done—if technically possible—using physical process control parameters. Validation of gas sterilization techniques of biological indicators is used according to current applicable standards. Temperature-pressure-measurement protocols, batch protocols and results of physical, chemical or biological inspections should be kept for 10 years.

Requirements for sterilization apply equally in the hospital and the resident doctor's surgeries!

5.2.9 How Long Can You Store Sterilized Items?

Depending on the packaging material and the storage conditions, maximum storage times need to be defined by the responsible reprocessing personnel on site.

For industrial produced medical devices, the manufacturer's instructions need to be followed.

Suggested Readings

McDonnell GE. Antisepsis, disinfection, and sterilization: types, action, and resistance. 2nd ed. Washington, DC: ASM Press; 2017, ISBN-10: 1555819672, ISBN-13: 978-1555819675.

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6 Basic Principles and Introduction to Disinfectants and Antiseptics for Skin, Mucosa, and Wounds

Elisabeth Presterl, Magda Diab-El Schahawi, Luigi Segagni Lusignani, Helga Paula, and Jacqui S. Reilly

6.1 Antiseptic vs. Disinfectant

Definition Antiseptic
An antiseptic is a chemical used in medicine to prevent wound infection and, subsequently, sepsis.

Antimicrobial Agent (Disinfectant)
Antimicrobial agents are applied to the surface of nonliving objects to destroy microorganisms that are living on the objects.

Nonliving surfaces = disinfectants

Live tissue = antiseptics

Unlike antimicrobial therapeutics ("antibiotics"), systemic administration is not possible as systemic side effects would exceed the antimicrobial effect.

Requirements for antiseptics: Various pathogens must be killed with sufficient certainty without damaging the patient.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_6

Requirements for Skin Antiseptics/Hand Disinfectants

- Fast action, short exposure time
- Broad spectrum of action (complete removal of transient flora)
- Reduction of the resident flora as much as possible
- Low to no absorption
- Good tolerability and low risk of allergic reactions
- Moisturizing substances (only with hand disinfectant)
- Immediate effect or residual effect according to indication
- Lack of irritation and allergenic potential
- Indications for skin antisepsis

The indication for the application of skin antiseptics is when intact skin is damaged. The purpose is to prevent the introduction of microorganisms into primarily sterile tissue, e.g., injection, puncture, surgical procedures, and set of intravascular catheters.

An exception is the eradication of pathogens, e.g., MRSA eradication.

First-choice skin antiseptics are alcohols, since they have the highest organism reduction factor (n-propanol > isopropanol > ethanol).

Depending on the indication, other substances may also be used. If one wishes to achieve a residual effect, the use of chlorhexidine or a combination of alcohols with other active ingredients is possible.

6.2 Preoperative Skin Antisepsis

Because of the risk of fire and the fastest reduction potential, alcohol with a higher flash point should be used (iso-/n-propanol). Advantage of alcohol: Fast action, easy handling, cheap.

Concentration and exposure time of the manufacturer must be taken into account with all antiseptics, and the alcohol must be allowed to evaporate completely. The performance of a preoperative skin antiseptic is obligatory.

Based on various recommendations, the following reaction times for alcoholic antiseptics should be taken into account, depending on the risk classification (Table 6.1):

Summary skin antisepsis:

- Alcohols are 1st choice drugs for skin antisepsis.
- Order of potency: n-propanol > isopropanol > ethanol.
- Microorganism reduction is more potent with longer exposure time and higher concentrations of antiseptic.
- Alcohols have no residual effect; after evaporation they have no effect. By combination with residual effect (e.g., chlorhexidine), a quick- and long-term effect can be achieved (intravascular catheters!).

Table 6.1 Reaction time for alcoholic antiseptics according to risk classification

Risk classification	Application	Alcohol-based skin antiseptic
Low risk	Blood collection, s.c., insulin injection, blood collection from fingertip, acupuncture	Min. 30 s (one application)[a]
Medium risk	i.m. injection, insertion of a peripheral venous catheter, puncture (cerebrospinal fluid, ascites, pleural puncture)	Min. 1 min (two applications)
High risk	Insertion of CVC, iliac crest puncture, puncture in regions of or in patients at particular risk of infection	Min. 5 min (three to six applications)
Sebaceous skin	Lumbar puncture	Min. 10 min

[a]Observe manufacturer instructions for contact time!

- The necessary exposure time depends on the indication and the risk.
- The rule of thumb is 30 s—1 min—5 min.
- The safest recommendation is always follow the manufacturer's instructions !!!

6.3 Wound Antisepsis

A wound infection can throw back the previous healing process significantly and can also develop into a life-threatening situation.

The classic indications of wound antisepsis are:

Prevention of wound infection—if contamination or colonization of the wound must be assumed from the outset.

Therapeutic—if there is already a clinical infection and, in addition to the systemic antimicrobial therapy, a local fast and high pathogen, elimination may be necessary.

In wound antisepsis, the transitions between a prophylactic and a therapeutic goal are usually interchangeable. The decisive criterion for selecting the wound antiseptic is the ratio between the desired microbicide and undesired cytotoxic effect. Since every acute or chronic wound has at least one or often several causes, in addition to the actual wound therapy, treatment should be considered for accompanying comorbidities. The one-sided reliance on local or systemic treatment agents is probably the most common error encountered in practice.

In addition to wound cleansing and consistent debridement, the following measures may be indispensable: a consequent venous compression (chronic venous insufficiency), the reduction of circumscribed pressure (pressure ulcers), the optimal adjustment of the blood sugar level, elimination of malnutrition, and improvement of the arterial blood circulation.

6.3.1 Co-dependence of Surgical Wound Treatment and Antiseptic

Successful wound antisepsis is inextricably linked to proper surgical wound care, including wound aftercare with appropriate dressings.

Wound debridement: The prerequisite for rapid wound healing is the debridement of dead tissue. Otherwise, the risk of infection increases due to optimal bacterial colonization conditions. Furthermore, inflammatory processes can be maintained, resulting in delayed proliferation and repair. Surgical debridement is the most effective method of removing necrotic tissue and has the advantage that further wound management can commence immediately afterward.

6.4 Frequency of Wounds and Wound Infections

6.4.1 Acute Injuries

In primary care facilities, the medical attention of acute traumatic wounds accounts for approximately 25–30% of treatments. Lacerations most commonly occur as a result of blunt trauma, cuts, abrasions, and burns, with most of these injuries responding quickly to treatment and healing without complications. Wound infections, with an incidence of approximately 3.5% in Europe and North America, are among the major complications of acute wound injury.

6.4.2 Chronic Wounds

It is estimated that approximately 5% of inpatients in hospitals and rehabilitation facilities account for chronic wound prevalence. Common infectious chronic wounds are ulcus cruris, ulcer decubitus, diabetic foot, and secondarily healing traumatic wounds (burn wounds).

6.5 Definitions

Wound Cleansing
The aim of wound cleansing is to remove possible contaminants (e.g., dirt, cell detritus from dried wound exudate, toxins, microorganisms) from the wound so as not to hinder wound healing.

Wound Decontamination
By wound decontamination, all measures are understood to mean a wound that has been contaminated with vital or avital particles. Decontamination of wounds is based solely on physical effects. Microorganisms are only removed from the wound

surface—a microbicide effect is not the primary intent. First choice agents are amphoteric surfactants.

Wound Antisepsis
Antiseptics are all antimicrobial measures on living tissue that are either prophylactic indication of an unwanted colonization or infection to prevent or treat it from a therapeutic point of view. The aim is to reduce the number of microorganisms by killing and/or inactivation or to stop their propagation definitively or at least for as long as possible. The microbiological minimum requirement for the term wound antiseptics is a reduction by 5 log levels (or 4 log levels for yeasts or under blood or exudate load ("protein error") by 3 log levels).

Disinfection
The objective of disinfection is the interruption of the infection chains by targeted or untargeted killing of pathogens on contaminated inanimate objects. See also chapter Surface, Instrument and Hand Disinfection (hand disinfection: hands—although animated tissue—are considered "instruments").

- Reliable microbicide effect (>5 log-steps reduction)
- Rapid onset of action (1–5 min)
- Effective effect in the presence of organic stress (>3 log-steps reduction)
- Low absorption, no allergy
- No induction of resistance
- No interference with normal wound healing
- Low to no cytotoxicity

6.6 Recommended Wound Antiseptics

- Short-term antiseptics: PVP-iodine, octenidine
- Long-term antiseptics: Polyhexanide, taurolidine

The criterion for selecting the wound antiseptic is the ratio between the desired microbicide and undesirable cytotoxic effects. To compare the tolerability of wound antiseptics, the biocompatibility index (BI) is suitable. Taking into account the application concentration of the active substance, testing for microbicide and cytotoxicity is carried out under the same experimental conditions.

BI = quotient of IC50 and CRF > log 3

IC50 = concentration that kills 50% of cells (fibroblasts)

CRF > log 3 = concentration which is necessary to min. 3 log levels to achieve reduction of the test organisms.

The BI is thus a dimensionless number and allows a comparison of the compatibility. A value >1 describes a good compatibility and a value <1 a poor microbicide activity combined with a high cytotoxicity.

6.6.1 PVP-Iodine

Advantages
- Rapid onset of action (30 s)
- Low loss of activity in the presence of proteins (low protein error)
- Broad spectrum of activity (bacteria, fungi, most viruses, spores, protozoa)
- Acceptable cytotoxicity
- First choice for puncture/cut injuries (HIV, hepatitis B, hepatitis C): ethanol/2-propanol with PVP-iodine

Contraindications
- Patients with overt hyperthyroidism
- Dermatitis herpetiformis
- Iodine allergy
- Not before and after radioiodine therapies

6.6.2 Octenidine Dihydrochloride

Advantages
- Onset of action (30 s to 1 min).
- No loss of effect by proteins.
- Spectrum of activity does not cover spores, but all relevant pathogens.
- No absorption.

Contraindications
- Must not be administered in the abdominal cavity, bladder, ear canal
- Allergy to octenidine

Note: Octenidine must NEVER be used in conjunction with PVP-iodine, as octenidine releases iodine radicals and results in brown discoloration and irritation of the tissue!

6.6.3 Polyhexanide

Advantages

- Very good tissue compatibility ⋄ 1st choice for chronic, poorly healing/sensitive wounds.
- Concentration of 0.04% takes 5–20 min to onset of action.
- No effect against spores, partly reduced effect against viruses.

Disadvantage

- Cartilage toxicity.
- There is a contraindication for use in the first 4 months of pregnancy.

Basics of Medical Microbiology

7

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Clinical microbiology classically focuses on microorganisms that make people sick "pathogens". Founders of clinical microbiology were Louis Pasteur and Robert Koch.

Until the first half of the nineteenth century, cleanliness and disinfection in medicine were not considered necessary, because the causative agents of infection were unknown. However, clinical microbiology was advancing rapidly revealing the pathogens of tuberculosis, diarrhoea, sepsis and many more. Koch and Henle published postulates linked microorganisms with infectious disease (Henle-Koch postulates):

- The pathogen always elicits the same pathological changes and the same clinical course of the infectious disease.
- Pathogens are cultivated from the infection site in a pure culture. The pathogen causes identical disease in humans and in animals. The pathogen must not be isolated in other diseases as part of the normal flora and in healthy individuals.

For diagnosis of an infection detection and identification of pathogens from patient, samples and susceptibility testing of antibiotics are pivotal.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_7

Bacteria have been existing for more than 3 billion years. They have adapted in their life cycle to changing conditions and for adaptability. Frequent use of antibiotics can lead to the development of resistance mechanisms and the selection of resistant bacteria and other microorganisms. As a result, antibiotics, which are used for standard treatment, non-toxic and well tolerated, become increasingly ineffective.

In the clinical microbiology laboratory, methods and techniques for diagnosis of infections are performed. Clinical samples from nearly all body sites are sent to this laboratory. However, there are some rules of "pre-diagnosis" to be obeyed:

- Material has to be clearly labelled with the name of the patient, the original body site where it was taken, the date and time when it was taken, the clinical diagnosis (presumed infection) and the name and availability of the sender.
- Material from superficial body sites may not be yield a reliable result. Thus, consultation with clinical microbiologist what samples to send in should be made.
- Any material should be sent as quickly as possible to the microbiology laboratory. There may be special agreements with the microbiology laboratory.
- For some materials (blood, tissue, swabs, respiratory samples, etc.), there may be special transport media. Information about it is usually supplied by the respective clinical microbiology laboratory. These media may differ between laboratories because of technical reasons but are based on the same principles.
- Material should never be contaminated with blood, faeces, etc. on the outside.
- All transport vessels should be closed firmed and should not leak.

7.1 Classification of Microorganisms

Infections can be caused by bacteria, viruses, fungi, prions, protozoa, worms (helminths), arthropods (insects), etc.

Bacteria (size 1–5 μm) are single-celled organisms without a cell nucleus (prokaryotes). The bacterial cell has no nucleus. The annular genetic material (chromosomes, DNA) is without a nucleus in the cytoplasm. The cytoplasm is a plasma membrane and a cell wall (multilayer) surrounded. Other components are ribosomes, mesosomes and endoplasmic reticulum, so-called cell organelles. Bacteria can be flagellated for better mobility. Mycoplasma and chlamydia are bacteria with an obligate intracellular development cycle.

Fungi (10–50 μm) are unicellular organisms with a cell nucleus containing the DNA (eukaryotes). Cells in mammals including the human race have the same organisation: cell and cell nucleus containing the DNA.

Viruses (20–200 nm) are particles containing genetic information but needing other cells and particularly their cell organelles to propagate.

Parasites are a heterogeneous group including protozoa (protozoa) and higher organisms (worms, arthropods, etc.). The size of the parasite is variable and depends on the site of parasitism. Protozoa are about 10 μm; worms may have a length of 10 m. Parasitism is a strategy to live and propagate needing a host.

Prions (infectious proteins) are subcellular biological objects. They are proteins and have particular secondary structure (folding). Examples are scrapie (encephalitis in sheep) or Creutzfeldt-Jakob disease in humans.

In the scientific literature, names of the microorganisms give the genus first and then the species, e.g. *Staphylococcus* (genus) *aureus* (species). For easier reading (and writing), the genus may abbreviated to the first letter (S. for *Staphylococcus*) in the further text.

The morphological classification of bacteria is according to the form of the bacteria: there are spherical bacteria (coccus = ball) and rod-shaped bacteria (bacillus = rods). Typical representatives of the spherical bacteria are streptococci (chain bacteria, *Streptococcus* species) and staphylococci (*Staphylococcus* species, "grape-shaped bacteria"). The most important rod-shaped bacterium is *Escherichia coli*. Other shapes are spirals (e.g. *Vibrio*, *Spirillum* or *Spirochaeta*).

The classification of bacteria in clinical microbiology is carried out according to the clinical aspect (pathogen or non-pathogenic); according to the dyeing method, the "Gram stain" (Gram-positive, Gram-negative); according to the scientific microbiological taxonomy; and according to the growth behaviour, e.g. aerobic bacteria require oxygen to produce energy and grow. Anaerobic bacteria produce energy and grow without oxygen.

The Gram stain is a fundamental method in medical microbiology. In the Gram stain, the cell wall is coloured. One differentiates Gram-positive (Gram staining by dye – crystal-violet – dark blue) and Gram-negative (discolouration of the Gram dye, maintaining the counterstaining with a red dye, Gram-negative bacteria). The Gram stain can be carried out on every material or sample sent into the laboratory. The material has to be smeared thinly on a glass slide; then it is fixed on the slide, stained with crystal violet, fixed with iodine solution, discoloured with alcohol and counterstained with a red dye. The Gram stain takes a few minutes and can therefore be considered as a fast, direct diagnosis.

Gram-positive bacteria have a thick cell wall composed of peptidoglycan (murein) and teichoic acid or lipoteichoic acid. In contrast Gram-negative bacteria have two cell walls: an inner and an outer cell wall consisting of lipids. In between the two cell walls, there are some small amounts of peptidoglycan. The outer cell wall of Gram-negative bacteria additionally contains so-called lipopolysaccharide (LPS). These lipopolysaccharides are important for the septic shock. Through these outer and inner membrane structures, enzymes transport molecules into the cytoplasm of the bacterial cell. The structure of the cell wall is critical for antibiotic therapy since the most effective antibiotics (e.g. beta-lactams antibiotics) bind to cell wall components, thus inhibiting the building of the stable cell wall and destroying the bacteria.

Classification of frequent medical pathogens according to the colour by Gram staining:

- Gram-positive cocci: e.g. *Staphylococcus* species, *Streptococcus* sp., *Enterococcus* sp.
- Gram-negative cocci: e.g. *Neisseria* sp. (*N. meningitidis*, *N. gonorrhoeae*)

- Gram-positive rods: e.g. *Bacillus* spp., *Listeria* spp., *Corynebacterium* sp., *Clostridium* sp., *Nocardia* sp.
- Gram-negative rods: e.g. *Escherichia* sp., *Klebsiella* sp., *Haemophilus* sp., *Brucella* sp., *Bordetella* sp., *Francisella* sp., *Campylobacter* sp., *Helicobacter* sp., *Pseudomonas* sp., *Bacteroides* sp. (anaerobic bacterium)

Humans have a normal (physiological) microflora on the skin and the mucosal membranes of the respiratory, gastrointestinal and urogenitary tracts. This is now called the human microbiome. The normal flora of humans is decisive for health. These bacteria not only have a kind of barrier function against the invasion of pathogens but also have an important role in the breakdown of nutrients and in the immune defence. The normal microflora is polymicrobial, thus consisting of many bacterial species. The normal flora of the oral cavity (more than 10e6 bacteria/ml) consists of about 200 different species, e.g. *Viridans streptococci*, *Neisseria*, *Veillonella* and *Porphyromonas*. The stomach has a bacterial colonisation of about 10e1–10e2 bacteria/ml. The small intestine (ileum) has a bacterial colonisation of about 10e3–10e6 bacteria/ml including *Viridans streptococci*, *Enterococcus* sp., *Pneumococci*, *Escherichia* coli, *Bacteroides* sp., *Lactobacillus* sp. and *Bifidobacteria*. The flora of the colon includes between 10e10 and 10e18 bacteria per gram of stool. There are 400–500 and more species present including *Peptostreptococcus* sp., *Enterococcus* sp., *Bacteroides* sp., *Eubacterium* sp., *Enterobacter* sp., *Escherichia coli*, *Klebsiella* sp., *Proteus* sp., *Bacillus* sp., *Fusobacterium* sp., *Clostridium* sp. and *Lactobacillus* sp. The numbers vary because many microorganisms do not grow in cultures. However, by using molecular methods, many new species are detected.

On the skin there is transient and resident flora. Transient florae are microorganisms that stay only for a short time on the skin, e.g. *Staphylococcus aureus* and *enterobacteria*. Resident microbial skin flora are microorganisms that live on the skin or in the skin structures, e.g. perspiratory glands. These microorganisms live there, multiply and are interacting with each other. Examples are *Staphylococcus epidermidis*, *Corynebacterium* spp. and *Propionibacterium* spp.

7.2 The Most Important Pathogens and Infections

Bacterial Meningitis (Infection of the Meninges)
Streptococcus pneumoniae, *Neisseria meningitidis*, *Haemophilus influenzae*, *Streptococcus agalactiae* (beta-haemolytic streptococci group B), *Listeria monocytogenes*

Infection of the Middle Ear (Otitis Media)
Streptococcus pneumoniae

Pneumoniae
Streptococcus pneumoniae, *Haemophilus influenzae*, *Staphylococcus aureus*, *Mycoplasma pneumoniae*, *Legionella pneumophila*

Tuberculosis
Mycobacterium tuberculosis

Skin Infections
Staphylococcus aureus, *Streptococcus pyogenes* (beta-haemolytic streptococci group A), *Pseudomonas aeruginosa*

Eye Infections
Staphylococcus aureus, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*

Infections of the Upper Respiratory Tract (Tonsillitis, Sinusitis)
Streptococcus pyogenes, *Haemophilus influenzae*

Gastritis
Helicobacter pylori

Infection of the Gastrointestinal Tract (Diarrhoea)
Campylobacter jejuni, *Salmonella* sp., *Sheela* sp., *Clostridium difficile*, diarrheagenic *Escherichia coli*

Urinary Tract Infection
Escherichia coli, *Klebsiella* sp., *Proteus* sp., *Enterobacter* sp., *Serratia* sp. and other *enterobacteria*, *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*

Sexually Transmitted Diseases
Neisseria gonorrhoeae, *Chlamydia trachomatis*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Haemophilus ducreyi*

7.3 Diagnostic Detection Methods of Microbiology

The basic techniques in clinical microbiology are explained below.

7.3.1 Microscopy

Microscopy is a standard method of medical microbiology and serves to direct detection of pathogens. Microscopy is still an important rapid method for pathogen detection in clinical material (suspected meningitis, tuberculosis) and also for preliminary determination and systematic classification of bacteria. Bacteria are barely visible in the light microscope at 1000× magnification. Immersion oil for improving the resolution is required. Fungi and protozoa are already visible at 400× magnification. In microscopy, materials can be visualised in a wet mount (unstained, living germs) as well as a fixed and stained specimens (dead germs). Unstained specimens

are used for diagnosis of primary syphilis to visualise the spirochaete bacterium *Treponema pallidum* in dark-field microscopy. Other stains are methylene blue staining or the staining for the detection of mycobacteria (Ziehl-Neelsen stain). Direct visualisation is a rapid test but needs some expertise.

7.3.2 Culture

Cultural methods are the mainstay of clinical microbiology. Clinical material is put into or onto nutrient medium leading to the growth of the bacteria within commonly 24 h for detection. Bacteria are then streaked on a surface of an agar plate. Single colonies are selected for identification of the bacteria and testing for susceptibility to antibiotics. These classical techniques for identification and susceptibility testing need at least 48 h sometimes even more. Recently, more rapid techniques allow the identification and susceptibility testing within few hours for specific pathogens.

7.3.3 Tissue Section (Histology)

This includes conserving the material in formaldehyde and staining of tissue sections and microscopy with direct detection of pathogens. Here the immune response is visualised.

7.3.4 Molecular Biology

With molecular biological methods for the detection of microbial genetic material, the most common technique is polymerase chain reaction (PCR), but there many other similar techniques for the detection of genetic material. Future molecular techniques for diagnostics to identify, classify or characterise microorganisms or to prove their presence in a human sample or in the environment will be based on whole-genome sequencing or next-generation sequencing methods of the genetic material.

7.3.5 Serology

Immune response (production of antibodies of the patient) to the invasion of the pathogen is detected in blood (serum) but also in other body samples like urine or sputum. Sometimes there may be detection of part of the pathogen surface. This is however referred to as “serology”. Detecting the pathogen-specific immune response is considered to be an indirect method for diagnosis. There are different techniques including immunofluorescence, complement fixation and enzyme-linked immunostaining assay (ELISA) for the detection of antibodies (IgG, IgM) to an infectious agent (see Chap. 20: Basic Immunology).

7.4 Description of Selected Basic Methods

7.4.1 Gram Stain

- Step 1: The thin head-fixed smear of the sample on the glass slide is dyed with carbolic gentian violet "Gram stain". All bacteria, Gram-positive and Gram-negative, are coloured in this step.
- Step2: After removing the carbolic gentian violet, the specimen is submerged in Lugol solution.
- Step 3 (differentiating): The specimen is decolourised with 96% ethanol. Here, Gram-positive and Gram-negative bacteria behave differently: Gram-negative bacteria are discoloured, while the blue dye complexes of Gram-positive bacteria cannot be washed out.
- Step 4 (counterstaining): To stain the Gram-negative bacteria, the specimens are dyed with diluted fuchsine or safranin solution, whereupon they appear red or red orange.
- Staining of acid-resistant bacteria by Ziehl-Neelsen (modified from Kinyoun)
- Step 1: The thin head-fixed smear of the sample on the glass slide is dyed with fuchsine red. Acid-fast bacilli, e.g. mycobacteria, and all other bacteria are red. Then the glass slide is rinsed with water.
- Step 2: The specimen is rinsed with a mixture of hydrochloric acid and alcohol for discolouring. All bacteria except mycobacteria, which keep the red stain in their lipid-rich membrane, are discoloured.
- Step 3: After rinsing with water, the specimen is counterstained with methylene blue. All other material including bacteria except the acid-fast bacilli is coloured blue.

7.4.2 Culture Methods

Cultivation is used for multiplication of the bacteria outside their natural location in inanimate substrates, called culture media.

The prerequisite for a successful detection of pathogens is the correct sampling of the specimen (no disinfectant, no antibiotic prior to taking the sample), immediate and adequate sample transport (duration less than 1 h, adequate transport medium) and the proper handling in the laboratory due to the carefully completed assignment with clinical information.

The most important condition for bacterial growth is the proper nutrient medium, optimum temperature and pH and the right environmental atmosphere (aerobic, anaerobic or microaerophilic conditions). There are liquid and solid culture media (agar plates). Among the nutrient media, there are optimal growth media (growth of almost all bacteria) and selective media (detection of specific bacteria) or minimal growth media (growth of certain relatively undemanding bacteria). Furthermore, there are differential growth media that use the metabolic competence of particular bacteria.

For identification and further determination of the bacterial susceptibility to antibiotics, a single and a pure culture containing only one sort of bacteria is required. A pure culture is obtained by isolating a single colony from the culture of the primary material. This is done for the each bacterial species present in a clinical specimen. By this fractional plating, it is possible to isolate bacteria from mixed cultures.

Identification of the bacteria starts with determining the morphological characteristics (colouring by Gram stain, shape, size, presence of a capsule, colony shape and colour), physiological characteristics (detection of metabolic enzymes) and chemical characteristics. Additionally determination of cell wall antigens by antisera or detection of certain species-specific DNA sequences using PCR may be applied.

7.4.3 Susceptibility Testing

At the same time, the susceptibility testing of bacterium is performed. An aqueous solution of certain concentration of the bacteria is made and streaked on agar plates. Then filter paper discs (diameter about 5 mm) soaked with antibiotics at determined concentrations are placed on the agar with streaked bacteria solution. After 24 h, the zone of inhibition around the filter paper discs is measured. There are manuals and guidelines on how to perform these tests. Inhibition diameter has to have a size defined for the antibiotic. Other methods are the determination of minimum inhibitory concentration by the microdilution method or the strip dilution method.

Other identification methods are antigen and toxin detection by latex agglutination, enzyme-linked immunosorbent assay, radioimmune assay, immunodiffusion and tissue culture, by hybridisation of the genetic material and polymerase chain reaction (PCR).

All laboratory tests for identification and susceptibility testing have to be validated in different clinical settings to get the sensitivity and specificity of the method. New methods have to be compared to establish methods.

Bacteriology: Selected Bacteria and Diseases

8

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8.1 *Staphylococcus* Species (Commonly: Staphylococci)

Staphylococci are Gram-positive cocci bacteria, size 5 micrometre, ubiquitously occurring. In the Gram stain, staphylococci are Gram-positive cocci. The cell wall is coloured dark blue because the cell wall is stained with the dark blue stain gentian violet. There are several species of the genus *Staphylococcus*. The most important are:

Staphylococcus aureus
S. aureus is the most frequently isolated pathogen from infection sites in the skin, soft tissue, mucous membranes and internal organs. *S. aureus* is a coagulase-positive *Staphylococcus* and can produce many other antigens and toxins eliciting significant immune response in the human host. *S. aureus* is common pathogen of puerperal mastitis (gestational mastitis), boils and carbuncles. But *S. aureus* is also the primary pathogen of osteomyelitis (bone inflammation) and endocarditis (heart valve inflammation). In food, e.g. not well-cooled vanilla ice cream, *S. aureus* may produce a heat-stable toxin and cause food poisoning with vomiting and diarrhoea. Certain strains of *S. aureus* produce the toxic shock syndrome toxin (TSST-1 or TSST-2), causing a severe illness, toxic shock syndrome and exfoliative dermatitis.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_8

In the early times, *S. aureus* became resistant to the standard antibiotic against staphylococci, methicillin. It was called then methicillin-resistant *S. aureus* (MRSA). Resistance against methicillin means that MRSA is resistant against nearly all beta-lactam antibiotics. Treatment with beta-lactam antibiotics (penicillins, cephalosporins) is then ineffective. MRSA spread over many hospitals in the United States and the Western world. MRSA is a common cause of hospital infections and can cause epidemics because staphylococci survive well in the environment and are therefore easily transmitted via the items and devices in the environment and hands of the personnel.

Staphylococcus epidermidis
S. epidermidis is a resident on the normal human skin. In contrast to *S. aureus*, *S. epidermidis* is coagulase-negative. However, when transferred to artificial surfaces in the human body (catheters, prostheses), *S. epidermidis* can cause infections of implanted or foreign material. These infections are particularly unpleasant when affecting orthopaedic prostheses. *S. epidermidis* forms a bacterial biofilm consisting of bacterial cells and amorphic material ("matrix") on the material. The treatment of these biofilm-associated infections is nearly not curable without removal of the infected foreign material.

Staphylococcus saprophyticus is a common pathogen of urinary tract infections in women.

There is a large group of other coagulase-negative staphylococci, which can cause infection associated with implanted or accidentally inserted foreign material, similar to *Staphylococcus epidermidis*. There is one species that may be a persistent pathogen like *S. aureus*: *Staphylococcus lugdunensis*.

8.2 *Streptococcus* Species (Commonly: Streptococci)

In the microscope streptococci are looking like a string of pearls. Streptococci have a distinctive property for haemolysing blood in the growth agar:

- α ("alpha")-haemolysis: partial haemolysis of erythrocytes. The *Streptococcus* colonies are surrounded by a green zone.
- β ("beta")-haemolysis: complete haemolysis of the erythrocytes. The *Streptococcus* colonies are surrounded by a yellow zone. Beta-haemolytic streptococci are important pathogens. There are several groups: A, B, C, E and G. Beta-haemolytic streptococci group A and group B are the most important pathogens.

Beta-Haemolytic Streptococci Group A
Classical infections by beta-haemolytic streptococci group A (also called *Streptococcus pyogenes*) are skin infections:

- Wound infections, erysipelas, cellulitis.
- Tonsillitis.

- Scarlet fever, rheumatic fever (hypersensitivity reactions).
- Sepsis (puerperal sepsis, puerperal fever). In puerperal sepsis diagnosis via the vaginal smear with the mother takes place. In neonatal sepsis *Streptococcus pyogenes* can be detected in blood culture, cerebrospinal fluid and urine of new-borns.

Beta-Haemolytic Streptococci Group B

Beta-haemolytic streptococci group B (also called *Streptococcus agalactiae*) can live as normal part of the flora on the mucous membranes (e.g. the vagina–birth canal).

They can cause the following infections:

- Neonatal sepsis and meningitis: Approximately 15% of pregnant women are asymptomatic carriers. In the new-born, it can cause early-onset perinatal infection when the new-born is infected via the birth canal. Neonatal sepsis occurs approximately 3–6 infections per 1000 births. New-borns develop clinical sepsis at 5 to 8 days of age, sometimes associated with meningitis and pneumonia. Left untreated, the mortality rate is as high as at 50%. Alternatively, there can be postnatal late-onset infection via unclean hands or contaminated objects. Here, the incidence is estimated at 2 infections per 1000 births. The symptoms occur from the 2nd week of life.
- Urinary tract infections.
- Pneumonia.
- Atypical erysipelas.

Streptococcus pneumoniae

Streptococcus pneumoniae is also found as a commensal in the normal flora of the respiratory tract. It is the most important causative agent of infection of the upper respiratory tract (infection of the middle ear (otitis media)), pneumonia and sepsis and meningitis (especially in splenectomized patients).

Viridans streptococci

The *Streptococcus viridans* group is an inhomogeneous mixture of alpha-haemolytic streptococci. They are normally part of the oral flora and the intestinal tract. They include the *Streptococcus milleri* group, *Streptococcus mutans*, *Streptococcus sanguis* and many others. They are important pathogens of native valve endocarditis, a very rare infection of heart valves.

Enterococci (*Enterococcus faecalis*, *Enterococcus faecium*)

Enterococcus species is a normal part of the gut flora. *Enterococcus* species can cause urinary tract infections (often associated with urinary catheters), but also endocarditis and wound infections.

The controlled use of vancomycin (VRE) leads to the emergence of vancomycin-resistant enterococci (VRE). Vancomycin-resistant enterococci can cause HAI.

8.3 Gram-Negative Cocci

Neisseria species is the most important example of Gram-negative cocci. There are two predominant pathogens within this genus: *Neisseria meningitidis* and *Neisseria gonorrhoeae*.

*Neisseria meningitidis (***Commonly Called Meningococci***)*
N. meningitidis is the causative agent of epidemic meningitis. This serious infection affects infants and young people in particular. Typical signs include high fever, lethargy/coma and a typical bright rash on the trunk and extremities. This is a very dangerous disease. The patient has to be sent to the hospital. Health authorities have to be notified immediately to install preventive measures. Prophylaxis has to be given to close contact persons.

There are serotypes A, B, C, Y and W135. Serotype B is the most frequent serotype in Central Europe, while serotype C is common in Great Britain or Greece. There are more than 20 different serotypes. 5–10% of the population are asymptomatic carriers with colonization of the nasopharynx; in the cold season, the number may be up to 30%. Transmission is by droplet or contact.

Meningococcal meningitis
After an incubation period of 2–5 days after contact, the infection begins with sudden malaise, high fever, headaches and neck stiffness. The severe course progresses to sepsis and septic shock due to endotoxinemia (spread of bacterial endotoxins in the human body) and disseminated intravascular coagulopathy. Clinical signs on the skin are petechial haemorrhages and also the typical meningococcal rash with map-shaped necrosis in the skin and all organs (purpura fulminans). The most severe form is called the Waterhouse-Friderichsen syndrome (fulminant meningococcal sepsis) with the loss of function of the adrenal glands. The mortality of the Waterhouse-Friderichsen syndrome is up to 95%. If the meningitis remains untreated, the mortality is up to 70%.

A rapid diagnosis is possible by examining a Gram-stained sample of cerebrospinal fluid in the microscope. There are also rapid antigen tests and rapid molecular methods. For correct identification and susceptibility testing, cultures of cerebrospinal fluid and blood have to be done. Close contacts (family, mother, father, siblings and playmates) have to get a chemoprophylaxis.

Vaccination is highly recommended. There are vaccines active against the serotypes A, B, C, Y and W.

Neisseria gonorrhoeae
Neisseria gonorrhoeae is the causative agent of the most common sexually transmitted bacterial infection, gonorrhoea. The reservoir is an infected, often asymptomatic person. Transmission occurs during sexual intercourse. New-borns are infected during birth by their mother.

Gonorrhoea
Approximately 50% of women have symptomatic infection in contrast to 80–90% of men who have ailments like burning painful urination and slimy, creamy discharge (urethritis, prostatitis). Nevertheless, in women gonorrhoea can lead to infection of the annexes and to peritonitis (pelvic inflammatory disease). The inflammation leads to formation of scars and adhesions. Sterility is the consequence. In pregnant women, there is risk of infection of the unborn and amniotic sac (chorioamnionitis), and there is the increased risk of miscarriage. Apart from the urogenital tract and conjunctiva, the pharynx and rectum can be infected too. Besides the infection, *N. gonorrhoeae* elicits immune response in certain individuals, called Reiter's triad (arthritis, conjunctivitis, urethritis).

To prevent eye infection and scarring, new-borns used to be given the so-called Credé's eye prophylaxis. Applying silver nitrate into the eyes of new-borns was carried out since 1881 by the German obstetrician Carl Sigmund Franz Credé (1819–1892). Thus the incidence of purulent conjunctivitis potentially leading to blindness was greatly reduced. Originally Credé's eye prophylaxis was performed with 1% silver nitrate solution. Later on, topical erythromycin or 2.5% povidone-iodine solution was applied within the first hour after birth in the conjunctival sacs of the new-born.

Diagnosis of gonorrhoea is made by examining the Gram-stained smear of the cervix or the urethra in the microscope. Gram-negative diplococci (cocci lying in pairs) are seen. There are also rapid molecular tests.

8.4 Corynebacteria

Corynebacteria are common non-pathogenic commensals being part of the normal microflora on the human skin. However, there is a classic pathogen: *Corynebacterium diphtheriae*, causing diphtheria, a systemic infection involving the upper respiratory tract, particularly the larynx, but also the heart and the nervous system.

Diphtheria
Infected with a phage (virus that infects bacteria), *Corynebacterium diphtheriae* forms a composite toxin (Toxin A and Toxin B). Toxin B has the toxic activity and binds to receptors in the body. The clinical signs and symptoms of diphtheria begin 3–5 days after infection. *C. diphtheriae* is transmitted by droplets in the air or by contact. There is a typical sweet halitosis. In the pharynx there are so-called diphtheritic pseudomembranes that obstruct the airway in young children and lead to breathing difficulties. The patient has massive malaise, fever and swelling of the cervical lymph nodes. The diphtheria toxin is a systemic "intoxication" and causes myocarditis, polyneuritis and even paralysis. The treatment of choice is an antitoxin (horse serum) plus antibiotic therapy with penicillin or macrolide.

Due to the severity of the disease, vaccination with an inactivated vaccine is highly recommended. Diphtheria does not exist in many developed countries, including Austria, due to the vaccination. Cases recorded in developed countries tend to be imported and travel associated. The vaccination is recommended especially when travelling in countries with war, poverty and a poor health system.

8.5 *Bacillus* Species

Bacillus species are anaerobic bacteria. *Bacillus* species are Gram-positive bacteria which grow under anaerobic (without oxygen) conditions and form spores under aerobic (normal air) conditions. Spores are insensitive to heat (up to cooking temperature), to radiation and to disinfectants. There are some sporicidal disinfectants (see Chap. 5 "Disinfection").

The following *Bacillus* species are of clinical importance:

- *Bacillus subtilis*: *B. subtilis* spores are used to test for the activity of a disinfectant against spores in the microbiology laboratory.
- *Bacillus cereus* causes food poisoning, diarrhoea and vomiting. *B. cereus* grows in old food and forms a toxin.
- *Bacillus anthracis* is the causative agent of anthrax. Anthrax is a serious local and systemic infection that can affect the skin, the intestine and the lungs. The lung infection with a septic course form is the most severe form with high mortality. Spores of *Bacillus anthracis* can survive for decades. Anthrax is a notifiable disease and agent of bioterrorism!

8.6 *Clostridium* Species

Clostridium sp. are also anaerobic bacteria and form spores when exposed to ambient air. The most important pathogens of the group *Clostridium* sp. are *Clostridium perfringens*, *C. tetani*, *C. botulinum* and *C. difficile*.

- *Clostridium perfringens* causes gas gangrene (skin, intestine).
- *Clostridium tetani* causes the lockjaw (tetanus). Tetanus occurs not only in adults but also in new-borns. Spores in the dust penetrate into the wounds and form toxin in the tissue under anaerobic conditions. The symptoms are paralysis and muscle spasms (increase of the muscle tone without impairment of consciousness). Typical signs of tetanus are the so-called risus sardonicus and trismus (lockjaw). Neonatal tetanus is very rare and is only found in developing countries. The portal of entry is the umbilical cord wound (it is therefore called the disease of 8th day). Neonatal tetanus has a high fatality rate. Treatment is the application of human hyperimmune serum, muscle relaxants and surgery (debridement). Prophylaxis is vaccination of the mother (transfer of antibodies through breast milk). Vaccination can be applied also during pregnancy. Due to the severity of the disease, the vaccination is highly recommended.

- *Clostridium botulinum* can anaerobically in contaminated food (canned) grow and cause botulism. Botulism is a food poisoning (*botulus* = sausage). *C. botulinum* produces neurotoxin A under anaerobic conditions, e.g. in cans, sausages and other meat products. Neurotoxin A is a potent toxin that leads to paralysis (death by respiratory paralysis) in the amount of 0.1 μg. Symptoms are initially diarrhoea and blurred vision. In wound botulism spores penetrate into the wound and produce toxins that enter the blood stream and cause botulism. Infant botulism: bacterial spores are ingested with food, and after an incubation period of 18–36 h, typical symptoms of dysphagia and diarrhoea start. The therapy used was polyvalent antitoxin.
- *Clostridium difficile* may cause severe diarrhoea in susceptible hosts (see Chap. 14, Infections). *Clostridium difficile* is ubiquitous (anywhere) in the environment and also in small numbers in the intestines of healthy humans. Approximately 50% of children at an age <1 year are colonized with *Clostridium difficile*. *Clostridium difficile* in asymptomatic children should not be treated. Risk factors to develop *Clostridium difficile* infection are age >65 years, renal failures, chemotherapy and antibiotic therapy. The spectrum of *Clostridium difficile* infection ranges from uncomplicated diarrhoea to severe pseudomembranous colitis, perforation of the intestine and death. Infection control measures include the isolation of symptomatic patients, adequate cleaning and disinfection of the environment with a sporicidal disinfectant. Frequent handwashing is required from staff members, visitors and the patients themselves.

8.7 Gram-Negative Rods

Escherichia coli, *Klebsiella* spp. (*K. pneumoniae*, *K. oxytoca*), *Proteus mirabilis*, *Enterobacter* spp. (*E. cloacae*, *E. aerogenes*), *Citrobacter* spp. (*C. freundii*), *Serratia* spp. (*S. marcescens*) and many others are summarized under the term "enterobacteria". They are the most common cause of bacterial infections in humans. The most common infections caused by enterobacteria are urinary tract infections, sepsis, wound infections and even pneumonia in patients with mechanical ventilation.

Enterobacteria are normally part of the gut flora. They are just a very small fraction of it compared to anaerobes. The most common representatives of enterobacteria are listed below:

There is a group of bacteria called "non-fermenters". These non-fermenting bacteria cleave only a few sugars and amino acids in contrast to enterobacteria. The most common pathogens among the non-fermenters are *Pseudomonas aeruginosa*, *Acinetobacter baumannii* complex and *Stenotrophomonas maltophilia*.

8.7.1 *Escherichia coli*

E. coli was the first bacterium to be detected. The laboratory strain K8 is still one of the working horses for laboratories. *E. coli* grows very well under aerobic conditions. *E. coli* can multiply very quickly. One bacterial *E. coli* cell multiplies so often during 12 h that after 12 h there are 343 597 383 680 *E.coli* cells.

Escherichia coli is part of the normal physiological intestinal flora. *E. coli* is a faecal contamination in drinking water. *E. coli* is the most frequent cause of healthcare-associated infections (44%). *E. coli* is the common pathogen of urinary tract infections and sepsis. Other infections are peritonitis, cholangitis and sepsis and meningitis in new-borns.

Some strains of *E. coli* may cause diarrhoea. They are therefore called diarrhoeagenic *E. coli*:

- Enterohaemorrhagic *E. coli* (EHEC) O157, O104 causes the haemolytic uremic syndrome.
- Enteropathogenic *E. coli* (EPEC) causes diarrhoea in infants.
- Enteroinvasive *E. coli* (EIEC) causes non-*Shigella* dysentery.
- Enterotoxigenic *E. coli* (ETEC) causes traveller's diarrhoea.

Improper storage, improper production and use of food (beef, raw milk) can lead to food poisoning by *E. coli*. The therapies of choice are broad-spectrum penicillins, cephalosporins of the second or third generation or quinolones. However, resistance to quinolones may be as high as 20% of the isolates or up to 30% to third-generation cephalosporins. These enterobacteria produce extended-spectrum beta-lactamases (ESBL) that can be up to 30%.

8.7.2 *Klebsiella* Species (*Klebsiella pneumoniae*, *Klebsiella oxytoca*)

Klebsiella sp. can also cause urinary tract infections, sepsis, cholecystitis, as well as pneumonia, lung abscess and otitis media. *Klebsiella pneumoniae* has higher resistance to third-generation cephalosporins and quinolones.

Klebsiella granulomatis is the causative agent of a sexually transmitted disease (STD) called granuloma inguinal or donovanosis. Normally localized in the intestinal tract, *Klebsiella granulomatis* is unremarkable. However, if it is translocated to genital tract, there are painless ulcers with tissue destruction and severe bleeding without swollen glands in the groin. The treatment of choice consists of tetracycline or macrolides.

8.7.3 *Proteus* Species

Proteus species include *P. mirabilis*, *P. vulgaris* and *P. penneri*. *Proteus* species is highly mobile and forms typical appearance on culture plates with a very unique smell. *Proteus* species are found in the gut and in the groundwater. Like *E. coli*, *Proteus* species is often the pathogen of urinary tract infections, sepsis or wound infection.

8.7.4 *Salmonella* Species

Salmonella species are pathogens causing diarrhoea in most cases. Only *Salmonella typhi* and *Salmonella paratyphi* cause a sepsis-like illness, typhoid fever.

There is a number of *Salmonella* species. The majority of *Salmonella* sp. cause diarrhoea, primarily *Salmonella enteritidis* and many others. Generally, this diarrhoea is self-limiting. Treatment is oral rehydration. *Salmonella typhi* and *Salmonella paratyphi* are the causative agents of typhoid and paratyphoid fever. Usually, typhoid or paratyphoid fever is acquired in tropical regions. The diagnosis is made by blood culture or by serological testing. Treatment of choice depends on the susceptibility pattern because there are resistant strains.

Salmonella diarrhoea is a zoonosis. *Salmonella* sp. can be found on poultry meat and eggs. There can be asymptomatic intestinal colonization in humans. Salmonellosis has to be reported to the health authorities. Serving, handling or cooking of food is prohibited for patients with *Salmonella* disease or colonization.

8.7.5 *Shigella* Species

Shigella dysenteriae is the causative agent of bacterial dysentery. Bacterial dysentery is a serious disease of the colon (colitis) with muco-bloody diarrhoea, painful bowel motions and occasional vomiting. *S. sonnei*, *S. flexneri* and *S. boydii* cause diarrhoea, but rarely a dysenteric colitis. The source of infection is contaminated food and sometimes via contact with contaminated items. Flies may be vectors. Actions like handling, cooking or serving of food are prohibited for patients with *Shigella* infection.

8.7.6 *Yersinia* Species

Yersinia are Gram-negative rods. There are three medically relevant *Yersinia* species.

In humans *Yersinia pestis* causes the plague, a serious sepsis with involvement of the lymph nodes (bubonic plague) and sometimes of the lungs. But plague is a zoonosis because *Y. pestis* is found in asymptomatic gerbils. These gerbils are restricted to some parts of the world, e.g. Mongolia or Southeastern United States. If rat fleas (*Xenopsylla cheopis*) feed on gerbils and on rats, *Y. pestis* is transmitted to rats. However, *Y. pestis* causes disease in rats and fleas. Fleas start to feed on other mammals and thus spreading plague even to humans.

In the Middle Ages, plague was a feared epidemic. However, plague can be treated with antibiotics. Nowadays, there may be individual cases of plague in endemic areas if there is a transmission when handling wild symptomless gerbils carrying the *Y. pestis*.

Y. enterocolitica causes enteritis with colicky pains and loose stools. Usually it is isolated in children with severe diarrhoea. Infection with *Y. enterocolitica* can lead to sepsis and abscess formation, but also attack bones or the heart.

Y. pseudotuberculosis causes enlarged mesenteric lymph nodes and pain in the right lower quadrant of the abdomen. Because of the localization, it is mimicking appendicitis; thus it is also called pseudoappendicitis.

8.7.7 *Vibrio* Species

Vibrio are Gram-negative rods that can commonly occur in tepid, salty water.

Vibrio cholerae is endemic in tropical areas. Cholera outbreaks occur primarily in areas with poor hygienic conditions (lack of sanitation, no fresh water), environmental emergencies or major population movements (refugees). *V. cholerae* is the causative agent of Asiatic cholera. Cholera is a toxic diarrhoea with up to 20 l of fluid loss per day. Left untreated, the mortality is up to 50% particularly in children. *V. cholerae* produces a heat-stable cholera toxin which stops the water reabsorption in the colon. The transmission of *V. cholerae* occurs through contaminated water. Outside of water the pathogen dies rapidly. There are virtually no healthy carriers. Infection control and prevention measures include strict water hygiene (boil water in countries with unsafe water) and adequate sewage. The treatment of cholera is rehydration. Antibiotic therapy kills the pathogen but has only small effect on the diarrhoea because diarrhoea is due to the toxin. For practice, it is important to take the travel history of expectant mothers with watery diarrhoea. *V. cholerae* is a notifiable disease to healthcare authorities.

8.7.8 *Haemophilus* Species

Haemophilus are Gram-negative rods that are part of the normal flora of the respiratory tract. *Haemophilus influenzae* is a pathogen of upper and lower respiratory infections but also of bacterial meningitis. In small children between 6 months and 4 years, *H. influenzae* can cause acute tonsillitis (angina), sinusitis, otitis media and pneumonia but also a bacterial purulent meningitis and endocarditis. The treatment of choice consists of aminopenicillin plus beta-lactamase inhibitor or cephalosporins. There is an efficacious vaccine.

Haemophilus ducreyi is the causative agent of the sexually transmitted disease, chancroid. This sexually transmitted disease is mainly found in tropical regions. The patients with chancroid present with roundish greasy-occupied ulcers on the genitals and swelling of the local lymph nodes. The treatments of choice are quinolones, macrolides and third-generation cephalosporins.

8.7.9 *Bordetella pertussis*

Bordetella pertussis is the causative agent of whooping cough (pertussis). Whooping cough is common in children. But also adults may acquire and spread pertussis. The bacteria are easily spread in droplets through the spasmodic cough attacks. In infants these coughing fits can lead to apnoea. Therefore, mortality can be up to 2% in first year of life. There is an effective vaccine against *Bordetella pertussis* (acellular vaccine) for children and adults.

8.7.10 *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is a non-fermenting Gram-negative rod and commonly found in the humid environment but also in the gut of humans and animals. *P. aeruginosa* is an opportunistic pathogen and causes severe sepsis in patients with leukaemia. *P. aeruginosa* is an important pathogen of healthcare-associated infections and in infections associated with implanted material because it easily forms biofilms on material surfaces. The most common infections caused by *P. aeruginosa* are urinary tract infections, wound infections, infections of the outer ear and infections of large burn wounds. Children with cystic fibrosis, an inborn genetic disease with failure to clear the mucus from the respiratory tract, become colonized and infected with *P. aeruginosa*.

In the microbiology laboratory, *P. aeruginosa* is identified at the first glance to the agar plate because it has an impressive colour that ranges from lime green to petrol blue and his sweet pungent odour. *P. aeruginosa* produces the enzyme oxidase. Test strips with an oxidase substrate that are commonly used in microbiology become a blue colour when pressed on the colonies of *P. aeruginosa*.

A prominent feature is that *P. aeruginosa* is not susceptible to many antibiotics. Exposed to antibiotics *P. aeruginosa* rapidly develops resistance.

Acinetobacter baumannii complex and *Stenotrophomonas maltophilia* are non-fermenters, but they are oxidase-negative. The colonies on the agar plate are unspectacularly greyish. However, both are resistant to most antibiotics commonly used for treatment. They can be selected by the extensive use of antibiotics and cause serious infections, sepsis, pneumonia and urinary tract infections, in immunocompromised and intensive care patients.

Acinetobacter baumannii complex survives well in the environment and may be easily transmitted and cause outbreaks in the hospital setting. Thus, infection prevention and control measures including hand hygiene and environment cleaning and disinfections have to be observed meticulously.

8.8 Other Rod-Shaped Bacteria

There are bacteria which are not characterized by Gram staining because their cell wall has different compositions, e.g. mycobacteria, or they are living within the human cells, e.g. chlamydia.

The most important pathogens are mycobacteria, *Treponema pallidum*, *Rickettsia* and *Borrelia* species.

8.8.1 Mycobacteria

Mycobacteria are acid-fast bacilli because they keep the red stain in the Ziehl-Neelsen staining. Their lipid-rich outer cell membrane makes mycobacteria resistant to environmental noxes. The treatment of mycobacterial diseases differs significantly from the treatment of other bacterial infections. Therefore, a distinction between bacteria and mycobacteria is pivotal.

There are many mycobacterial species. A distinction between "fast-growing" and "slow-growing" mycobacteria gives the first clue to identification. "Rapidly growing" mycobacteria grow within 14 days on the special growth media. "Slow-growing" mycobacteria require up to 6 weeks to grow. Therefore, for the diagnosis of mycobacterial diseases, molecular PCR-based diagnostic tests are particularly important.

Human pathogens of the genus *Mycobacteria* are *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum*, *Mycobacterium microti*, *Mycobacterium leprae* and *Mycobacterium ulcerans* (Buruli ulcer). Among the so-called atypical mycobacteria, the most important is *Mycobacterium avium intracellulare* complex.

Mycobacterium tuberculosis
Mycobacterium tuberculosis is one of the most important pathogens worldwide. It is the causative agent of tuberculosis, a world-occurring disease. For 90% of healthy people, infection with *M. tuberculosis* is asymptomatic. However, there is no complete elimination of the bacteria. Mycobacteria can survive intracellularly in macrophages for life. When the immune system is weakened, e.g. in AIDS, alcoholism, iatrogenic immunosuppression or very old age, there may a reactivation of the endogenous infection.

Tuberculosis
Tuberculosis is common in countries with low income and a high rate of AIDS. About 150 years ago, tuberculosis was very common in Europe, especially in urban areas due to famine and poor housing conditions. By improving living conditions, and with other preventive measures, the tuberculosis epidemic in Europe was contained in the early twentieth century. Currently, there are up to 1.7 billion people infected. Not all infected people have a visible disease but a latent infection that can erupt

easily when the patient becomes immunocompromised. Estimates show that 20 million people have a so-called open tuberculosis of the lungs. Open pulmonary tuberculosis is associated with a high risk to spread *M. tuberculosis* by coughing. Transmission of mycobacteria is airborne meaning that the infectious particles remain longer in the air. Thus open pulmonary tuberculosis is of hygienic relevance. Patients with open pulmonary tuberculosis have to be isolated in a special isolation room that should only entered with special tightly fitting masks (class 2, FFP-2, N90). Contact persons have to be identified and followed up. Three million persons die each year from the effects of tuberculosis.

Classification of Tuberculosis

- Primary tuberculosis: Infection occurs via air directly through droplets. Primary infection affects usually the lungs. There is a small initial lesion and lymph node.
- Secondary tuberculosis: When reactivated there is an endogenous spread of pathogens in immunocompromised host in almost all organs. Symptoms are nonspecific.

Signs and symptoms include subfebrile temperatures (below 38.3°), night sweats, weight loss, swollen lymph nodes, fatigue and weakness, cough or dry cough with little expectoration.

In immunocompromised persons, a severe disease may occur in varying manifestations including sepsis, tuberculous meningitis or organ involvement which looks like a tumour in the computed tomography.

Diagnosis of Tuberculosis

Microbiological diagnosis includes direct detection and visualization of acid-fast bacilli by staining of the material (sputum, aspirate, etc.) using the Ziehl-Neelsen stain. The test is easy but less sensitive compared to the PCR test. Cultures will be positive after up to 6 weeks. Serology testing is done using specific lymphocyte reaction to a *Mycobacterium tuberculosis* antigen (IGRA, interferon-gamma reaction assay). This test replaces the tuberculin from the screening of people at risk.

Previously a tuberculin test was performed (Mantoux text). This test is based on the cross-reaction of an infected with tuberculosis people to the intracutaneous administration of *Mycobacterium bovis*—antigens. The test is nonspecific and only says that the individual had contact with *Mycobacterium tuberculosis* or *Mycobacterium bovis* (BCG). The test does not indicate whether an acute clinical infection or years past healed, clinically silent, infection. A negative test indicates that a patient has never had contact with tuberculosis. However, in severely immunocompromised patients, the reaction is also negative despite active clinical infection.

Tuberculosis has to be reported to health authorities under the Tuberculosis Act. Patients with tuberculosis are regularly monitored by the health authorities.

Treatment of Tuberculosis
The treatment of tuberculosis consists of a combination of 3–4 antituberculous over 3–6 months. Initially a combination of isoniazid, rifampicin, pyrazinamide and ethambutol is administered for 2 months, followed by a combination of isoniazid and rifampicin for the next 4–7 months. In South and East Asia, Eastern Europe and some African countries, there are *Mycobacterium tuberculosis* strains that are resistant to this standard therapy, multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). For practice it is important to know the travel history or the country of origin of the expectant mothers to identify a possible risk for these infections and to refer them to a dedicated tuberculosis centre for further diagnostics and treatment if indicated.

8.8.2 *Treponema pallidum*

Treponema pallidum is a spirochaete bacterium. Spirochaetes have a helical form and look like a screw. *T. pallidum* is the causative agent of syphilis, one of the most important sexually transmitted infections. The transmission from an infected person is through sexual intercourse. The incubation period of syphilis is about 21 days (10–90 days). *Treponema* enters the bloodstream and is distributed in the whole body and all organs and the brain. Congenital syphilis develops when infection occurs during the later stages of pregnancy. *Treponema* is transmitted to the foetus through the placenta, infecting the foetus, and the child is born with congenital syphilis.

The diagnosis is made with dark-field microscopy looking on material from syphilitic lesion on a glass slide. *T. pallidum* can be seen as corkscrews moving rapidly around. However, be careful to use always gloves for examination and sampling because *Treponema* are very infective and may enter through very tiny lesions of the skin or the mucosa.

More commonly the diagnosis is made using serological tests. There is a screening test, the VDRL test, the TPHA (*Treponema pallidum* haemagglutination test) and the treponemal antibody tests (FTA-ABS) that can detect both IgG and IgM antibodies. FTA-ABS-IgM antibodies are present in a very recent infection.

Syphilis
There are four stages of syphilis.

- Stage I:
  About 3 weeks after infection, a painless firm papule develops and evolves to an ulcer with firm ground and sharp borders at the site of the primary infection as well as a painless swelling of the local lymph node. The ulcer ground is infested heavily with *Treponema* bacteria and very infectious. The painless ulcer is also called hard chancre, and ulcer plus the lymph node is called primary complex of syphilis.

- Stage II:
  About 4–10 weeks after infection, there is generalization of the diseases with fever, malaise, weakness, weight loss, hair loss and headache. There are typical red flat to papulous lesions on the skin of the trunk, extremities and particularly on palms and soles. Further there are wart-like lesions, so-called condylomata lata, on the mucosae of the mouth and at the genitalia. These lesions are full with bacteria and thus very infectious. The symptoms resolve after 6–10 weeks even without therapy.
- Latent syphilis:
  After stage II syphilis may become latent, i.e. symptomless. The latency period can last up to years. Latent syphilis is defined as a positive serologic test but no symptoms of disease.
- Stage III:
  The final stage of syphilis is also called lues or gummatous syphilis. In this stage gummas develop. Gummas are painless tumours consisting of granulomatous immune reaction to the *Treponema*. The gummas can be very large. The symptoms are dependent on the localization of the gummas because gummas can develop in all organs including the central nervous system. Neurosyphilis manifests as meningitis (involvement of the meninges), meningovascular syphilis, general paresis or tabes dorsalis with various neurological symptoms. The symptoms are neuropathic pain, ataxia, apathy, seizures, general paresis and dementia. About a third of untreated patients develop stage III symptoms. Stage III syphilis is not infectious.
- Congenital syphilis:
  Two-thirds of new-borns infected with syphilis are born without symptoms. Symptoms develop during the first years of life and include enlargement of the liver and spleen, rash, fever, neurosyphilis and pneumonia. If untreated, children may develop the typical saddle nose deformation or sober shins. Infection during pregnancy is also associated with miscarriage.
  Because of these serious sequelae, syphilis test is done during pregnancy in Austria under so-called mother-child pass.

In some developed countries, cases of syphilis have to be reported to health authorities if the patients deny treatment of him-/herself and the partners. Treatment must also include the sexual partners.

8.8.3 *Rickettsiae*

Rickettsia is a genus of nonmotile bacteria that can have the shape of cocci, rods or threads (up to 10 μm long). They are obligate intracellular parasites because *Rickettsia* survive, grow and replicate within the cytoplasm of eukaryotic host cells (typically endothelial cells). They cannot live in the environment. *Rickettsia* cannot be cultured on agar plates but on tissue cell cultures only. Culture is therefore not done in the routine clinical microbiology laboratory.

Diagnosis is made by serology tests only.

Rickettsia species are transmitted by vectors, commonly arthropods, including chigger, ticks, fleas and lice. *Rickettsia* species are the pathogens of "spotted fevers" including rickettsialpox, African tick bite fever, Rocky Mountain spotted fever, Queensland tick typhus (Australian tick typhus) and fever boutonneuse. The patients have fever, rash and most often a typical lesion at the site of tick bite (eschar). *Rickettsia prowazekii* causes epidemic typhus (trench fever), recrudescent typhus and sporadic typhus, and *Rickettsia typhi* (worldwide) causes endemic typhus (murine typhus). A rickettsia-like pathogen *Orientia tsutsugamushi* causes scrub typhus.

In Austria, rickettsial disease is uncommon and only to be suspected in travellers returning from outdoor activities in Africa, Australia, the United States and Asia.

8.8.4 *Borrelia* Species

Borrelia sp. are *Spirochete* bacteria. Like *Rickettsia* they are obligate intracellular parasites. They cannot live in the environment. Culture of *Borrelia* is only done in specialized research laboratory. In the clinical routine, serology test (antibodies against *Borrelia*) is performed.

B. recurrentis (vector: lice) and *B. duttonii* (vector: ticks) are pathogen causing relapsing fever. These diseases occur in humans in bad circumstances before (wars, prisons, refugees).

Borrelia burgdorferi in the United States and *Borrelia afzelii* or *Borrelia garinii* in Europe are pathogens of tick-borne borreliosis. The vectors are ticks. There are two sylvatic cycles linked to life cycle of the tick vectors and wild animals.

Lyme Disease (Borreliosis)

Borreliosis is a zoonosis. First, borreliosis was named Lyme disease after the geographical site of the first diagnosis. At the site of the tick bite, a typical lesion with a reddish border and pale centre erythema chronicum migrans develops about 2–3 weeks later. If spreading of the borrelia into whole body occurs, there may be several manifestations like acrodermatitis atrophicans involving the fingers and the hand as well as myocarditis, cardiomyopathy, arrhythmia, arthritis, arthralgia, meningitis, neuropathies and facial nerve palsy.

Treatments of choice are penicillins and tetracycline.

8.8.5 *Chlamydia* Species

Chlamydia are cell wall-less bacteria. There are several *Chlamydia* or *Chlamydia*-similar species, but the most important *Chlamydia* is *Chlamydia trachomatis*. *Chlamydia* are characterized by a complex life cycle. They live a "parasitic" life in cells. They are obligate intracellular parasites because *Chlamydia* survive, grow and replicate within the cytoplasm of eukaryotic host cells. *Chlamydia* can therefore

survive in the cells. For propagation the chlamydia are released from the cell and infect the next cell.

Chlamydophila psittaci is the causative agent of psittacosis. The reservoirs are birds, so it is a zoonosis (ornithosis, psittacosis). Transmission to humans can lead to pneumonia and rarely a haematogenous spread in the liver, spleen and central nervous system. The transmission is airborne dust, rarely minor injuries in the laboratory. The incubation time is 4 to 14 days. The diagnosis is a serological blood test by detecting antibodies to *Chlamydophila psittaci*. The treatments of choice are macrolides and tetracycline.

Chlamydophila pneumoniae is occasionally exciting an atypical pneumonia in humans. There will be an increase with age colonization of the respiratory tract with *Chlamydophila pneumoniae*, so it is unclear whether this bacterium is causative pathogen. It is estimated that 10% of the atypical pneumonia is caused by *C. pneumoniae*. Transmission is airborne from person to person. 70% of all infections with *C. pneumoniae* are asymptomatic.

Chlamydia trachomatis is a common cause of chlamydia infections associated with different serotypes. There are distinct clinical syndromes:

- Scarring conjunctivitis

  Chlamydia trachomatis serovars A, B, Ba and C cause scarring conjunctivitis that leads to blindness in dry subtropical zones (desert). According to WHO it is estimated that 1.9 million people are affected by blindness or visual impairemetn due to trachoma. Overall about 158 million people currently live in endemic areas for trachoma and are therefore at risk of blindness due to this disease. The underlying causes are poor sanitation and lack of water, and the transfer is made by contaminated items, by flies or by direct contact among people.
- Chlamydial urethritis (unspecific urethritis)

  Chlamydia trachomatis serovars D–K are the most frequent cause of sexual disorder which is known as urethritis or cervicitis in the United States and Western and Northern Europe. The test has been done by means of molecular-biological tests in the smear from the urethra or cervix. The sessions are held with macrolides and tetracycline and will include all partners. New-borns can be infected during birth. Possible long-term consequences are chronic scarring caused by chronic inflammation and consequent infertility. In case of an excessive immune response reactive arthritis can occur. The symptom complex in urethritis, arthritis and conjunctivitis is called Reiter's syndrome. Epidemiologically, it is estimated that there are 3–5 million new infections of STD *Chlamydia trachomatis* D–K in the United States. Two-thirds of women are asymptomatic. In men, it is more common to clinical symptoms with urethral discharge. In the women occur subacute infections with nonspecific abdominal pain, sometimes urethritis, but also endometritis, salpingitis. Scarring can cause ectopic pregnancies and infertility. The incidence of arthritis is 1–3%.
- Lymphogranuloma venereum

  Chlamydia trachomatis serovars L1–L3 are the causative agent of the venereal disease lymphogranuloma venereum. It creates small ulcerative primary lesion ("herpetiform"). Finally, there is a painful swelling and purulent melting of the regional lymph nodes.

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Hospital Infections

9

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9.1 Infections

Infection is the adherence of pathogens and their multiplication in a host as well as the associated triggering of reactions of the host organism.

The pathogens of an infection may be bacteria, viruses, fungi, worms, protozoa or ectoparasites. The clinical picture of an infection is expressed on the basis of specific or unspecific symptoms:

- Systemic infection (sepsis): fever, chills, low blood pressure, "shock"
- Local: redness, swelling, heat, impaired function
- Organ specific: e.g. cough, headache

Laboratory test suggestive of infection:

- Increased granulocytes
- C-reactive protein
- Microbiology results

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
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By definition, fever is a body temperature above 38.2 °C. The causes may be inflammation (infection, disease of the rheumatoid type) or malignant tumours, but also postoperative and traumatic events can cause fever.

Infectious diseases can be classified in several ways:

- Pathogen-related
- Organ-related (pneumonia, urinary tract, etc.)
- Systemic located
- Transmitter-related (vector)
- Behaviour-related (travel diseases, venereal diseases)
- History-related (acute, subacute, chronic, recurrent, etc.)
- Immunosuppression
- Community-acquired ("outside" the hospital) vs. hospital infections (healthcare-associated infections, HAI)

Regardless of the classification of infection, the general target of infection is a rapid diagnosis including rapid pathogen identification and the initiation of targeted therapy for treatment.

9.2 Diagnostics

An indispensable diagnostic measure is the collection of a detailed medical history and clinical examination (including blood pressure, pulse and temperature measurement) to determine the status of the patient. As further standard diagnostic possibilities, laboratory chemical examinations can be requested (blood count, inflammatory parameters) and blood cultures taken (each two blood culture vials), and urine culture and lung X-ray can be carried out. Specific, mostly symptom-related diagnosis includes stool culture, wound swab, lumbar puncture, etc.

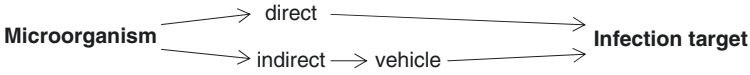
The microbiological diagnostics include:

- Direct: visualization natively (e.g. stool for worms) and microscopic (malaria, *Treponema*, Gram colour for bacteria).
- Culture.
- Tissue section (histology, special stains) with direct visual detection and/or staining.
- PCR (polymerase chain reaction). PCR is a molecular technique that allows for the rapid detection and characterization of microorganisms, including those difficult to culture; PCR methods are used in a broad range of medical diagnostic fields, including bacteriology, virology, mycology and parasitology.
- Indirect: serological tests.

If no pathogen is detected, so-called "empirical" therapy is initiated to prevent an uncontrolled progression of the infection.

9.3 Transmission of Infections

The basic model for the *transmission* of infections is as follows:



By direct transmission is meant direct contact with the agent, e.g. by aerosol formation when eating or coughing. Indirect contact infection occurs between a noninfected person and their environment. This can, e.g. be a contaminated object. The pathogens enter, e.g. about open wounds or the mucous membranes in the host. One form of indirect contact infection is the smear infection. It takes place faecal-orally via the excretions of infected persons. So-called living sources of infection can be patients, visitors or hospital staff. Inanimate objects such as aqueous solutions, foods or instruments may also be a medium for pathogenic microorganisms.

The most important vehicle for indirect transmission is the *hands*. Hands are our most common working tool and are therefore most likely to be at risk of contamination. Further vehicles for the indirect transmission path are professional clothing (stomach region, sleeves), catheters, instruments, rinsing fluids, body bowl, stethoscope, dust and air (rather rare). In practice, the pathogens often find the source of infection via several vehicles: bandage → hand → instrument → patient.

9.4 Healthcare-Associated Infections (HAI)

A nosocomial infection (NI) is any infection that is causally related to treatment in the hospital (or other healthcare facilities). The word nosocomial derives from the Greek "nosos" (disease) and "komein" (care). NI is the most common complication of medical care and affects all healthcare facilities (long-term care facilities, rehab centres). NI is worldwide referred to as "healthcare-associated infections" (HCAI, HAI). Nosocomial pathogens are thus pathogens of hospital infections.

By definition, an HAI is any infection that occurs in the hospital after 48 h and on entering the hospital not yet incubated. The reasons for HAI are multifactorial:

- *Patient factors* (severe underlying disease, treatment-specific factors)
- *Microbiological factors* (pathogenicity, virulence, infectivity)
- *Environmental factors* (proximity of patients to each other, lack of dispenser)
- *Technical factors* (medical devices)
- *Hygiene factors* (contamination, cleaning defects, poor hand hygiene)

Certain factors influence the transmission of a healthcare-associated infection. Reduced immune response or breaches of natural barriers (skin defects, wounds) facilitate the colonization by pathogenic or facultative pathogenic microorganisms.

Risk factors for healthcare-associated infections	*Health status*
• Age (new-born, old people)	Advanced age
• Invasive measures (surgery, catheter, etc.)	Malnutrition
• Metabolic disorder (diabetes, etc.)	Alcoholism
• Cardio-circulatory diseases	Smoke
• Neurological (paralysis, etc.)	Chronic respiratory diseases
• Oxygen deficiency in the tissue	Diabetes
• Immunosuppression	*Acute factors*
• Antibiotics	Operational intervention
• Most complicated examination and surgical instruments (flexiscopes)	Trauma
	Combustion
• Blood vessel catheter	*Invasive procedures*
• High immunosuppression (stem cell transplantation)	Endotracheal or nasal intubation
	Mechanical ventilation
• Organ transplantation	Central venous catheterization
• Etc. (see table on the right)	Extracorporeal renal replacement therapy
	Lying drains
	Feeding tube
	Tracheostomy
	Urinary catheter
	Associated treatment
	Blood transfusions
	Recent antimicrobial therapy
	Immunosuppressive therapy, e.g. cortisone, etc.
	Stress ulcer prophylaxis
	"Lying position"
	Parenteral nutrition

9.5 Epidemiology

According to the European Centre for Disease Prevention and Control (ECDC), around 80,000 patients in Europe suffer daily from HAI. The prevalence of HAI in Europe is currently about 6%; the incidence is 7 HAI/100 hospital admissions.

The most common HAI are:

- *Urinary tract infections*: up to 35%
- *Surgical site infections*: up to 25%
- *Pneumonia*: up to 20%
- *Septicaemia*: up to 7%

Around 8% of these infections are ultimately the direct cause of death of those affected.

The consequences of an HAI have great individual as well as socioeconomic significance. Not only is the hospital stay extended by the infection (on average 7 days), but the treatment takes longer and becomes more expensive (rehabilitation). For working patients, this leads to a loss of earnings or production, and elderly

people often end up in disability or retirement. Eight out of 100 patients die as a result of NI.

Hospital infections rarely occur epidemically (only about 5%); there is rarely an outbreak of HAI. The vast majority (95%) of NI is sporadic (endemic) and must be sought to fully capture them.

9.5.1 Surgical Site Infection (SSI)

Surgical site infections (SSIs) are the most common type of nosocomial infections in low- and middle-income countries (from 1.2% to 23.6%) and affect up to one third of patients who have undergone a surgical procedure. Although SSI incidence is much lower in high-income countries, it remains the second most frequent type of HAI in the USA and the most common type in some European countries. According to 2015 European Centre for Disease Prevention and Control (ECDC) surveillance report, colon surgery has the highest prevalence in Europe with 9.6 episodes per 100 operations, followed by 2.9 for coronary artery bypass graft, 1.7 for caesarean section, 1.4 for cholecystectomy, 1.1 for hip prosthesis, 0.8 for laminectomy and 0.6 for knee prosthesis. The distribution of microorganisms that cause SSIs varies by type of surgical procedure. Gram-positive cocci are the most commonly reported for coronary artery bypass graft, hip and knee prosthesis, laminectomy and caesarean section. For gallbladder and colon operations, the majority of the responsible microorganisms are *Enterobacteriaceae*. SSI may cause poor wound healing, further antibiotic treatment, additional surgical procedures, organ failure, longer postoperative hospital stays, higher mortality and higher healthcare costs. It can occur in the incision skin area (superficial SSI), beneath the incision area in the muscle and the tissues surrounding the muscles (deep SSI) or in a body organ or a space between organs (organ SSI). SSI typically occurs within 30 days after surgery, and the proportion of SSI diagnosed in-hospital varied from 17% in caesarean sections to 67% in colon operations.

9.5.2 SSI Post Caesarean Section

Surgical site infection (SSI) is one of the most common complications following caesarean section and has an incidence varying worldwide from 3% to 15%.

Most wound infections do not become clinically apparent until postoperative days 4–7, when most women have already been discharged from the hospital. Since early treatment has an important role in preventing severe consequences, it is essential to instruct these women on signs and symptoms requiring further evaluation.

Risk factors can be divided into three categories:

1. Host-related factors (age, morbidity, pregestational diabetes mellitus and previous caesarean delivery)

2. Pregnancy and intrapartum-related factors (hypertensive disorder, gestational diabetes mellitus, twin pregnancy, preterm rupture of membranes, greater number of vaginal examinations)
3. Procedure-related factors (emergency delivery, caesarean hysterectomy, surgery duration of more than 60 min).

The infections after caesarean section are usually caused by Gram-positive cocci, although a polymicrobial infection consisting of both aerobic and anaerobic organisms is not rare.

Besides daily inspection of the caesarean incision, evidence-based interventions may significantly reduce post-caesarean delivery wound complications:

1. Appropriate timing of perioperative prophylaxis (before the skin slit)
2. Alcohol-based antiseptic solutions based on chlorhexidine for surgical site skin preparation

9.6 Antimicrobial Resistance and Healthcare-Associated Infections

The abusive administration of broad-spectrum antibiotics led to the development of resistance to standard antibiotics. Today, the development of new antibiotics does no longer keep in pace with the development of resistance of the microorganisms. This can lead to expensive, elaborate therapies. Increasingly, there are untreatable infections.

The WHO published a list of multiresistant bacteria for which new antibiotics are urgently needed, the WHO priority pathogens list for research and development of new antibiotics (see Chapter 11, multidrug-resistant microorganisms).

The complications of NI can range from localized wound infection to fulminant sepsis.

9.7 Prevention of Healthcare-Associated Infections

As the effects of antibiotics are decreasing, the focus is on prevention through basic hygiene measures:

- Hand hygiene.
- Spatial separation between infectious and non-infectious patients.
- Adequate cleaning and reprocessing of medical devices and objects with which patients come in contact.
- In the prevention of HAI, two important approaches are antisepsis and asepsis:

- Asepsis: measures to prevent contamination, e.g. through barriers (gloves, tweezers)
- Antisepsis: control of microorganisms by disinfection, sterilization and conditional cleaning

For details on hygiene measures in hospitals, see also chapter "Multidrug-Resistant Pathogens and Hygiene". For hand hygiene, see chapter "Hand Hygiene".

9.8 Surveillance of HAI

There are several tools available to detect and monitor HAI. *Prevalence* studies (1 day, 1 week), *incidence* studies (continuous monitoring of all incidences for extended periods, surveillance) or *outbreak* investigations with case-control or cohort studies are used as appropriate to describe HAI and to recognize HAI (see chapter "Epidemiology").

Surveillance is the systematic, continuous collection, analysis and interpretation of relevant data on healthcare-associated infections. This data collection can be used to provide feedback to the medical and nursing staff, thus reducing the frequency of HAI. Surveillance is also a form of internal quality assurance. The informative value and effectiveness is increased if one's own data on infection frequencies are compared with those of others (clinics, departments, etc.). Only in the context of the data of other departments, the measure of their own infection frequency is assessable. In order not to draw wrong conclusions, a comparison is only possible if identical methods are used to collect the data.

HAI-Net (Healthcare-Associated Infections Surveillance Network) is a network that has been providing anonymized data on healthcare-associated infections in European hospitals since the beginning of the 2000s. The network is now coordinated as a permanent agenda of ECDC, which publishes Austrian data at regular intervals compared to data from other European countries (http://ecdc.europa.eu/).

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Antimicrobial Agents (Antibiotics)

10

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Antimicrobial agents (antibiotics and antifungal agents) are active against bacteria or fungi. Antiviral agents are active against viruses. Commonly the antimicrobial agents work specifically against some types of bacteria, fungi or viruses. Thus, the diagnosis should be confirmed by microbiological testing, e.g. microscopy, culture and susceptibility testing, etc. However, when the patient is severely ill, there is no time to wait for the results. Then, immediate antimicrobial therapy, so-called empirical therapy, is administered which is based on evidence-based recommendations of expert medical societies ("guidelines").

Overuse of antimicrobial agents leads to development of bacterial resistance. Thus, antimicrobial agents, antibacterial agents in particular, should be used only when the infection is due to bacterial pathogens.

10.1 Antibacterial Agents

Antibiotic are produced classically by microorganisms, e.g. the fungus *Penicillium* produces penicillin, and acremonium produces cephalosporins. Penicillins and cephalosporins have a similar core structure, the beta-lactam ring. The compounds are the basis of many new antibiotics commonly used for treatment of infections. Other antibiotics are glycopeptides or aminoglycosides.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_10

Chemotherapeutics are antimicrobial compounds that are chemically produced. Examples are trimethoprim or quinolones.

The commonly used antibiotic classes are:

- Beta-lactam antibiotics (penicillins, cephalosporins, carbapenems)
- Quinolones
- Macrolides
- Glycopeptides

There are different modes of action for antibiotics:

- Inhibition of cross-linking of the cell wall components (beta-lactam antibiotics, glycopeptides)
- Inhibition of protein synthesis (aminoglycosides, macrolides)
- Interaction and inhibition of DNA transcription (quinolones)

Beta-lactam antibiotics are the most commonly used antibiotics. The most commonly used penicillins are penicillin V, piperacillin, amoxicillin and amoxicillin combined with clavulanic acid. The most commonly used cephalosporins are cefuroxime, cefamandole, cefoxitin, cefalexin, mecillinam, cefotaxime, ceftriaxone, cefepime and cefpirome and carbapenems are meropenem and imipenem. Beta-lactam antibiotics are well tolerated, and some can be used safely in pregnancy.

Other antibiotics are macrolides (erythromycin, azithromycin, roxithromycin, clarithromycin), clindamycin, fusidic acid, fosfomycin and oxazolidinones.

10.2 Antibiotics in Pregnancy

Generally, there are no prospective studies of the use of antibiotics in pregnancy. However, there are more than 50 years' experience in the use of some beta-lactam antibiotics in pregnancy as well as of macrolides erythromycin and josamycin. They are therefore classified as safe for use in pregnancy. For newer substances (e.g. oxazolidinone, fosfomycin), there is less experience. Tetracyclines, aminoglycosides and oxazolidinones must not be used in pregnancy.

When taking antibiotics during pregnancy, the advice of prescribing doctors and drug information must be observed.

10.3 Side Effects of Antimicrobial Agents

The most frequent are abdominal pain and diarrhoea caused by irritation of the intestinal flora, nausea and vomiting.

Rash is an occasional side effect. Antibiotic may sometimes act as a so-called hapten during a viral infection. This causes rash, but does not occur without virus infection. The most common form of allergy is an urticarial rash. This sort of rash has been distinguished from the allergy.

The most severe form of allergy is anaphylaxis. Anaphylaxis may occur with penicillins and cephalosporins. Anaphylaxis is a very rare, acute allergic reaction with very low blood pressure and respiratory distress. This emergency situation with shock and respiratory distress happens when antibiotics are intravenously administered.

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Multiresistant Microorganisms and Infection Control

11

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Multidrug-resistant microorganisms (MDRO) are bacteria that are insensitive to the mode of action of most antibiotics [1]. Bacteria has the ability not only to modify themselves to resist antimicrobials but also to propagate these resistance traits and even share resistance genes with other contemporary bacteria within their environment, enabling them to overcome host strategies aimed against them. This microorganisms' resistance is a biological property that is defined in the genome of the microorganisms and is passed on in their multiplication. The use of antibiotics for decades has eventually led to the selection of bacterial strains that are resistant to a range of drugs. Thus, even sensitive bacterial strains could be displaced.

Bacteria may use four major bacterial resistance strategies in order to disrupt the essential steps required for the effective action of the antimicrobial agents:

1. By prevention of the antimicrobial from reaching its target by reducing its ability to penetrate into the cell
2. By expulsion of the antimicrobial agents from the cell via general or specific efflux pumps
3. By inactivation of antimicrobial agents via modification or degradation
4. By modification of the antimicrobial target within the bacteria

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_11

No single mechanism of resistance is considered responsible for the observed resistance in a bacterial organism, but several different mechanisms may work together to confer resistance to a single antimicrobial agent.

MDRO are a serious health problem in all healthcare facilities. Multidrug-resistant microorganisms are present not only in hospitals but also in rehabilitation centres, long-term care facilities, medical practices, etc. What is most alarming today is the rate at which antibiotic resistance often develops and how quickly it spreads across the globe and among different species of bacteria. In addition, no European country can claim to be unaware of the problem of MDRO. It is crucial to promote healthcare with high-quality standards, thereby reducing the risk of MDRO and limiting their spread through control measures.

The majority of all infectious agents in the EU are accounted for by the nosocomial pathogens. An estimated 4 million people a year in Europe acquire a nosocomial (= hospital-acquired) infection, of which approximately 80,000 die from it. Here, MDRO represent an increasing danger due to the limited therapeutic spectrum due to their multiresistance behaviour (Table 11.1).

In 2017 the World Health Organization has grouped the pathogens according to the species and the type of resistance and then stratified the results in three priority tiers: critical, high and medium:

1. Critical
   - *Acinetobacter baumannii*, carbapenem-resistant
   - *Pseudomonas aeruginosa*, carbapenem-resistant

Table 11.1 Relevance and transmission of multidrug-resistant microorganisms

Effective hygiene measures		
Microorganism	Transmission	Relevance
ESBL (extended-spectrum β-lactamase producers CAR (carbapenem-resistant Gram-negative rods) MDRGN (multidrug-resistant Gram-negative microorganisms)	*Direct*: hands *Indirect*: contact with pathogen-containing secretions, stool, wounds, contaminated objects	• Often asymptomatic carriers • Mostly Gram-negative microorganisms • Occurrence as an endogenous infectious agent in the intestine → Eradication not possible
MRSA (methicillin-resistant *Staphylococcus aureus*)	*Direct*: hands, from skin to skin (dandruff) *Indirect*: contaminated objects	• Healthcare-associated infections, i.e. sepsis, pneumonia, urinary tract infections, surgical site infections • Eradication possible!
VRE (vancomycin-resistant enterococci)	*Direct*: hands, from skin to skin *Indirect*: contaminated objects	• Healthcare-associated infections • There are healthy carriers (intestinal microorganisms) • → Eradication not possible • High mortality by infections

   - *Enterobacteriaceae*, carbapenem-resistant, 3rd-generation cephalosporin-resistant
2. High priority
   - *Enterococcus faecium*, vancomycin-resistant
   - *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and vancomycin-resistant
   - *Helicobacter pylori*, clarithromycin-resistant
   - *Campylobacter*, fluoroquinolone-resistant
   - *Salmonella* spp., fluoroquinolone-resistant
   - *Neisseriagonorrhoeae*,3rd-generationcephalosporin-resistant,fluoroquinolone-resistant
3. Medium priority
   - *Streptococcus pneumoniae*, penicillin-non-susceptible
   - *Haemophilus influenzae*, ampicillin-resistant
   - *Shigella* spp., fluoroquinolone-resistant

The most important MDRO in healthcare settings are:

- MRSA (methicillin-resistant *Staphylococcus aureus*)
- ESBL (extended-spectrum β-lactamases) producers *Enterobacteriaceae*/ MDRGN (multidrug-resistant Gram-negatives)
- VRE (vancomycin-resistant enterococci)

11.1 Methicillin-Resistant *Staphylococcus aureus*

Methicillin-resistant *Staphylococcus aureus* (MRSA) strains have been known since 1961. Since 1975, a worldwide increase of MRSA has been observed. The frequency of MRSA is regional but also varies from hospital to hospital and from department to department. Increased MRSA occurrence may be indicative of inadequate sanitary measures and is associated with therapeutic problems and increased costs. The incidence of MRSA increases with the size and specialties of a hospital, as well as with the severity of the underlying diseases of the patients. MRSA strains are not only resistant to methicillin and oxacillin but also to all other β-lactam antibiotics (penicillins, cephalosporins, carbapenems).

Infections with MRSA are a serious medical problem. They usually affect critically ill people who are impaired in their defence and thus contribute to increased infectious morbidity and mortality in this patient group. Although from a clinical perspective, the mere colonization with MRSA has a much lower relevance compared to the infection, it is important for the retransmission to determine whether an infection or just colonization exists. Hospital hygiene measures designed to prevent transmission of MRSA to other patients are therefore equally applicable to infected as well as populated patients. As in the case of the spread of other multidrug-resistant microorganisms, the emphasis is on compliance with basic hospital hygiene measures (hand hygiene, protective clothing, supply and disposal, reprocessing of medical devices).

Staphylococcus aureus can survive very well in inanimate environment, in dust and in dry conditions; therefore, the pathogen is predestined as a hospital microorganism. In humans, it occurs in the nose, throat and perineum. About 1/3 of the normal population is carrier of the microorganisms. This is colonization, not infection. Especially wounds, eczema and ulcers (or decubitus ulcers) are susceptible to infections with *S. aureus*. Most of the infections caused by *S. aureus* usually develop endogenously, that is to say via autoinfection through the pre-existing microorganisms' colonization on the body. In Austria about every 10th, *S. aureus* is an MRSA. Approximately 30–40% of patients colonized with MRSA develop infection by previous colonization. Most infections occur locally superficial on the skin in the form of (soft tissue) abscesses, folliculitis, cellulitis, carbuncles or wound infections. In rare cases, *S. aureus* can also trigger deep processes, e.g. pneumonia with multiple abscesses. In new-borns and infants, *S. aureus* may in rare cases be the cause of SSSS (staphylococcal scalded skin syndrome) (also called *dermatitis exfoliativa neonatorum Ritter von Rittershain*, Ritter's disease for short). This is a rare staphylococcal skin infection that causes haematogenous spread of staphylococcal toxins to cause skin detachment that is fatal if left untreated.

The *transmission* of MRSA is primarily by contact (*hands*, instruments, dressings, clothing, work surfaces), if usual, general hygiene measures are not sufficiently observed. Person-to-person transmission primarily occurs through the hands of the staff after contact with colonized/infected MRSA patients.

A nasal colonization of staff with MRSA is usually temporary. With permanent nasal colonization, the risk of colonization of the hands and thus transmission to patients is increased, whereby the risk of colonization is increased in personnel with dermatitis or skin lesions.

In special cases, microorganisms are also strongly released into the ambient air and spread. This includes patients with massive colonization or respiratory infection, large MRSA-colonized wound areas (e.g. burn victims) or MRSA-populated, scaly skin diseases. Such patients (= spreaders) must be strictly isolated (single room), and the caring staff (as well as relatives, visitors) must wear complete protective clothing in the *isolation room*.

Protective equipment by MRSA: Gloves, disposable plastic apron, long-sleeved disposable gown with cuffs, face mask.

Duty to inform: It is important to ensure that all employees in one area (doctors, carers, physiotherapists, cleaners) are aware of both the patients concerned and the appropriate hygiene measures. Everyone needs to know about the MRSA status of the patient so that appropriate precautions can be taken (protective equipment). Visitors to the patient must also be informed about hygiene measures before and after entering the patient room.

Screening: In principle, MRSA screening should only be performed in patients with specific evidence or suspicion of colonization/infection. The *primary screening is done via a nose/throat swab* or (in previously known positive patients) from the former positive localization (wounds, secretions, etc.). Patients who meet a certain risk profile (see Risk Factors) are primarily screened.

Risk factors for colonization/infection with MRSA in the hospital:

- Previous KH stay
- Length of the KH stay
- Previous antibiotic therapy
- Use of catheters, drains, etc.
- Surgical intervention (wounds)
- Decreased immune system (oncological patients, intensive care patients, etc.)
- Other patients with MRSA (cohabitation)
- Poor compliance regarding hygiene measures
- Admission from countries with a high rate of MDRO

Therapy MRSA can be effectively eliminated in asymptomatic carriers by eradication. These are local applications in the nose (mupirocin, chlorhexidine), on colonized wounds and on the colonized skin (daily antiseptic wash or baths with chlorhexidine, PVP iodine soap). Systemic MRSA eradication is not intended for prophylaxis or rehabilitation and is indicated only in rare cases. The resistance behaviour of the microorganisms eliminates all β-lactam antibiotics as a therapeutic option!

Hygiene measures:

- *Hand disinfection* after contact with patients or with objects close to the patient (even after the gloves have been removed)
- Single room (desirable, absolutely necessary for spreaders)
- Gloves (for all actions at the place of infection/settlement)
- Protective equipment (with spreaders, plastic apron, protective coat, face mask)
- Use used bandage material, laundry, used instruments, etc. without interim storage or contact with objects in the disposal bag or transport container
- Daily maintenance disinfection of the patient room
- Obligation to inform employees, the patient and the visitors

Proof of MRSA should definitely be documented in the medical history and in the doctor's brief!

11.2 Multidrug-Resistant Gram-Negative Bacteria

The term ESBL (extended-spectrum β-lactamases) refers to an enzyme that cleaves β-lactam rings, thereby rendering an important group of antibiotics, the β-lactam antibiotics, ineffective. Most commonly, these enzymes are found in Gram-negative bacteria of the *Enterobacteriaceae*, which live in the gut. Thus, those bacterial strains having this enzyme are *referred to as ESBL producers* (e.g. *E. coli* ESBL). Gram-negative bacteria have built-in abilities in the last decades to find new ways to

be resistant: they can pass along genetic materials that allow other bacteria to become drug-resistant as well. Multidrug-resistant Gram-negative (MDRGN) bacteria are a type of Gram-negative bacteria that are resistant to more than one drug in three or more antimicrobial drug classes (acylureidopenicillines, cephalosporins, quinolones, carbapenems). The increasing incidence of serious infections due to antimicrobial drug-resistant Gram-negative bacteria has increased, and MDRGN strains of *Enterobacteriaceae*, *P. aeruginosa* and *A. baumannii* have become of most concern because they have been reported by hospitals all around the world. Infections with these microorganisms are very difficult to treat and can lead in some cases to death of up to 50% of the infected patients.

Since carbapenems are so far the last choice against infections caused by ESBL producer bacteria, last decade increase in carbapenem resistance rates, together with the lack of newly emerging antimicrobial drugs, has resulted in the revisit of old antibiotic drugs such as colistin and fosfomycin and carbapenem-resistant strains which represent nowadays a significant threat to public health. These bacteria have the potential for widespread transmission of resistance via mobile genetic elements; while some strains are innately resistant to carbapenems, others contain mobile genetic elements (i.e. plasmids) that result in the production of carbapenemase enzymes (carbapenemases), which break down most β-lactam antibiotics, including carbapenems. These carbapenemase-producing genes are frequently co-located on the same mobile element with other resistance genes, which can result in co-resistance to many other antibiotic drug classes and make them difficult to manage.

MDRGN can cause a variety of infections, most commonly urinary tract infections caused by bacteria in the digestive tract, which can easily enter the urinary system due to their anatomical proximity. Other common infections are respiratory infections (pneumonia), wound infections (postoperative) and sepsis. A colonization of the intestine with MDRGN pathogens can be quite asymptomatic and is harmless for the person concerned. Due to the fact that most bacteria living in the intestine are Gram-negative, a complete eradication of MDRGN pathogens in affected individuals is not possible. Thus, the spread of the pathogens is prevented solely by hygienic measures.

Like all other hospital microorganisms, the transmission of MDRGN pathogens takes place *via direct contact* (Stool!) or *indirectly via contaminated objects* (patient environment, instruments, laundry, care utensils, sanitary facilities, etc.). Even asymptomatic carriers represent a source of infection (stool, anogenital area)!

Risk factors' colonization with ESBL/MDRGN microorganisms:

- Previous antibiotic therapy
- Previous hospital stays (including length of stays)
- Immunosuppression after organ transplantation
- Invasive aids (catheters, drains, intubation, probes)
- Stay in an intensive care unit (including neonatology and haematology-oncology stations)
- Surgical procedures or wounds

- Severe underlying disease or comorbidities
- Stay in a hospital abroad

The preventive measures for MDRGN agents are defined as bundles. Primary is to ensure compliance with the *standard infection control measures* (*five moments of hand hygiene*, *aseptic operation*, *protective clothing where required*, *compliance of the staff*). In patients who are a source of litter (urinary/faecal incontinence, open wounds, scaly skin diseases, severe cough, lack of compliance), isolation in a single room (with its own toilet) is essential. Colonized patients who do not represent a source of scattering should be evaluated according to the situation. A cohort of populated patients is quite possible but in consultation with hospital hygiene.

Further strong recommended infection control measures by MRGN:

- Contact precautions
- Implementation of multimodal IPC strategies
- Surveillance of MDRGN infection and surveillance cultures for asymptomatic CRE colonization
- Environmental cleaning

Measures in isolated MDRGN carriers: Single room with own toilet, long-sleeved disposable gown with cuffs, face mask and gloves for all actions in the isolation room, co-ordination in consultation with hospital hygiene.

Therapeutic indication: Colonization with MDRGN pathogens without clinical signs of infection is not an indication for antibiotic therapy. An eradication scheme is currently not established. In some cases, a wash with an antiseptic washing lotion to reduce the superficial colonization of the skin (after consultation with the hospital hygiene) is considered. Due to the high probability of reinfection with the own enterobacteria, therapy/eradication in asymptomatic MDRGN carriers is not meaningful or not feasible.

Screening: Screening is only to be carried out if there is a corresponding suspicion (see Risk Factors). Primary screening in high-risk patients is done by smears from the stool or by rectal swab. Depending on the clinical manifestation (urine, wounds, bronchial secretions), the smear may be taken at the infected body site if there are signs of inflammation. Patients of a newly discovered MDRGN carrier should in principle always be screened.

Proof of ESBL/MDRGN should definitely be documented in the medical history and in the doctor's brief!

11.3 Vancomycin-Resistant Enterococci

Vancomycin-resistant enterococci (VRE) are colonies of bacteria that are resistant to the antibiotic vancomycin and thus can only be treated with reserve antibiotics. Enterococci are part of the physiological intestinal flora in humans and are considered to be only conditionally pathogenic. Clinically, *E. faecalis* and *E. faecium* are

the most important. Enterococci are very environmentally stable and form numerous resistances to antibiotics. In *E. faecium*, e.g. can be expected with an ampicillin resistance in 90% of cases. Resistance to glycopeptide antibiotics (e.g. vancomycin or teicoplanin) has also increased in recent years, resulting in the nomenclature of VRE. As with MDRGN microorganisms, gut rehabilitation is not possible with VRE, which is why intestinal colonization with VRE can persist for a long time (months, even years).

VRE do not cause *any pathogen-specific symptoms* that can be used to make a diagnosis. VREs are recognized by the presence of enterococci in clinically relevant test materials and the resistance to vancomycin in the antibiogram. Local infections caused by VRE are often difficult to treat due to vancomycin resistance, which is why this bacterial group is one of the healthcare-associated infections. In particular, VRE causes infections of chronic wounds such as decubitus, urinary tract infections in indwelling catheters or the respiratory tract in artificial respiration and tracheostomy and in severe cases also sepsis. Of course, the symptoms depend solely on the location and severity of the infection.

The *transmission* from person to person is mostly by contact over the hands (with stool) as well as over contaminated objects or near-patient surfaces. Contamination of the environment is at, e.g. open wounds possible (stray sources). Since enterococci are environmentally stable, disinfection measures in the hospital (hand, instrument, surface disinfection) are of great importance.

Risk factor colonization with VRE microorganisms:

- Immunosuppression
- Severe underlying disease or co/multi-morbidity
- Surgical procedures or open wounds
- Invasive aids (catheters, drains, intubation)

As in the case of MDRGN and MRSA, a *screening* for VRE is only carried out on suspicion based on the risk profile and in addition, when receiving known VRE carriers (from previous or previous examinations), with fellow patients of a VRE carrier.

Therapeutic indications: Colonization with VRE without clinical signs of infection does not constitute an indication for antibiotic therapy. An eradication scheme (with topical agents) is currently not indicated.

11.4 Hygiene Measures with Vancomycin-Resistant Enterococci

- Hand hygiene:
  - Personnel: hand disinfection before and after each patient contact (five moments of hand hygiene) and also between cohorted VRE patients
  - Patient: hand disinfection after the toilet visit, after contact with excreta and before leaving the room

  - Visitors: Hand disinfection before and after contact with other patients and before leaving the room
- Single room isolation.
- Own toilet always necessary!
- Co-patients stay in the room until the primary screening and have their own toilet. With VRE freedom they can be moved out of the room.
- Protective clothing (gloves and apron for all medical and nursing activities on the patient).
- Use all utensils only for the patient and wipe them after use.
- Do not take medical documentation with you into the room.
- Routine and targeted cleaning and disinfection of near-patient surfaces.
- Discard waste directly at the patient's bed in closed containers.
- Prepare bowl dishes and urine bottles in the dishwashing unit immediately after use.
- Plan work processes so that activities take place in the "MDRGN room" or at MDRGN providers at the end of the routine (while ensuring good preparation and, if necessary, involvement of a second person to avoid unnecessary interruptions [contamination risk!]).
- Obligation to inform patients, employees in the area, cleaning staff, visitors, etc.

Proof of VRE should definitely be documented in the medical files and in the doctor's letter for the patient!

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General and Specific Virology

12

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12.1 General Virology

Viruses are subcellular particles of nucleic acid and proteins that do not have their own metabolism. In order for them to multiply, they must infect a suitable host cell and allow it to multiply. They contain only one type of nucleic acid, either DNA or RNA. They multiply obligatorily intracellularly and are themselves not capable of energy production or protein synthesis. Viruses occur in at least two states. They have a double existence, depending on whether they are inside or outside the host cell. Outside the virus cell, the virus exists as a virus particle, also called virion.

12.2 Virus Assembly

Biochemically, viruses are composed of carbohydrates, proteins, nucleic acid, and, in the case of enveloped viruses, lipids. The infectious virus particle (virion) consists of a few basic elements such as DNA or RNA, a capsid of viral proteins and often a shell derived from cellular membranes.

Depending on the nucleic acid type, the viruses are classified as RNA viruses or DNA viruses. Most DNA genomes are double stranded (ds) and are genetically

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_12

relatively stable. RNA viruses usually have a single-stranded (ss) genome and are subject to a high mutation rate. Thanks to mutation and selection, the RNA viruses are extremely adaptable. Another part of the virus is the capsid, which consists of viral proteins. The genome in many viruses is surrounded by the capsid like a protein coat. In some viruses, the capsids are again surrounded by a shell. The envelope is derived either from the host cell plasma membrane or from intracellular membranes. The envelope carries viral glycoproteins, which are responsible for the attachment of the virus to its host cell and the fusion of the virus envelope with the host cell membrane. The glycoproteins of the virus envelope serve neutralizing antibodies as a target and are subject to strong selection pressure from the immune system.

Enveloped viruses are sensitive to external influences such as heat or dehydration. This has a significant influence on the transmission paths, as "naked" (unencumbered, non-enveloped) viruses are usually much more resistant than viruses with shell.

12.3 Taxonomic Classification of Viruses

The classification is based on biological, biochemical, morphological, and increasingly also on genetic characteristics. Main criteria are:

- Type of genome: According to the nucleic acid type (RNA or DNA), they form as a single or double strand. Furthermore, a distinction is made whether the genome is in pieces (segmented) or contiguous (not segmented).
- Symmetry of the capsids: Cubic, helical, or complex.
- Possession of a shell: Covered or uncovered.
- Place of propagation: Assembly of the nucleocapsid in the nucleus or cytoplasm.
- Location of the envelope: Nuclear membrane, endoplasmic reticulum, plasma membrane.
- Virion size: The diameter can vary from 18 to 250 nm.

12.4 Classification of Viruses (Simplified)

	DNA	RNA
Non-enveloped	Adenovirus Parvovirus	Enterovirus, rhinovirus Reovirus Echovirus
Enveloped	Herpesvirus (HSV, EBV, CMV, etc.) Hepadnavirus (HBV)	Arbovirus, RSV Mumps virus, retrovirus (HIV) Measles virus, *Flavivirus* (HCV) Rubella, parainfluenza virus Influenzavirus, rabies virus

12.5 Virus Propagation

Virus propagation works equally well for all viruses in specific phases. These are:

- The attachment of the virus to the host cell
- The penetration of the virus
- The release of the genome from the capsid
- The multiplication of viral components
- The assembly of virus components
- The release of the progeny viruses

12.6 Pathogenesis

Viruses differ in terms of their entry into the body, their spread in the organism as well as the organ manifestations and reactions of the host. The amount of virus transferred or the pathogenicity, the virulence of the virus, and the susceptibility/resistance of the host largely determine the course of the infection. Apathogenic viruses do not cause disease. In the case of pathogenic viruses, depending on the amount of virus administered and/or the resistance situation of the host, there are also infection courses without disease symptoms. Such events are referred to as unapparent or subclinical infection. Infection with manifest disease, by contrast, is termed apparent or clinical.

Pathogenicity refers to the disease-causing properties of the virus.

Virulence refers to the degree of expression of the pathogenic properties of a virus.

12.6.1 Transmission Routes

The most common entry ports into the body are:

- Mucosal epithelia (of the respiratory tract, the gastrointestinal tract, and the genital tract)
- The conjunctiva of the eye
- The placenta
- The skin

12.6.2 Oral Versus Parenteral Transmission

Oral: Over the oropharynx and gastrointestinal tract, mostly fecal-oral transmission. Other carriers are saliva, urine, semen, cervical secretions, and breast milk.

Parenteral: The infection usually occurs via microtrauma and transmission of virus-containing blood (no oral intake).

The respiratory tract: Many viruses reach the mucous membranes of the nose, mouth, and throat by droplet infection and multiply in the upper and lower respiratory tract. The excretion and retransmission take place by aerosol formation during speech, sneezing, and coughing.

The gastrointestinal tract: Acid-stable viruses can enter the gastrointestinal tract via smear infection or contaminated food. The excretion takes place via the stool; this allows the fecal-oral transmission.

The urogenital tract: Some viruses prefer venereal transmission. Here, the genital mucosa serves as a portal of entry.

The skin: The intact skin is impenetrable to viruses. But the smallest skin lesions and microtraumas form a suitable portal of entry. Another possibility is the direct inoculation through the intact or injured skin. Examples include stings or bites of infected arthropods or the bite of a rabid animal and contaminated syringes in drug addicts and iatrogenic puncture wounds with contaminated cannulas or the transfusion of infectious blood products.

The placenta serves as the portal of entry for the intrauterine transmission from the mother to the child. Prerequisites for this are a maternal viremia and the ability of the virus to infect the placenta. In this case is transplacental infection.

12.6.3 Vertical Transfer From the Mother to the Child

Virus transmission is possible at different times of pregnancy. The time of infection is often critical to the consequences of infection and the extent of childhood harm.

Prenatal infection: The infection occurs before birth. Virus transmission is intrauterine, i.e., always transplacental. If there is an infection of the embryo during organogenesis, this can lead to a developmental disorder of the affected organs, called embryopathy.

Embryopathogenic viruses include rubella virus, parvovirus B19, and cytomegalovirus.

Perinatal infection: The infection occurs at the time of birth. Perinatal infections with herpes simplex virus, hepatitis B virus, or HIV require appropriate preventive measures.

12.6.4 Clinical Manifestation of the Infection

An infection does not necessarily lead to the full picture of a viral disease in all cases. It can lead to a mild or even no symptoms. A distinction is made between the apparent (clinical, symptomatic) infection with clinical symptoms and the unapparent (subclinical, asymptomatic) infection without disease symptoms. In measles and poxvirus infections, there are almost always classic signs of disease; Polio virus or herpesviruses plus infections are usually unapparent.

12.7 Antiviral Defense Mechanisms and Counterstrategies of the Viruses

12.7.1 Innate Unspecific Immunity

The unspecific response occurs as soon as the viruses have overcome the outer barriers. The defense mechanisms consist of:

- Phagocytosis
- Inactivation by the complement system
  - Activation of NK cells (natural killer cells)
- Non-specific fever reaction

12.7.2 Acquired Specific Immunity

Specific immune response is essential for the long-term control of a viral infection and the permanent elimination of the virus. Furthermore, it is essential for the protection against reinfections and a significant protection factor in the first months of life in the form of maternal antibodies. The goal of all vaccinations is to build up a specific immune system. This is the only reliable means to eradicate certain human pathogenic viruses worldwide.

Humoral immune response: Antibodies are especially important in acute infections. They block the spread of virus and, in most cases, the seeding into the end organs and ensure the elimination of the virus. The maternal antibodies transmitted via the placenta protect the newborn for months and are one of the reasons why the teething troubles occur later ("nest protection").

Cellular immune response: The cellular immune response is directed against virus-infected cells and causes their elimination by cytotoxic T cells. The sooner virus-producing cells are destroyed; the sooner chronic-persistent viral infections are avoided.

12.8 Prevention and Eradication

The most important prophylactic measure is vaccination, which provides both effective individual protection and collective protection through control and prevention of epidemics. A distinction is made between active and passive immunization. For the prevention of viral infections, exposure prevention (such as isolation, quarantine, disinfection, sterilization, etc.) and chemoprophylaxis with antiviral drugs are required in special cases.

Specific Virology: Viruses as Diseases

13

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13.1 Historical Overview of the Development of Virology

1796: Jenner transfers cowpox material from a milkmaid to a boy and shows evidence of immunity generated by re-vaccination with virulent pox material.

1885: With the development of a rabies vaccine and the implementation of the first vaccination in a person at risk, Pasteur founds rabies research.

1892: Ivanovsky notes the transferability of tobacco mosaic disease by the bacteria-free filtrate from pressed juices of infested leaves.

1956: Crick and Watson come to the conclusion by evaluating the X-ray structure of analytical studies and by theoretical considerations that in smaller viruses the nucleic acid is surrounded by regularly arranged protein subunits. This starts the research into the fine structure of viruses.

Discovery of New Viruses

- 1965: Hepatitis B-virus
- 1981: Parvovirus B19
- 1983: HIV-I, HHV-6/7
- 1988: Hepatitis C-virus

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_13

- 1993: Herpes virus Typ 8
- 2003: SARS-coronavirus
- 2012: MERS-coronavirus

13.2 Adenoviruses

- No enveloped DNA virus
- 51 human-pathogenic serotypes
- High environmental resistance

Path of infection: transmission by droplets or smear infection in the water or instruments.

Incubation period: varies from a few days to 10 days.

Clinical manifestation: Adenoviruses can infect the epithelial cells of the oropharynx, respiratory, gastrointestinal tract and eye. The infection is often asymptomatic or with mild symptoms.

The various human-pathogenic serotypes cause numerous diseases which mainly affect the respiratory tract ("influenza infection"), the eye (conjunctivitis) or the gastrointestinal tract (diarrhoea). Respiratory tract infections: a noteworthy part of all "colds" of infants is caused by adenoviruses. Young adults can develop from respiratory infections to life-threatening pneumonia. School-age children may experience febrile pharyngitis and conjunctivitis as part of pharyngoconjunctival fever.

Eye infections: Acute follicular conjunctivitis (so-called swimming pool conjunctivitis), there is a one-sided, often painful reddening of the eye on both sides and periauricular swelling of the lymph nodes. Inadequate quality of the pool water or inadequate sterilization or disinfection of instruments during ophthalmological activities may lead to transmission of adenoviruses.

Intestinal infections: Pronounced diarrhoea. In infants, adenoviruses are the second leading cause of diarrhoea after rotaviruses.

Other infections: Infections of the urogenital tract (acute haemorrhagic cystitis), less commonly intestinal invaginations and meningoencephalitis.

13.3 Parvoviruses: Parvovirus B19

No enveloped DNA virus

Path of transmission: Infected respiratory droplets.

Pathogenesis and clinical presentation: The virus damages the erythroblasts, and there is a drop in reticulocytes along with transient anaemia. In childhood, erythema infectiosum generally referred to as the "fifth disease", pertaining to the five major exanthematous childhood diseases: scarlet fever, measles, rubella and exanthema subitum. Parvovirus is characterized by a rash which begins classically on the face ("slapped cheek syndrome") and spreads on the extensor sides of the extremities in a ring-shaped pattern.

Delayed complications: Arthritis and arthralgia.

Parvovirus B19 in pregnancy: Can cause intrauterine infection in about 20% of cases. In early pregnancy, this can lead to spontaneous abortion of the foetus. In the second and third trimester, there is a hydrops fetalis, which, if left untreated, usually leads to the death of the foetus. Hydrops fetalis characteristically presents with pronounced cerebral oedema and soft tissue oedema, ascites and maceration of the foetus due to the severe oxygen deficiency of the tissue due to virus-induced anaemia.

Prophylaxis and treatment: Exposure prophylaxis for pregnant women (it should be noted that the exanthematous stage rarely poses a risk of infection). There is no specific antiviral therapy. In the case of exposure to the virus during pregnancy, maternal serostatus (immunity) should be ascertained. In the case of suspected transplacental infection, detection of the virus in maternal blood/serum as well as in umbilical cord blood, amniotic fluid or in chorion biopsy material should be considered.

13.4 Enteroviruses

- No enveloped RNA viruses
- Part of the enterovirus group:
  - Poliovirus type 1–3
  - Coxsackie virus A and B
  - Echovirus
  - Human enterovirus
- High environmental resistance
- Transmission faecally–orally
- Massive viral shedding through asymptomatic but infectious persons

Increased incidence in the summer months; also referred to as "summer flu". Most enterovirus infections are asymptomatic or with the nonspecific clinical presentation of a flu infection.

Typical Clinical Manifestations of Enterovirus Infections

Pathogenesis: Enteroviruses multiply after ingestion first in the local tissue of the nasopharynx and later in the intestine. The viruses reach the target organs either via the bloodstream (viremia) or via neural spread. However, only in a very small percentage does organ manifestation occur with the above clinical signs (see Table 13.1).

Clinical Presentation

Poliovirus: The spinal form of poliomyelitis causes irreversible flaccid paralysis of the limb musculature, the chest muscles or the diaphragm, and thus poses a risk for suffocation. The bulbar form of poliomyelitis causes disruption of the respiratory and circulatory centre. There is also an encephalitic form which, like the bulbar form, can quickly lead to death. Infections in pregnant women acquired shortly before birth can be transmitted to the child and lead to sepsis-like illnesses of the new-born.

Table 13.1 Clinical manifestations of enterovirus infections

Viruses	Clinical manifestations
All enteroviruses	Fever, head and joint aches ("summer flu")
Poliovirus	Paralysis, myelitis, meningitis, encephalitis
Coxsackie-A-viruses[a]	Respiratory diseases, pneumonia (infants), herpangina (toddlers), hand-foot-mouth illness, gingivostomatitis, myocarditis, haemorrhagic conjunctivitis, exanthema
Coxsackie-B-viruses[a]	Diarrhoea, myocarditis, pericarditis
ECHO-viruses[a]	Maculopapular rash, myocarditis, gastroenteritis
Other enteroviruses[a]	Bronchiolitis, pneumonia, hand-foot-mouth illness, haemorrhagic conjunctivitis

[a]All enteroviruses have the ability to cause polio-like symptoms (meningitis, meningoencephalitis, paralysis)

Coxsackie-A-viruses: Causes herpangina especially in infants, which manifests itself by the formation of painful small blisters on the oral mucosa, high fever and loss of appetite. The hand-foot-mouth disease, which is also caused by Coxsackie A viruses, causes blisters on the hands, feet and in the mouth.

Coxsackie-B-viruses: Cause myositis of the abdominal and chest muscles with a dry pleurisy (breathing extremely painful).

Enteroviruses: Often cause of aseptic (abacterial) meningitis, and often cause more or less discrete rashes.

Prophylaxis: Prophylaxis of poliomyelitis through active immunization.

Parenteral vaccine by inactivated polio viruses according to Salk, which contains inactivated polioviruses of all three serotypes. Primary immunization should be done in infancy. Booster vaccinations should be in accordance with the Austrian vaccination plan. Sabin's oral polio vaccine, which is no longer available in Austria, contains attenuated, replicable viruses of all three types.

All other enteroviruses: Prophylaxis consists of hygienic measures.

13.5 Hepatitis A Virus

- No enveloped RNA virus
- Transmission: Faecally–orally

This virus is extremely stable against heat and other environmental factors. The virus can enter the food chain through fertilization of crops with faecal matter or through contaminated wastewater, which can lead to an accumulation in mussels and oysters and play a role in outbreaks. Hepatitis A virus is endemic in countries with poor hygienic conditions.

Incubation period: 2–6 weeks.

Pathogenesis and clinical presentation: The hepatitis A virus enters the gastrointestinal tract through smear infection or through contaminated food/drinking water and reaches the liver via the bloodstream.

In children: Over 90% of cases manifest subclinically.

In adulthood: In 70–80% of cases acute hepatitis occurs (loss of appetite, fatigue, fever, vomiting, diarrhoea, bilirubinuria and jaundice).

There are no chronic courses. There is low lethality (in children about 1%, in adults about 5%).

Diagnosis: Hepatitis A antibody detection in serum, detection of virus antigen from stool, detection of the viral RNA genome by PCR in serum or stool.

Prophylaxis: Active vaccination with an attenuated vaccine (2 doses in separate intervals of at least 4 weeks) provides long-term protection. Vaccination is recommended for people working in health care, day care, kitchens as well as sewerage and sewage treatment workers and travelers in endemic areas.

13.6 Human Rhinovirus

- No enveloped RNA virus
- Transmission: Through droplet or smear infection directly from person to person
- Incubation period: 1–4 days
- Over 100 serotypes
- Propagation in the mucous membranes of the nasopharynx

Clinical presentation: Runny nose with sneezing, coughing and watery to mucous secretion discharge. Disease duration is usually 1 week.

13.7 Rotavirus

- No enveloped RNA virus
- High environmental resistance
- Transmission: Faecally–orally
- Most common pathogen of diarrhoea in children!

Clinical presentation: After an incubation period of 2–3 days, patients present with watery diarrhoea, vomiting and fever for about 4–7 days. Humans excrete the viruses over a period of up to 14 days!

Diagnosis: Antigen detection in stool.

Prophylaxis: Oral vaccination from the sixth week of age, depending on the vaccine will be given 2 or 3 doses with a minimum interval of 4 weeks.

13.8 Herpes Viruses

- Herpes simplex virus 1&2
- Varicella-zoster virus (VZV)
- Human cytomegalo virus (CMV)
- Epstein–Barr virus (EBV)
- Human herpes virus 6–8

General
- Enveloped DNA virus
- Herpes viruses are widespread in humans and animals
- Persist lifelong in the infected host
- After initial infection, the virus genome remains in the body for life (latent infection)
- Latency is periodically interrupted by reactivation and viral regeneration
- The frequency and duration of virus reactivation depends on the type of herpes virus, the latent site and the immune status

13.8.1 Herpes Simplex Virus Type 1 (Herpes Labialis)

Primary infection usually occurs in infancy and is predominantly asymptomatic; it rarely manifests as stomatitis aphthosa (= oral blight).

Acute herpetic gingivostomatitis: painful clinical picture with fever, lymphadenopathy and ulcerative lesions of the oral mucosa, tongue and lips, occurring in about 1% of primary infections.

In the course of the asymptomatic or symptomatic primary infection, neuronal spread occurs via the axons and latent infection of the neurons of the trigeminal nerve. During the later reactivation, infectious virions reappear in the area of the nerve endings, resulting in cold sores near the original site of infection (herpes labialis). The blister content is an important source of new infections.

13.8.2 Herpes Simplex Virus Type 2 (Herpes Genitalis)

Path of infection: The transmission takes place through sexual contacts; the primary infection usually takes place in adolescence or adulthood.

Clinical manifestation: Blistering and small ulcers occur in the male genital area and in the area of the vulva and vagina in women, occasionally also perianal and rectally. In herpes simplex virus–type 2 lifelong latent in the lumbosacral ganglia and upon reactivation presents as genital herpes.

Complications: Herpes simplex virus encephalitis can occur both at primary infection and at reactivation.

- *Keratoconjunctivitis herpetica*: Primarily an inflammation of the cornea of the eye (keratitis) and possibly also the conjunctiva (keratoconjunctivitis) by herpes simplex infection. Herpes simplex virus 1 (HSV-1) is predominantly the causative agent, rarely HSV-2. Recurrence can lead to irreversible scarring.
- *Eczema herpeticatum*: In atopic dermatitis or chronic eczema, pre-damaged (and thus particularly virus-sensitive) skin can present with extensive blistering.
- *Herpes neonatorum*: It is especially problematic when a woman's first contact with herpes simplex virus type 2 occurs during pregnancy, since it increases the risk of a perinatal infection of the new-born child with herpes neonatorum. Since there are no maternal antibodies yet in a primary infection, the virus can spread particularly well in the immature new-born. Infections of the new-born can range from local infections of the skin and mucous membranes to generalized infection involving the internal organs and the CNS. Most of the therapy comes too late to prevent a fatal outcome. If genital herpes is suspected, delivery by caesarean section is indicated.

  However, if the pregnant woman experiences recurrence of genital herpes at the time of birth, the child may become infected in the birth canal, but the maternal antibodies transferred by the placenta prevent subsequent viremia. Nevertheless, neonatal encephalitis with a high lethality may occur.

Varicella Zoster Virus

Path of infection: The virus is transmitted aerogenically via droplets of blister fluid and leads to a lifelong persistence. Since the virus is highly contagious, already a short-term stay in a room in which a varicella patient is exposed is sufficient for disease transmission. Contagiousness begins 1–2 days before the onset of the rash and ends 5–7 days after the onset of last rashes. Herpes zoster sufferers are contagious until the encrustation of the blisters (smear infection).

Clinical Symptoms

The varicella zoster virus causes two different clinical pictures:

Varicella (chicken pox) during initial infection and herpes zoster (shingles) in a reactivation.

Varicella: After an uncharacteristic prodromal stage (1–2 days before onset of illness), the disease begins with itchy rash and fever for a period of 3–5 days. The skin lesions consist of poplars, vesicles and scabs at various stages of development ("starry sky"). The lesions may quickly develop into blisters that appear first on the trunk and face and can spread rapidly to other parts of the body, including the mucous membranes and hairy scalp. Varicella usually has a benign course in healthy individuals and usually heals without scarring. However, severe scratching or bacterial superinfections can cause scarring. New-borns and immunocompromised individuals may experience severe haemorrhagic disease progression, often with a fatal outcome.

Complications
- Bacterial superinfection mostly caused by *Streptococcus pyogenes* or *Staphylococcus aureus*
- Varicella pneumonia
- CNS manifestation

In isolated cases myocarditis, corneal lesions, nephritis, arthritis, bleeding tendencies, acute glomerulonephritis and hepatitis.

Foetal Varicella Syndrome
If varicella occurs in the first and second trimesters of pregnancy, there may be a foetal varicella syndrome characterized by segmental skin lesions (ulcers, scars), neurological disorders and malformations (atrophy of the brain, paresis, seizures), eye damage and skeletal abnormalities.

Severe neonatal chickenpox: May result from a primary infection of the susceptible mother within 5 days of birth or up to 48 h thereafter. Since the new-born has an immature immune system and in these cases no protective is among new-borns who contract varicella between the fifth and 12th day of life.

Herpes Zoster
Herpes zoster is not an exogenous new infection, but an endogenous recurrence. The virus can only reactivate in people with a prior varicella zoster virus infection. The virus persists in the spinal or cranial nerve ganglia and can eventually lead to a reactivation in the form of herpes zoster. It occurs predominantly in immunocompromised or elderly persons. Herpes zoster is characterized by a unilateral vesicular eruption that is limited to a dermatome with sometimes very severe pain. Infestation of the trigeminal nerve (ophthalmic nerve) leads to the zoster ophthalmicus. Furthermore it can exhibit in the form of zoster oticus, zoster maxillaris or zoster genitalis.

Preventive measures: A varicella vaccine is available from the age of 2, two vaccinations are given at intervals of at least 4 weeks. It is also recommended to vaccinate unvaccinated 9–17-year-olds without varicella history, as the disease is associated with a higher complication rate.

Post-exposure prophylaxis by passive immunization with varicella zoster immunoglobulin is recommended within 96 h of exposure (face to face contact or household contact) for persons at increased risk of varicella complications. This group includes unvaccinated pregnant women without varicella history, immunodeficient patients with unknown or missing varicella immunity, new-borns whose mothers have varicella 5 days before to 2 days after confinement.

Remember
- *Primary infection of the mother with varicella zoster virus*: Viremia → dangerous for the child!
- *Endogenous reactivation (herpes zoster)*: No viremia → safe for the child!

13.8.3 Cytomegalovirus (CMV)

CMV exclusively infects human cells and proliferates slowly.

After primary infection, the CMV virus persists for life in latent form in various cells and organs and often reactivates. Both primary infection and reactivation are usually asymptomatic. However, it can lead to severe disease courses under immunosuppression. CMV infection remains one of the most important prenatal viral infections (congenital disease).

Infection

Since the virus may be present in tear fluid, saliva, urine, genital secretions as well as breast milk and blood, possible transmission upon contact with infectious bodily fluids, e.g., by breastfeeding, kissing, sexual contacts, but also by blood products and organ transplants is possible. During lactation, CMV is excreted by almost all seropositive women with milk and passes to the children at a rate of about 35%.

Mostly, oral transmission is by saliva or other bodily fluids (urine, breast milk, cervical secretions, seminal fluid). Sexual contacts are another important source of infection. Other important transmission pathways are the prenatal or perinatal infection from the mother to the child.

Clinical Manifestation and Pathogenesis

In immunocompetent individuals, CMV infection is usually asymptomatic or has nonspecific symptoms (such as flu-like respiratory symptoms, fatigue, fever, cough). Even women who become infected with CMV during pregnancy have the majority (about 75%) no symptoms.

Complications may occur especially in new-borns or those with congenital or acquired immunodeficiency, as well as immunosuppressive therapy, in which the infection can damage many organ systems. These include in particular the lungs with the risk of developing pneumonia, the liver, the intestine and the eye, which can lead to retinal infection (retinitis) with blindness.

In new-borns that have been infected in utero, growth delays and especially hearing damage may occur, also often late neurological damage is observed.

Prenatal infection: In the first infection of pregnant women with high viremia, the virus is transmitted diaplacentally in about 40–50% of cases. In about 5–10% of cases there is a clinical manifestation.

For Clinical Manifestations

Cerebral damage (microcephaly, hearing loss, optic atrophy, seizures, spasticity or motor disorders), hepatosplenomegaly with jaundice, haemorrhage, haemolytic, anaemia Interstitial pneumonia, in the worst case intrauterine foetal death.

Perinatal infection: Infection occurs either at birth or through breast milk. The perinatal infection of the new-born usually proceeds subclinically with occasional long-term consequences such as hearing disorders or behavioural problems. Premature babies are very at risk and must be protected by exposure prophylaxis.

Postnatal infection: It is usually subclinical in children and often mild in adults. In most cases, a long-term fever (status febrilis) occasionally shows a similar mononucleosis with involvement of the liver.

Complications occur mainly in immunocompromised individuals (pneumonia, retinitis, nephritis, encephalitis) and in prenatal infections.

13.8.4 Epstein–Barr Virus (EBV)

Path of infection: Transmission is mainly via saliva.

EBV affects the lymphocytes which are stimulated for proliferation. The EBV primary infection therefore leads to lympho-proliferation which cannot be controlled by immunosuppression or genetic immune deficiencies. Burkitt's lymphoma and part of Hodgkin's lymphoma are EBV-associated B-cell lymphomas. Worldwide, about 90–95% of the adult population is infected.

Clinic and pathogenesis: As the virus is transmitted mainly in the saliva, the primary infection usually occurs in early childhood and is usually asymptomatic. In older children and young adults, it often comes to the clinical picture of infectious mononucleosis (Pfeiffer's glandular fever, kissing disease). Infectious mononucleosis is characterized by fever, swelling of the lymph nodes, hepatosplenomegaly, white matter tonsillitis, and in some cases maculopapular rash of the skin occurs, especially after the administration of certain antibiotics.

13.8.5 Human Herpes Viruses 6, 7 Und 8

13.8.5.1 Human Herpes Virus 6

The virus is widespread and transmitted by saliva in early infancy. The prevalence rate for the 3-year-olds is already up to 95%. HHV-6 is the causative agent of the exanthema subitum (roseola infantum, 3-day fever).

Clinic: Primary infection in infancy usually remains asymptomatic. In infancy, exanthema subitum (3-day fever) may occur after an incubation period of 5–15 days. Classically, there is an abrupt increase in fever to 40–41 °C with febrile convulsions and a rapid defilement after 3 days. Afterwards a fleeting rash appears.

Complications: Rarely, meningitis, encephalitis, hepatitis severe events occur especially in immunosuppression in organ or bone transplant patients.

13.8.5.2 Human Herpes Virus 7

Like the HHV-6, it is widespread and transmitted by saliva. Primary infection of infants occurs somewhat later than with HVV-6 and may occasionally go below the exanthema subitum picture. Both initial infection and reactivation in immunosuppression are usually asymptomatic.

13.8.5.3 Human Herpes Virus 8

Transmission occurs probably through saliva and sexually. Participation in the development of Kaposi's sarcoma and other lymphomas in serous body cavities (pleura, pericardium, peritoneal cavity) is considered a definitive diagnosis.

13.9 Influenza Viruses

These are enveloped RNA viruses. Pathogens of influenza are orthomyxoviruses which are subdivided into types A, B and C. Especially relevant to humans are influenza A and B viruses. Influenza C viruses are virtually meaningless and cause only mild childhood disease.

Influenza A and B viruses are characterized by spike-like surface structures formed by the surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA). There are 16 different HA and 9 NA known. Influenza A viruses are named by type and subtype, e.g., A (H1N1). There are no subtypes of influenza B, but in recent years there are two genetically distinct lines circulating worldwide (Yamagata line and Victoria line).

Reservoir: Influenza A viruses occur in humans and in addition also in mammals (for example, pigs, horses). Influenza B viruses only occur in humans. The actual reservoir of influenza A viruses are birds, especially waterfowl, in which all previously known subtypes could be detected. A distinction is made between avian influenza viruses (which occur in birds) and human ones (which circulate in the human population) differ in that they bind very specifically to different receptors in the upper respiratory tract of humans and birds, whereas in the respiratory tract of the pig receptors for both human and avian influenza viruses.

Mutations and Antigen Drift, Reassortment and Antigen Shift
On the one hand, the great genetic variability of the influenza viruses is based on the fact that the eight gene segments are freely combinable and, on the other, on the high mutation rate. Point mutations lead to antigenic drift (antigenic shift). If the surface antigens HA and NA, which are important for the immune response, are affected by point mutation, the viruses are poorly or no longer recognized by the antibodies present. Since there is only a long-lasting immunity against viruses with a very high genetic relationship, the continuously occurring drift variants can cause annual flu outbreaks. Therefore, every year for all vaccine antigens must be checked whether they differ from the previous viruses and vaccinations must be adapted to the drift variant.

In contrast, antigen shift results in a complete replacement of an entire HA or NA genome segment by reassortment. The antigen shift leads to a complete re-equipment of the surface of the virus with hemagglutinin and/or new neuraminidase molecules, against which surface molecules there is no immunity in the population.

Occurrence: Influenza virus infections are common worldwide. In the temperate zones of the northern and southern hemisphere, influenza waves occur regularly in the respective winters. Due to the seasons set by 6 months, the winter influenza wave in the southern hemisphere occurs when summer is in the northern hemisphere and vice versa. It can also occur out of season flu outbreaks.

Transmission: Influenza viruses are transmitted by droplet infection (cough or sneezing) and smear infections (hands). The viruses multiply locally in the epithelial cells of the upper and lower respiratory tract lead to a direct damage to the infected cells. The destruction of the cells causes a strong inflammatory reaction as a result of which bacterial superinfections (for example, with *Staphylococcus aureus*, *Streptococcus pneumoniae* or *Haemophilus influenzae*) can occur.

Incubation Period: 1–2 Days
Duration of contagiousness: On average about 4–5 days from the onset of the first symptoms. A longer duration is possible, e.g., in children, persons with chronic pre-existing conditions. From a pragmatic point of view, individuals with influenza are recommended to be isolated for 7 days.

Clinical manifestation: The typical influenza symptoms are characterized by:

- Sudden onset of illness with fever (≥38.5 °C)
- Dry, irritating cough
- Sore throat
- Muscle and/or headache
- Other symptoms may include: General weakness, sweats, nausea, vomiting and diarrhoea

It should be noted, however, that not all affected influenza patients experience the above symptoms. Roughly speaking, one-third of infections lead to a febrile manifestation, one-third to mild and the last third to asymptomatic clinical presentation.

Complications
Rarely, severe courses occur, with pulmonary complications (pneumonia!) In the foreground. If other organs are involved, myositis, rhabdomyolysis, encephalitis, myocarditis may occur. In children, complications of the CNS were also observed.

Diagnosis
Gold standard is the genome detection by means of PCR from nasal or throat swab, bronchial lavage. Furthermore, rapid tests for the direct virus antigen detection from nose/throat material are available. But with a lower specificity and sensitivity than the PCR virus isolation by culture is usually reserved for specialized laboratories. Further methods for the detection of viral antigens are the immunofluorescence and ELISA test which are comparable in their sensitivity with the fast text.

Therapy
Nowadays almost exclusively neuraminidase inhibitors are used therapeutically. They are active against both influenza A and influenza B viruses.

Prophylaxis
Vaccination–Recommended is the annual active immunization using the dead vaccine prior to the influenza season in the fall. Target group for vaccinations: persons over 60 years, pregnant women and women who want to become pregnant during the influenza season, children from the age of 6 months, all persons with increased risk as a result of chronic diseases (chronic lung, heart and circulatory diseases, kidney disease, neurological diseases, metabolic diseases and immune deficiencies), caregivers (e.g. in hospitals, nursing homes) and household contacts of risk groups, in particular persons from health professions.

Parainfluenza Virus
Enveloped RNA virus.

Four serotypes – Type 1–4, Type 1–3 are distributed worldwide, Type 4 mainly in the Americas.

Transmission: By droplet infection and direct contact.

Incubation period: 3–5 days.

Clinic: The viruses lead to a strong inflammation and swelling of the mucous membranes and trigger flu-like symptoms. Feared are severe cases, which occur more frequently in infancy, resulting in acute laryngotracheobronchitis with inspiratory stridor, barking cough, hoarseness and dyspnoea (pseudo-krupp). In infants, the descending infection can lead to bronchiolitis and pneumonia. Serious diseases occur in highly immunosuppressed patients (bone marrow transplantation).

Diagnostics: Serological procedures (seroconversion or a significant title increase in paired sera), virus isolation or PCR or immunofluorescence.

Prophylaxis and therapy: Currently none available. Treatment is based on symptomatic measures.

Respiratory-Syncytial Virus (RSV)
The enveloped RNA virus belongs to the family Paramyxoviruses.

Transmission occurs through droplet infection as well as smear infection (contaminated objects).

Clinical manifestation: The RS virus causes respiratory infections in infants and toddlers, which occur seasonally—often in late autumn and winter. RSV is the main agent of bronchiolitis in infants in the first months of life. Since it is highly contagious, it is often the cause of healthcare-associated infections in children's hospitals and preterm stations. The likelihood of contact with the virus in the first months of life is already very high. There are also reinfections possible. Particularly at risk are infants in the first months of life, as well as older infants and toddlers with pre-existing conditions (congenital heart defects cystic fibrosis, bronchial asthma).

Serious infections also occur in older persons with pre-existing conditions as well as in immunosuppressed patients. These patients can often cause fatal pneumonia. Often the virus also leads to a middle ear infection which can be superinfected bacterially.

Diagnosis: The virus can be detected by virus culture, PCR or direct immunofluorescence.

13.10 Mumps Virus

The enveloped RNA virus belongs to the family Paramyxoviruses and occurs only in humans.

Transmission: Aerogen by droplet infection and direct salivary contact, rarely by saliva-contaminated objects.

Incubation period: 16–18 days.

Duration of infectiousness: The infectious is greatest 2 days before to 4 days after onset of disease. Overall, an infected person may be contagious 7 days before to 9 days after the occurrence of parotid gland swelling. Clinically unapparent infections are also contagious.

Clinical manifestations: Mumps (Parotitis epidemica) is a systemic infectious disease and can occur at any age. A disease usually leads to lifelong immunity.

The mumps disease is typically characterized by a painful one-sided (20–30%) or double-sided (70–80%) inflammatory swelling of the parotid, lasting about 3–8 days. In up to 15% of cases, involvement of the submandibular or sublingual salivary glands is observed. The infection may be preceded by a multi-day prodromal stage with fever, headache, malaise, myalgia and loss of appetite. In children under 2 years of age, the majority of mumps infections are subclinical. In children under 5 years, the mumps infection often presents as an acute respiratory disease (up to 50% of cases). At least 30–40% of infections are clinically unapparent or subclinical.

In the context of the disease various complications can occur that become more common with age.

Complications include:

- CNS involvement (e.g. encephalitis, meningitis)
- Deafness
- Orchitis, which can lead to sterility in the adult male
- Mastitis
- Pancreatitis
- Nephritis
- Myocarditis

Diagnostics: Diagnosis is frequently done based on the typical clinical manifestation of parotic gland swelling. For a more reliable diagnosis serology and PCR are available.

Therapy: There is no specific antiviral therapy for mumps. The therapy is exclusively symptomatic.

Prophylaxis: A live vaccination (measles, mumps, rubella) is available. From the age of 10, all children should be vaccinated against mumps, measles and rubella with two vaccinations at least 4 weeks apart.

Measles Virus

The enveloped RNA virus belongs to the family Paramyxoviruses. The virus is extremely environmentally unstable (very sensitive to external influences such as elevated temperature, light and disinfectants). The measles virus is distributed worldwide, the natural reservoir are humans.

Pathway of infection: Measles is one of the most infectious diseases transmitted by inhalation of infectious droplets (talking, coughing, sneezing) – airborne transmission – as well as by contact with infectious secretions from the nose or throat. Already on short exposure the measles virus leads to an infection (contagion index

near 100%) and triggers clinical symptoms in more than 95% of the unprotected infected persons.

Incubation period: 8–10 days to the onset of the catarrhal stage, 14 days to the onset of the rash.

Duration of contagiousness: 3–5 days prior to the onset of the rash until 4 days after the appearance of the rash. Infectiousness is greatest immediately before the appearance of the rash.

Clinical manifestation: Measles is a systemic viral infection with a biphasic course. It starts with fever, conjunctivitis, runny nose, cough and an enanthema on the oral mucosa. These so-called Koplik spots (lime-like white to blue–white spots) are typical of measles. Measles maculopapular exanthema (brownish–pink confluent patches) is between the third and seventh day after the onset of the initial symptoms. Classically, it starts in the face and behind the ears and persists for about 4–7 days. When decaying, a bran-like scaling is often observed. The temperature drop occurs between the fifth and seventh day of illness. A measles disease leaves a lifelong immunity.

Complications: Infection with measles causes a transitory immunodeficiency for about 6 weeks. As a consequence, there is a temporary increase in susceptibility to bacterial superinfections (measles-associated otitis media, bronchitis, pneumonia and diarrhoea are common). In about 0.1% of cases, there is dreaded post-infective encephalitis. With disturbance of consciousness up to the coma which ends fatally in about 10–20% of the affected cases, about 20–30% must count on residual damage to the CNS.

Subacute sclerosing panencephalitis (SSPE) is a very rare late complication that manifests on average 6–8 years after infection. On average, there are 4–11 SSPE cases per 100,000 measles diseases. Children under 5 years old are at significantly higher risk. SSPE begins with mental and intellectual changes, develops a progressive course with neurological disorders and deficits to the loss of cerebral functions and ends always lethal.

In immunosuppressed patients often develop severe organ complications which end fatally in 30% of cases.

In developed countries, the lethality of measles is between 0.05% and 0.1%, according to the WHO. In the so-called developing countries lethality in some countries is up to 6%.

Diagnostics: Laboratory diagnostics is essential for the reliable detection of measles disease. Serological methods (ELISA, HHT) for the detection of IGM and IGG antibodies are available. Furthermore, a virus genome detection by PCR from urine or throat swab is possible.

Therapy: There is no specific antiviral therapy, only symptomatic therapy is possible.

Prophylaxis: The most effective preventive measure is the live vaccination against measles. A vaccination is possible from the 10th month of age with the measles-mumps-rubella vaccine. Two vaccinations should be administered at least 4 weeks apart.

13.11 Rubella Virus

It is an enveloped RNA virus of the togavirus family. Man is currently the only known host. The rubella virus is distributed worldwide.

Transmission route: Aerogenic by droplet infection. The virus invades the mucous membrane of the upper respiratory tract and subsequently leads to pronounced viremia with the possibility of diaplacental transmission in pregnancy.

Incubation period: 14–21 days.

Duration of contagiousness: It lasts 1 week prior to the onset of the rash and lasts up to 1 week after the appearance of the rash.

Clinical manifestation: In about 50% of infections, the disease is asymptomatic in childhood. The disease is characterized by a small speckled maculo- or maculopapular rash which begins on the face and subsequently spreads over the body and extremities and disappears after 1–3 days. Other symptoms may include subfebrile temperatures, headache, lymphadenopathy (often nuchal and retroauricular), mild upper airway catarrh and conjunctivitis. Rarely, complications often occur with increasing age (arthritis, bronchitis, otitis, encephalitis, myocarditis). Thrombocytopenia can cause purpura and haemorrhage.

Rubella infection during pregnancy (Congenital Rubella Syndrome): While postnatal rubella infection is rarely associated with complications, infection of the developing foetus through the mother's placenta causes severe damage. The frequency and severity are dependent on the time of infection in infections.

In the first 8 weeks of pregnancy, in 90% of the cases of infection during the second trimester, in 20–35% of cases, damage is observed. Primary infection in the first 4 months of pregnancy may result in spontaneous abortion, premature birth or GREGG's triad with defects in the heart (open ductus arteriosus), eyes (cataract) and ears (inner ear deafness). Other possible consequences include lower birth weight, thrombocytopenic purpura, hepatosplenomegaly, encephalitis, hepatitis, myocarditis or microcephaly. While infection of the foetus in the fourth week of gestation may trigger the full picture of the disease, e.g., infection in the 20th week may lead to isolated deafness.

Diagnostics: Detection of virus specific IgM antibodies, e.g., by ELISA. For prenatal diagnosis, a PCR is also available to detect the virus from chorionic biopsy material or amniotic fluid.

Therapy: A specific causal therapy does not exist.

Prophylaxis: Live vaccination see Measles, in addition, unvaccinated women or women with unclear vaccination status of childbearing age should be vaccinated. It is also recommended to vaccinate unvaccinated staff or people with unclear vaccination status in paediatrics, obstetrics, pregnancy care and community facilities.

13.12 Rabies Virus

Rabies is a zoonotic disease and is transmitted by an enveloped RNA virus, family of rhabdoviruses. Rabies is common in much of the world.

Reservoir: Wild animals (foxes, badgers, martens, deer) and domestic animals (cattle, sheep, goats, horses) as well as dogs and cats. Furthermore, bats are an important reservoir. Dogs and cats play an important role as human exposition animals.

Transmission routes: After the infection of the animal, at the end of the incubation period, virus replication occurs in the CNS, where it spreads to the pathogens, whereby the virus is excreted en masse in the saliva. The transmission to humans usually takes place through inoculation via a bite. However, transmission is also possible via skin injury or direct contact with infectious material (e.g. saliva) with the mucosa.

Incubation period: Usually 3–8 weeks, less often shorter than 9 days; in individual cases up to several years. The time to onset of clinical symptoms depends on the location of the bite site. Nearer CNS entry portals describe shorter incubation times. Duration of contagiousness in foxes, dogs and cats are usually 3–7 days before onset of clinical symptoms, as well as throughout the duration of the disease.

Clinical manifestation: The clinic divides into the following stages in humans:

Prodromal stage presents with characteristic discomfort, e.g., headache, loss of appetite, occasional fever. Furthermore, burning, itching and increased pain sensitivity in the area of the bite wound were reported.

Acute neurological phase and encephalitic form: Cerebral dysfunction, further there is a pronounced hydrophobicity. When swallowing, there are spasms of the pharyngeal muscles causing a considerable fear of drinking and the saliva flows out of the mouth. Even the visual or acoustic perception of water leads to restlessness and cramps that can spread to the entire musculature. Furthermore, there are alternating switches between aggressive and depressive moods.

Paralytic form: Increasing onset of paralysis, especially of the cranial nerves.

Coma: In coma and under the signs of respiratory paralysis, death occurs. Usually it takes 7 days between the onset of the first symptoms and the death of untreated patients.

Diagnosis: Suspicion arises first of all from the onset clinical symptoms and a thorough medical history. The antigen or rabies virus detection in epithelial cells of the cornea, in neck skin biopsies, in serum or in cerebrospinal fluid can be tried, but not infrequently it leads to false negative results. Confirmation of the clinical suspected diagnosis will be successful only post-mortem by immunofluorescence from samples of cerebellum and the brainstem.

Preventive action: Pre-exposure immunization by means of rabies vaccination on days 0, 7, 21.

Post-exposure measures: The contaminated wound should be immediately and extensively cleaned with water and soap solution (washing out of the pathogen). Furthermore, active and passive immunization against rabies should be performed by vaccination (on days 0, 3, 7, 14, 28) and administration of rabies immunoglobulin.

Gastroenteritis: Gastrointestinal Infections

14

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(Colloquially referred to as stomach flu)

Generally referred to as an inflammatory disease of the gastrointestinal tract, gastroenteritis is usually associated with vomiting and diarrhoea and has nothing to do with the "real flu" (influenza). Gastroenteritis of various causes is the most common cause of diarrhoea and nausea in children and adults. As a rule, symptom-relieving measures such as oral rehydration therapy are sufficient for the treatment. Gastroenteritis is still a leading cause of child mortality, with up to 1.5 million deaths per year worldwide. The causes are manifold and range from infections to poisoning to physical causes. In most cases, however, bacteria or viruses are the cause of gastroenteritis. The microorganisms damage the mucous membranes of the digestive system either directly or indirectly by bacterial toxins. The transmission of gastroenteritis occurs via the faecal-oral route (faecal-oral smear infection).

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_14

Typical pathogens of gastroenteritis are:

Viral	Bacterial	Protozoa
Rotavirus, adenovirus, norovirus, astrovirus	*Campylobacter* *Salmonella* *Shigella* *Yersinia* *Clostridium difficile* *E. coli* *Vibrio cholerae*	Amoeba (*Entamoeba histolytica*) *Giardia lamblia*

Toxins Toxins (bacterial toxins) can accumulate in spoiled food and lead via intake of the respective foods to inflammation of the intestinal mucosa, and it manifests clinically as the classic picture of food poisoning. For example, botulism (canned goods), *Bacillus cereus* (e.g. rice, spices) and medication and other toxins can trigger toxic gastroenteritis.

Ionizing Radiation Ionizing radiation (X-rays, radioactive rays) in the context of a reactor accident or cancer treatment may cause damage to the lining of the gastrointestinal tract (radiation colitis).

Definition of Diarrhoea More than three liquid stools per day with stool weight of at least 250 grams.

Transmission Transmission occurs in most infectious gastroenteritis by a faecal-oral smear infection. The infectious stool usually contaminates food mostly through insufficiently cleaned hands and gets passed into the gastrointestinal tract of the next patient via the mouth. An exception is *Norovirus*. The transmission takes place both faecally-orally and by oral uptake of virus-containing droplets that arise in the context of case-like vomiting (droplet infection).

Incubation period: The incubation period depends on the pathogen usually 4 to 48 hours.

Symptoms The disease usually begins with anorexia, nausea and/or vomiting. Diarrhoea usually sets in after a few hours, and at this time the symptoms can already begin to subside again. Depending on the extent of mucosal damage, it can also lead to bloody diarrhoea. Increased bowel movements cause another spasmodic abdominal pain, and also fever is common. Dizziness and fatigue may also occur at this stage. Vomiting and diarrhoea can contribute to dehydration as a result of high fluid losses and impaired fluid absorption.

Complications Especially in infants, children and the elderly, the loss of fluids and electrolytes can lead to increased dehydration of the body with corresponding weight loss, which if left untreated can lead to circulatory problems (shock), kidney failure or seizures.

Prophylaxis Prophylaxis consists primarily of line hygienic measures in particular the hygienic preparation of food. Further, for babies from the age of 6 weeks, an oral vaccine is available.

Therapy In most cases, the therapy is limited to symptomatic measures, with treatment in the form of elimination of the cause is usually not possible. First and foremost is the therapy in which fluid and electrolyte losses are compensated. Ideally, this is done through a standardized oral solution (oral WHO rehydration solution). If that is not enough, the rehydration must be done by intravenous infusion. Antimicrobial therapy is not necessary in most cases.

14.1 Rotavirus

Rotaviruses are non-enveloped RNA viruses that are extremely resistant to environmental influences. In children, rotaviruses are the most common cause of viral intestinal infections. In the western industrialized nations, infants and children most often fall ill at the age of 6 months to 2 years due to the particularly high susceptibility based on the lack of immunity. A rotavirus-specific immunity is built up during the first years of life by repeated infections. Rotaviruses are the most common cause of healthcare-associated intestinal infections in new-born infants. It shows a seasonal frequency which is highest in the months of February to April.

Reservoir: The main reservoir for rotaviruses is humans.

Route of infection: Rotaviruses are transmitted faecally-orally through smear infections and contaminated water and food. The viruses are easily transmitted because already ten virus particles are enough to infect a child. Acute infected people in turn excrete enormous virus loads (109–1011 viruses per gram of stool), and patients with subclinical infections (especially new-borns and adults) play a key role as vectors.

Incubation period: 1–3 days

Duration of contagion: Contagiousness is highest during the acute stage of the disease and as long as the virus is excreted in the stool. Viral excretion usually takes no longer than 8 days. In individual cases, however, it can also lead to a much longer virus excretion (e.g. premature babies, immunodeficiency).

Clinical manifestation: Symptoms range from subclinical infections to mild diarrhoea to serious illnesses. The disease usually begins acutely with watery diarrhoea and vomiting. Often there are also mucus admixtures in the stool. Fever and abdominal pain can occur. Rotavirus-related enteritis cannot be differentiated clinically from other types of gastroenteritis. The gastrointestinal symptoms usually persist between 2 and 6 days. And specific respiratory symptoms are observed in more than half of the cases. In case of complicated processes that lead to dehydration, this can lead to death if not treated adequately in time.

The immunity to rotaviruses usually develops in the first years of life. Most of the initial infections occur between the ages of 6 months and 2 years. But there are also known infections in new-borns and infants under 6 months. At the age of 3 years, about 90% of all children have already undergone a rotavirus infection; by the

age of 5, almost all children have been infected with rotavirus. Although almost all adults have antibodies against rotaviruses, repeated infections are possible in all age groups. Also transfers within families of sick children to the parents are not uncommon. In adults, however, most infections are asymptomatic. At higher ages (> 60 years of age), the number of symptomatic diseases increases significantly again. At the end of an infection, serotype immunity can be demonstrated, but it is not permanent.

Diagnostics: The method of choice is the detection of an antigen from the stool by means of enzyme immunoassay. Further, detection via PCR is possible.

Therapy: As a rule, an oral substitution of liquid and electrolyte is sufficient. If intravenous fluid intake is required, hospitalization is usually necessary. There is no antiviral therapy; antibiotics and agents that inhibit intestinal motility are not indicated.

Preventive measures:

1. Immunization against *Rotavirus* from the 7th week of life: the live vaccine can be administered orally. Depending on the vaccine used, 2 (Rotarix) or 3 doses (RotaTeq) are given at a minimum interval of 4 weeks.

2. Hygiene measures: To avoid transmission by faecal-oral route, the following hygiene measures must be followed:

Separation (isolation) of the sick person, if necessary cohort isolation/care

a. Other hygiene measures:
   - Hand disinfection before and after all nursing activities.
   - Disposable gloves when changing diapers and handling contaminated objects. Thoroughly disinfect hands after removing the gloves (high viral load in the stool!).
   - One-off apron for all nursing activities.
   - Patient-related use of care products (ointments, etc.) in the smallest possible packing units.
   - Immediate disposal of infectious items (diapers, laundry, etc.).
   - The measures of the cleaning and disinfection plan of the department must be strictly adhered to.
   - Thermometer: Basically no rectal measurements in patients with diarrhoea.
   - Patient-related surfaces: In case of contamination with stool, immediately wipe disinfection according to the station's cleaning and disinfection plan.
   - Feeding bottle and rubber nipple: Thermal disinfection by machine preparation at 95°C.
   - Patient dishes: Cleaning in a dishwasher.
   - Incubators: In case of contamination (intervention openings), immediately wipe disinfection; otherwise reprocess the incubator at weekly intervals.
   - Linens: Dispose the laundry contaminated with stool separately, and then treat baby clothes at 60°C by chemo-thermal laundry disinfection.
b. Cancellation of special hygiene measures: 5 days after the onset of the symptoms of diarrhoea, or after a negative stool finding, the hygiene measures can be lifted again.

c. For disinfection, only agents with proven virucidal activity according to the manufacturer's instructions' appropriate concentration and exposure time are suitable.

Norovirus Infection Noroviruses (formerly known as Norwalk-like viruses) are globally distributed non-enveloped RNA viruses. The noroviruses are responsible for a majority of nonbacterial gastroenteritis (up to 30% in children and up to 50% in adults) and are also the predominant cause of gastroenteritis outbreaks in community settings, hospitals and retirement homes. In infants and young children, they are the second leading cause of all acute gastroenteritis after rotavirus. Norovirus infections can occur all year round. However, there is usually a seasonal peak from October to March.

Reservoir: Humans are currently the only known reservoir.

Path of infection: The viruses are excreted both through the stool and via the vomit of human. The infectivity is very high, and the minimum infection dose is likely to be about 10–100 virus particles.

Transmission: Either follow faecal-oral (e.g. hand contact with contaminated surfaces, food) or by oral ingestion of virus-containing droplets, which arise as part of the gushing vomit (droplet infection). The transmission usually takes place directly from person to person and is the cause of high numbers of norovirus infections. However, infections can also come from contaminated food (salads, mussels and other raw foods or those requiring refrigeration) or drinks (contaminated water).

Incubation time: This is about 6–50 hours.

Duration of contagion: During acute illness, infected people are highly contagious. Therefore, for the prevention of retransmission, the symptomatic phase including the first 48 hours after the onset of symptoms (i.e. until the cessation of diarrhoea or vomiting) is most significant. As a rule, the virus is excreted through the faeces for 7 to 14 days, in exceptional cases but also for weeks after an acute illness. After the acute phase (after cessation, diarrhoea/vomiting), careful sanitary and hand hygiene is still required.

Clinical Symptoms Noroviruses are associated with acute onset gastroenteritis, characterized by severe vomiting and severe diarrhoea, which can lead to significant fluid and electrolyte deficiencies. In some cases, the symptoms may be limited to vomiting without diarrhoea or diarrhoea without vomiting. Mostly there is a marked malaise with abdominal pain, nausea, headache, myalgia and fatigue. Body temperature may be slightly elevated, but usually does not cause high fever. If there are no underlying diseases, the clinical symptoms will last around 12–48 hours. But also milder or asymptomatic courses are possible.

Diagnosis There are currently three detection methods for norovirus detection in stool:

- PCR
- Antigen enzyme immunoassay (EIA)
- Electron microscopic detection of virus particles

Therapy The therapy is symptomatic by balancing the significant loss of fluids and electrolytes. Currently there is no antiviral therapy; antimicrobial therapy is not indicated. For infants and the elderly, hospitalization will be necessary in severe cases.

Preventive Measures

1) Immunization: No vaccines available.
2) Hygiene measures: Measures for patients and staff during acute illness until 48 hours after the clinical symptoms disappear are the same as for *Rotavirus*. Because the virus remains infectious for a long time on contaminated surfaces or hands, agents with proven virucidal activity must be used for disinfection. To avoid outbreaks, the diseased staff should also be released from work for minor gastrointestinal complaints and resume work at the earliest 2 days after completing the clinical symptoms, with due regard for hand hygiene.

14.2 *Clostridium difficile*

Pathogen *C. difficile* (CD) is an anaerobic, gram-positive, endospore-forming rod bacterium that is ubiquitous in the environment and can colonize the intestines of humans and animals. The spores are excreted with the stool, are very resistant to the environment and therefore easily transferable. Due to the resistance of spores to many disinfectants, cleaning is of particular importance. Hypervirulent CD can cause very serious illnesses, especially in older people.

Epidemiology Between 1 and 3% of healthy adults and up to 80% of infants are colonized with CD; in hospitalized patients, asymptomatic support is found in up to 35% (risk factors: antibiotic therapy, hospitalization period).

Clinical Manifestation Consist of moderate to severe watery diarrhoea with sometimes fulminant course, possibly toxic megacolon or intestinal perforation. The cause of the disease is the toxins of CD, which cause massive damage to the enterocytes of the colon. Symptoms usually appear 3–10 days after the initiation of broad-spectrum antibiotic therapy. Often a CD-associated diarrhoea (CDAD) is a reason for admission of the patient (= out-of-hospital-acquired CDAD). This should be distinguished from hospital-acquired, nosocomial CDAD (symptoms later than 48 hours after admission and up to 4 weeks after discharge).

Infectious material: faeces; in diarrhoea massive excretion and dissemination of CD!

Transmission Faecally-orally. CD is highly infectious. Patients with diarrhoea excrete 107 to 109 pathogens per gram of stool. Transmission of CD is critical especially in those with poor intestinal control and hygiene deficiencies. Because of environmental resistance of the CD spores, not only articles with chair contact are relevant (Underwear, endoscope, hands!) but also frequently touched objects

(bed fittings, call button, telephones, etc.) and all poorly maintained surfaces (accumulation of CD-containing dust). Because of environmental and disinfectant resistance, there is long survival and accumulation of CD spores in the environment!

Contagiousness Contagiousness is particularly high in diarrheal phase. Correctly treated patients may excrete the pathogen after the onset of diarrhoea for a further 3–6 weeks in a smaller amount. The toxin test may also remain positive in up to 30%. Extended sponsorship and CDAD relapses occur.

14.3 Microbiological Investigations

14.3.1 Material

¬ Stool for toxin and germ detection. At least 2ml only of non-formed stools!!

Indication:

¬ Moderate to severe diarrhoea after AB therapy. Only heaped or soft stools are mostly not conditioned by CD.

¬ Risk groups (over 65 years, immunosuppression, severe underlying disease, gastrointestinal basic disease).

¬ Any diarrhoea lasting more than 3 days without other known pathogens.

After successful diagnosis, repeated stool tests to check for presence of CD are not necessary. The treatment success is purely defined by recession of clinical symptoms. Only if there is a suspicion of recurrence should a new investigation be made.

Therapy: In addition to the fluid and electrolyte replacements, the first-choice antimicrobial therapy is metronidazole. The uncritical use of glycopeptides (vancomycin, teicoplanin) should be avoided in order to prevent the development of VRE (vancomycin-resistant enterococci)!

Instruction for Patients For CDI patients we recommend primarily handwashing to rinse off the *Clostridium* spores and drying the hands carefully followed by hygienic hand disinfection after visiting the toilet and after contact with intestinal secretions. Furthermore, one should avoid environmental contamination with intestinal contents.

14.4 *Salmonella*

Pathogen *Salmonella* spp. are moving, Gram-negative rods. They are distributed worldwide and are transmitted by food. The most important human pathogenic *Salmonella* are (1) the causative agents of enteric salmonellosis *S. typhimurium* and *S. enteritidis* and (2) the causative agents of the sporadic typhoid salmonellosis *S. typhi* and *S. paratyphi*. This guideline deals exclusively with endemic and epidemic enteric salmonellosis.

Salmonella's main reservoir is the gastrointestinal tract of livestock (cattle, pigs, poultry) and animal foods derived therefrom. They multiply in a temperature range of 10–47 ° C, in some cases already from 6–8 ° C. They are able to survive in or on different foods for up to several months. Freezing does not kill them.

Typical Clinical Picture

- In 95% local, self-limiting inflammatory or secretory gastroenteritis
- In 5% systemic course with septic disease

Infectious Material

- Stool and/or vomit
- Blood (if septic)
- Contaminated food or drinking water

Transmission The infection is caused by oral pathogen absorption.

– By eating contaminated food (meat or eggs that are not sufficiently heated)
– By direct contact with infectious material of patients (see above)
– By indirect contact with infectious material of patients over contaminated objects or surfaces

Risk of Transmission The infection dose for adult humans is only 104 to 106 pathogens.

Incubation Period The incubation period is 6–72 hours.

Duration of Infectiousness The duration of contagiousness in adults is an average of 1 month and, in children under 5 years up to 7 weeks, often even up to several months. In some cases (<1%), *Salmonella* can be eliminated permanently (> 1 year) after having undergone infection with the stool.

Microbiological Detection

- Cultural pathogen detection from stool or rectal swab
- Blood culture suspected of systemic course

Hygiene Measures Isolation:

- Isolation in a single room with a proprietary toilet

Hand hygiene with alcoholic hand rub:

- Patients
- Visitors
- Healthcare personnel

Protective Gear

- Disposable gloves and disposable apron for all nursing and medical activities as well as for dealing with excreta and contaminated objects
- Protective coat and protective mask in case of danger of environmental contamination (vomiting, diarrhoea, lack of compliance, etc.)

Surface Disinfection Ongoing wipe disinfection according to sector-specific cleaning and disinfection plan of all hand contact surfaces and all objects and surfaces that come into contact with infectious secretions

Care utensils (ointments, etc.)

Patient-related use in packaging units that are as small as possible (see Hygiene File of the AKH/Ointments – Handling and Application)

Instruments (blood pressure apparatus, stethoscope, clinical thermometer, etc.):

- Patient-related use.
- Perform wipe disinfection after use.
- Basically no rectal measurements in patients with diarrhoea.

Disposal Disposal of disposable materials and used bandages without intermediate storage or contact with items in the disposal bag:

- Dispose used bed and underwear without intermediate storage or contact of objects in a laundry bag, and put wet laundry in a plastic bag and transport closed.
- Place used instruments without intermediate storage in the transport container and bring to treatment.

Excretions

- Prepare urine bottles and bowls in the bowl washer immediately after use.
- After use of the toilet, wipe disinfection on the toilet seat, the toilet lid and all hand-contact surfaces (sink, door handle, etc.).
- Training of the patient.

Patients' Dishes Processing in the dishwasher

Bottles and Rubber Nipples

- Thermal disinfection by machine treatment at 95 ° C for at least 1 minute

Duration of hygiene measures

Maintenance of hygiene measures for the duration of gastrointestinal symptoms

Cancel the hygiene measures in case of cessation of gastrointestinal symptoms and three times negative stool sample.

In case of the cessation of symptoms and further elimination of pathogens, seek the most somatic dismissal and consultation with KHH regarding adaptation of the hygiene measures.

Organization of Work Processes Plan work processes so that activities in the "Salmonella Room" take place at the end of the routine.

Ensure good preparation and, if necessary, involvement of a second person in order to avoid unnecessary interruptions (risk of contamination!).

Therapy For uncomplicated salmonella gastroenteritis, no antibiotic therapy is required.

In severe cases, infants/toddlers, the elderly and patients with immune deficiency, antibiotic therapy is indicated after consultation with the attending physician.

14.5 Diarrheal Diseases in the Hospital

What needs to be considered by the medical staff:

Diarrheal diseases can be caused by viruses, bacteria and parasites.

With an accumulation of diarrheal diseases in Vienna and the environment, the probability is given that such illnesses occur also with patients and personnel increasingly.

Although such infections are usually self-limiting, severe forms and complications, especially in immune-compromised patients, cannot be ruled out. In acute diarrhoea, it is to be expected that the pathogens are excreted in large numbers in the stool. To prevent a transmission, therefore, appropriate measures must be taken.

Transmission Routes The transmission of diarrhoea occurs in most cases faecal-oral (so-called smear infection on the hands). In *Noroviruses*, transmission also occurs via droplets (aerosols in the vomit)

Hand Hygiene The hands play a crucial role in the transmission of intestinal infections.

The correct implementation of hand hygiene, especially when dealing with excretions, is therefore essential. This applies to patients and medical staff, as well as aiding relatives and visitors.

The provision of a hand sanitizer to the affected patient and appropriate instruction from the care personnel supports the hand hygiene compliance. One exception is *Clostridium difficile*, a spore-forming bacterium. Spores of *C. difficile* are resistant to alcohol; therefore spores need to be removed mechanically by washing the hands with soap and water. For CDI patients we recommend therefore primarily handwashing to rinse off the *Clostridium* spores, drying the hands carefully followed by hygienic hand disinfection after visiting the toilet and after contact with intestinal secretions. Furthermore, one should avoid environmental contamination with intestinal contents.

Protective Clothing In dealing with diarrhoea patients, there is an increased risk of contamination of the clothing by spraying. Therefore, protective clothing must be worn.

This includes:

- Apron
- Disposable gloves

If increased risk of splashing is to be expected and in case of aerogenic transmission:

- Disposable gloves
- 1x protective coat
- Oral and nasal mask
- Safety goggles

Toilet Hygiene On a close-meshed cleaning and disinfecting the toilets is to be respected.

The diarrhoea patients have their own assigned toilet that is not shared with other patients.

Please also note the use of special disinfectants in the presence of Noroviruses and *Clostridia*.

Isolation Measures For massive diarrheal symptoms and also for many virally induced diarrheal diseases (triggered by, e.g. noroviruses), the affected patients should be isolated in a single room with their own toilet. Patients with the same pathogen can be cohorted.

Information to Patients and Their Visitors With the aid of separate leaflet for patients and visitors, they are informed that special attention must be paid to hand hygiene and surface disinfection in the toilets.

Instruct the patients and visitors of proper hand hygiene.

Any contaminants should be reported to the care staff.

Visitors should not bring home-cooked food or drinks to their sick relatives.

Food Hygiene Raw, semi-cooked and even cooked foods can be effective in spreading intestinal pathogens when in contact with faecal contaminated hands or objects. Therefore, hand hygiene plays a very prominent role in the kitchen.

In our central kitchen, strict attention is paid to compliance with these rules. More problematic than foods produced by the central kitchen are food and drinks brought from home or prepared and manipulated at the stations.

The tea kitchens of the stations only have basic equipment. Therefore, the manipulation of food there should be reduced to a minimum.

Any kind of preparation or manipulation with food must also be carried out in the tea kitchen under the necessary hygienic precautions. A particularly important role is played by hand hygiene.

Persons suffering from diarrhoea must not be engaged in the preparation or distribution of food. It is also important to note the hygiene at the dining areas and in the refrigerators for food outside the tea kitchen (e.g. in the staff rooms).

Blood-Borne Viruses: HIV, Hepatitis B, and Hepatitis C

15

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15.1 HIV Types 1 and 2

Course of Infection

The course of infection after infection with human immunodeficiency virus (HIV) is divided into several stages. Initially, there is a primary infection; here patients may have an acute retroviral syndrome or flu, or mononucleosis-like symptoms in the sense of a typical viral disease.

The next stage is a clinically symptomless variable-duration stage with continuous viral replication. At the next stage, there is persistent generalized lymphadenopathy.

The final stage—the full picture of acquired immunodeficiency syndrome (AIDS)—is characterized by opportunistic infections and tumors typical of HIV/AIDS.

HIV Transmission Routes

- Sexual
- Parenteral
- Intravenous (IV) drug use, (stab) injuries

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_15

- Vertical
- Perinatal
- Pre- and postnatal (breastfeeding)

Clinical Course of HIV

Phase I—acute infection: Here, the virus is present in the blood and it multiplies, causing viremia. This causes typical symptoms such as fever, headache, general weakness, and muscle and joint pain, so the viral infection is similar to a flu-like infection. The duration of this first phase is up to a few weeks. In the blood, one sees that the CD4 cells are still normal; a normal test result is about 800–1200 CD4 cells per milliliter of blood.

Phase II—asymptomatic disease: The virus is latently present in T helper lymphocytes (CD4 cells). This asymptomatic disease phase can last from 0 to 10 years or longer. During this stage a slow decline in CD4 cell numbers occurs. At the stage of asymptomatic disease, the CD4 cell numbers are slightly decreased to 1000 per milliliter of blood. At this stage, the patient has no symptoms; he is subjectively healthy, but he is very infectious. After about 6–8 weeks, seroconversion occurs, and only then are the antibodies serologically detectable.

Phase III—asymptomatic disease: This is due to virus multiplication within the host cells; with destruction of T helper cells and macrophages by the virus, signs of the disease become evident. A considerable reduction in CD4 cell numbers (to <600 per milliliter) is detectable in the blood. The symptoms of AIDS-related complex (ARC) start to present: chronic weakness, mild fever, night sweats, diarrhea, weight loss, and generalized lymphadenopathy. In addition, the first opportunistic infections may occur, such as bacterial pneumonia, meningitis, and oral and vaginal fungal infections, as well as tuberculosis. This phase can last for months to a few years.

Phase IV—AIDS: In this disease phase, CD4 cell numbers are severely reduced to <200 per milliliter of blood. Patients have severe opportunistic infections:

- Pneumocystis carinii pneumonia (PCP)
- Toxoplasmosis (especially with brain involvement)
- Cryptosporidiosis (diarrhea)
- Many bacterial and viral infections—e.g., cytomegalovirus (CMV) or herpes simplex virus (HSV)
- Tumors—e.g., Kaposi's sarcoma or lymphoma

HIV dementia, in the sense of a degenerative brain disease, can also occur during this stage of the disease. The antiretroviral therapy (ART) available today has turned HIV/AIDS into a chronic disease. Therefore, the duration of this disease is that of a chronic disease today.

HIV Transmission Routes

The following body fluids of the infected person are infectious: blood, seminal fluid, vaginal secretions, and breast milk. Therefore, the following transmission paths arise:

1. Unprotected sexual contact with an HIV-infected partner (depending on the prevalent viral load in the blood of the HIV-infected person)
2. Intravenous drug use with joint use of syringes and needles
3. Vertical transmission from an HIV-infected mother to her newborn

HIV viruses can also be detected in urine, saliva, and tears, but in concentrations too low to cause infection.

No transmission takes place through social contacts, droplet infections, or indirect infection routes. There is also no evidence of insect-borne transmission in the literature. The most common means of HIV transmission today is thus still through unprotected sexual intercourse. Transmission via blood transfusion or transplantation is particularly common in countries where blood donations are not routinely screened for HIV.

HIV Epidemiology

The prevalence in different countries varies greatly. AIDS has become the leading cause of death in sub-Saharan Africa. The disease is currently spreading fastest in the countries of the former Soviet Union and in South and Southeast Asia. By contrast, AIDS is a marginal health problem in the industrial regions of Western Europe. According to data from the Robert Koch Institute in Germany, at the end of 2013, an estimated 78,000 people were living with HIV or AIDS in Germany. Of these, about 51,000 were men who had had sex with men and about 17,000 had become infected via heterosexual contacts. About 10,000 were intravenous drug users and about 7300 people had come from high-prevalence regions and had mainly been infected through heterosexual contact in their countries of origin. Thanks to the currently effective drug treatment, fewer and fewer people in Germany are dying of HIV infection. In 2010 there were about 550 deaths. The number of new infections is significantly higher than the number of deaths. According to current estimates, in 2010 about 3000 people in Germany became newly infected with HIV, similar to the numbers in previous years.

Vertical Transmission of HIV

Without maternal ART, the risk of vertical transmission of HIV from mother to child is about 40%. This 40% risk is divided as follows:

- 5–10% via intrauterine infection
- 20–25% via infection at birth
- 10–15% via postnatal infection

However, effective interventions have reduced the risk of vertical transmission to 1–2%. Such interventions include:

- Risk-adapted ART for the mother
- Delivery via caesarean section before the onset of labor
- Weaning
- Risk-adapted postexposure prophylaxis (PEP) for the newborn

HIV and Birth

The prevalence of HIV in newborns differs greatly in different countries. AIDS has become the leading cause of death in sub-Saharan Africa. The disease is currently spreading fastest in the countries of HIV and birth.

Birth mode: In HIV-infected patients, caesarean section is still considered the birth mode of choice, with a laborless uterus plus weaning plus PEP for the newborn.

Note: Vaginal delivery is possible at selected centers, at the express request of the mother, but only if the mother is compliant with ART and has a viral load below the detection limit, which is currently <40 copies per milliliter of blood.

15.2 Hepatitis B Virus

Hepatitis B virus (HBV) leads to infection after transmission. After an incubation period of about 2–6 months, acute hepatitis occurs. This can be an anicteric, icteric or, in extreme cases (0.5–1% of cases), fulminant hepatitis can occur.

As a result, about 90% of hepatitis B infections are cured. Nine percent of patients have chronic hepatitis B (40% of the under-5-year age group and 8% of the over-5-year age group), and they either continue to heal or they suffer liver cirrhosis with possible progression to hepatocellular carcinoma. The remaining 1% of cases are fulminant and lethal.

Transmission of hepatitis B virus occurs parenterally via blood or via sexual intercourse, but also perinatally from the mother to the child. In body fluids such as blood, serum, and wound exudate, the concentration of hepatitis B virus is high. Moderately high concentrations are found in semen, vaginal fluid, and saliva. In urine, stools, sweat, tears, and breast milk, the concentrations are low or undetectable.

Hepatitis B in Pregnancy

Ascertainment of hepatitis B status is recommended in pregnant women up until the 28th week of pregnancy.

Prenatal hepatitis B transmission in pregnancy: The reported risk of intrauterine hepatitis B infection of the child by the mother during pregnancy is 3–5%.

Perinatal hepatitis B transmission in pregnancy: If the mother is hepatitis B surface antigen (HBsAg) positive and hepatitis B envelope antigen (HBeAg) positive, there is a very high (70–80%) risk of infection of the newborn.

If the mother is only HBsAg positive, the risk of infection of the newborn is 6%; thus, the mother's HBeAg status is highly relevant to the risk of perinatal infection of the newborn.

Hepatitis B and Newborns

In the case of hepatitis B antigen–positive mothers, the newborn will be vaccinated (active immunization), and hyperimmunoglobulins are administered immediately after birth (passive immunization).

A decision on whether the mother should breastfeed the child or not is dependent on the viral load and is subject to case-by-case assessment.

15.3 Hepatitis C

Hepatitis C virus (HCV) belongs to the family of flaviviruses. It is an enveloped, single-stranded RNA virus. Hepatitis C virus is distributed worldwide; there are six different genotypes and about 100 subtypes.

Clinical Manifestation of Hepatitis C
In acute hepatitis C infection, only about 25% of patients are symptomatic; i.e., 75% of those infected with hepatitis C are asymptomatic, but viral replication still occurs. In 60–80% of cases, hepatitis C becomes chronic. Possible sequelae include liver cirrhosis (which occurs in 15% of cases) with possible progression to hepatocellular carcinoma (1–5% probability per year). Another possible long-term consequence is immune disease.

Risk factors for hepatitis C acquisition include:

- Percutaneous exposure to contaminated blood.
- Transfusion of hepatitis C virus–containing blood or blood products (before 1992); because of blood screening, the risk today is about 0.01%.
- Intravenous drug use ("needle sharing").
- The role of tattooing and piercing in hepatitis C transmission is highly probable but controversial in the literature.
- Occupational infection—e.g., in the medical field (infection via needlestick injury).
- Nosocomial/iatrogenic infection due to insufficient disinfection of medical devices—e.g., acupuncture or dental equipment.
- Dialysis.
- Transplantation.
- Sexual contact; sex workers and men who have sex with men are especially at risk here.
- Bloody household products that are shared (commonly, wet razors; nail scissors; and also toothbrushes).

Vertical transmission (from mother to newborn) is rare and depends upon the viral concentration in the maternal blood.

Note: In approximately 40% of patients infected with hepatitis C virus, none of the previously known and listed risk factors apply. This means that there must be additional transmission paths, but they are not yet known.

Perinatal Hepatitis C Virus Transmission
Transmission of hepatitis C virus from an RNA-positive mother to her newborn can occur only at the time of birth, and here the mean infection rate is about 6%.

However, if the mother is coinfected with HIV, the infection rate is higher—up to 17%. No associations with the type of birth or with breastfeeding have been found. Infected newborns are symptomless. Fulminant hepatitis is rarely seen, but infected children are infectious and can spread the infection.

Epidemiology of Hepatitis C

Worldwide: Around 3% of the world's population is infected with hepatitis C virus, and around 170 million people worldwide are chronically infected.

Europe: The known hepatitis C prevalence in most countries lies between 0.5% and 2%. The dark figures are probably higher. In Europe, it is estimated that approximately 2–5 million individuals are hepatitis C virus–positive. The incidence of first hepatitis C diagnosis has increased in recent years.

Hepatitis C Screening for Pregnant Women: Why?

Hepatitis C virus infections are found mainly in the 20- to 40-year age group. Hepatitis C screening in pregnant women could identify asymptomatic infected women, which could reduce the risk of vertical transmission. Personal protective measures at birth could thus be undertaken. Of course, the protection of fellow patients also has public health significance. If one realizes early that an infection is present in a patient, treatment can be given earlier and thus possibly minimize the chronic consequences of this illness.

Nosocomial Transmission of Hepatitis C Virus Infection

Nosocomial transmission is usually recognized in the context of outbreaks. Causes are described in the literature, occurring especially via contaminated instruments or other medical devices in the field of hemodialysis, but also in the field of endoscopy. Sometimes, unhygienic injection pacts such as plasmapheresis, phlebotomy, and multiple use of injection solutions are to blame. All of the above can be avoided by complying with the correct basic hygiene measures.

Occupational Hepatitis C Infections

Affected persons in this cohort are those who work in invasive medical fields, such as surgical personnel and midwives performing activities with increased risks of injury.

Needlestick Injuries

The risk of infection after a needlestick injury with a contaminated needle depends on several factors:

- The size of the inoculum (the amount of blood)
- The size and nature of the needle (the lumen of the cannula)
- The depth of the inoculation
- The viral load of the patient of origin

It should be noted that gloves do not provide protection against needlestick wounds. However, they reduce the risk of infection by mechanically reducing the inoculated blood volume. Roughly speaking, one can reduce the risks of infection via needlestick injury to:

- About 30% for hepatitis B
- About 3% for hepatitis C
- About 0.3% for HIV

Preventing needlestick injury involves avoiding dangerous practices that can lead to such wounds, such as:

- Recapping (putting the protective cap back on a used cannula)
- Errors in disposal of used cannulas
- Defective disposal containers
- Overfilled disposal containers
- Insufficient numbers of disposal containers
- Needles or adapters being forgotten in the hospital bed

Preventive Measures with Regard to Needlestick Injuries

Where you can vaccinate, you should vaccinate. To prevent hepatitis B virus infection, there is the possibility to vaccinate; therefore, this vaccination is absolutely recommended to all exposed employees.

Preventive measures with regard to hepatitis C and HIV are:

- Exposure prophylaxis
- Consideration of hygiene measures with use of appropriate protective equipment
- Prevention of needlestick injuries

Protective Gear

When providing care to patients, always wear gloves when there is a risk of coming into contact with body fluids—e.g., during blood collection, during the birth process, or when handling a placenta.

Masks (covering both the nose and the mouth) and goggles should always be worn if there is a risk of formation of aerosols or splashing of blood or body secretions and excretions—e.g., the amniotic sac.

Moisture-proof protective gowns or clothing must be worn during work involving massive contamination with blood or secretions (moisture penetration)—e.g., during dirty work, such as disposal of fecal matter or urine. Protection of the forearms is of particular importance.

Health care personnel with injuries to the hands and/or arms should not be put to work caring for patients with blood-transmitted diseases while they are injured.

Puncture Wounds and Needle-Related Injuries

16

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People working in the medical field may be exposed to potentially infectious blood while working. The risk of infection from a cut or puncture wound with contaminated instruments depends on several factors. Among the most important are the type of injury, the amount of contaminated material and the quantity of the infectious agent.

In a retrospective, case-controlled study by the Centers for Disease Control and Prevention (CDC), the following four factors were identified that significantly increase the risk of becoming infected:

- Deep injuries
- Visible blood on a sharp object that was injured
- Hollow needles previously in contact with a vein or artery of the source patient
- Source patients in the state of maximum viremia/bacteraemia

In principle, exposure to blood or infectious bodily fluids can occur in two ways:

- Percutaneous exposure (needle injuries and injuries with sharp objects)
- Mucocutaneous exposure (splashing, spraying, direct skin/mucous membrane contact)

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_16

Mucocutaneous and percutaneous exposures have different transmission rates and require different preventive measures. The most common medical exposures leading to infections are percutaneous. Percutaneous puncture wounds are also the most effective way of transmitting infectious organisms.

The most relevant pathogens associated with cut and puncture wounds in the hospital include hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). For HBV there is the possibility of a vaccine that every healthcare worker should take advantage of!

The risk of acquiring infection with one of these 3 viral agents is 5–40% for HBV, 3–10% for HCV and 0.3% for HIV.

The most common causes of exposure to blood or body fluids by medical professionals include recapping of needles, administration of parenteral drugs, blood draws, disposal of i.v. catheters and infusion sets, injuries with used needles, injuries with misplaced needles, overcrowded sharps containers, blood contact from wearing gloves or torn gloves, needle injuries from the glove and accidental needle injuries during medical work. They break down as follows:

- Manual 'recapping' of needles 17%
- Wrong disposal of needles 14%
- Manipulations on the stylet of i.v. cannulas 36%
- During an invasive process 8%
- During an autopsy 2%
- Other approaches 17%
- Exposure of open wounds to infectious sources 6%

The most effective measure to reduce the annual incidence of needle injuries is undoubtedly the prevention thereof; this can be achieved first and foremost through the targeted training of correct blood collection technology on the one hand and regular education of the dangers for medical personnel on the other hand. It is also important to provide sufficient disposal facilities for needles and sharp objects. Should there nevertheless be a puncture wound with blood exposure, the following general guidelines should be implemented:

16.1 Immediate Wound Care

Immediately and sufficiently long (about 5 min) wound should be squeezed. Attention, the blood is considered infectious in this case! The efficacy of bleeding with the purpose to reduce the risk of infection, however, is not proven in any study. Then leave the puncture site with PVP-iodine or an alcohol-containing skin or mucous membrane antiseptic (for eyes with a suitable buffer solution) for about 30 s–1 min.

16.2 Pay Attention to Careful Documentation

Before seeking the competent body for a possible prophylaxis, it is necessary to obtain all the information that can be collected. On the part of the affected person, a HBs-Ak title should be known; on the part of the source patient, information about the underlying disease, social anamnesis, previous microbiological examinations and, of course, titles of HBs-Ag, HCV-Ab and HIV-Ab should be obtained from the patient documentation. If title values cannot be determined from the medical history, 5 ml of native blood must be taken from the source patient.

In any case, 5 ml of native blood must be taken from the person affected, for forensic reasons alone, in order to rule out hepatitis B (high prevalence) that has already existed before the stab wound.

16.3 Contact the Doctor in Charge

The in-house behavioural instructions should correspond to a detailed and precise plan in order not to lose time due to ambiguity. So that further supply is guaranteed, independent of the time of day, the emergency department of the respective home is recommended as the first point of contact. Further measures (HBV, HIV prophylaxis) should be considered there on the basis of a specific history and previous documentation. In any case, an occupational accident report must be filled in here at the latest.

Medical Mycology: Fungal Infections

17

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Mycology (μύκης, Greek: fungus) is the science on fungi.

Fungi are eukaryotes and have a cell nucleus. Like human cells they have mitochondria in their cell for energy production. They are heterotrophic and can live on many different nutrients. They can propagate either asexually by producing spores or dividing. Alternatively most of the fungi can propagate sexually depending on the environmental conditions. Sexual propagation means that two different fungal cells of the same fungal species combine their genetic material to form genetically new fungi. There are more than 100,000 species, but only 300 species are pathogenic for humans and animals. Many fungi are plant pathogens.

Fungi are pleomorphic. Pleomorphism means that they have a different morphology (appearance) dependent on the environment and the nutrient in spite of having the same biochemical and physiological properties. Fungi are commonly found in the environment. They live on and in plants, in the soil, often in symbiosis with bacteria or even higher organisms, e.g. leafcutter ants. This symbiosis works like this: The fungi digest the cellulose of the plant leaves sheets which serves as food for the ants. The ants care for fungi and carry them to new leaves to digest.

Overall, fungi cause biological degradation of organic material, a process that is commonly perceived as damage or rot. Fungi can produce carbohydrates, alcohol and carbon dioxide as raw materials for photosynthesis of plants.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_17

There is the science of fungal taxonomy classifying fungi according to several properties including metabolism, ecological features and genetics. However, the most common classification of fungi is based on the appearance of fungal colonies on nutrient media and the appearance in the microscope:

- Yeasts with creamy white to coloured colonies. Yeasts reproduce by budding. The most common genera are *Candida* species and *Saccharomyces cerevisiae*, a fungus that is widely used in food industry.
- Filamentous fungi (moulds, *Hyphomycetes*) have colonies with woolly appearance. In the microscope it can be seen that they form a true mycelium with long thread-like structures (hyphae). The most commonly known filamentous fungi are *Aspergillus* or *Penicillium*.

For medical mycology fungi are classified according to the disease that is caused by them. A fungal infection is referred to as "mycosis":

- Superficial mycoses

  Fungi cause superficial disease on the surfaces of the human body (skin, mucous membranes) without invading the body. The fungus lives as a genial parasite on the skin or in skin appendages. The most important superficial mycoses are dermatomycoses with infection of skin, hair and nails. Another type of dermal mycosis is intertrigo where it comes with redness within large skinfolds (e.g. under the breasts or under the buttocks). Mycosis of the oral mucosal membranes in critically ill patients with an impaired immune system is called thrush. Mycosis of the vagina and the outer genitalia occurs commonly in women, particularly in pregnant women.
- Invasive fungal infections

  Invasive fungal infection is infections of the severely ill and immunocompromised. Due to the impaired immune response, fungi may enter the human body. Invasive fungal infections are very rare and only seen in special medical centres that focus on these types of patients (transplantation, cancer, leukaemia). The most common pathogen of invasive fungal infection is *Candida* species. Filamentous fungi (moulds) are about a tenfold less frequent than *Candida*. They include the genus *Aspergillus* (*A. fumigatus*, *A. flavus*, *A. terreus*, *A. niger*) or Z*ygomycetes* (*Mucor*, *Rhizopus*) and very rarely other phaeo- and hyalohyphomycetes.

17.1 Fungal Toxins and Poisonous Mushrooms

Fungi may produce toxins, e.g. *Aspergillus flavus* produces aflatoxins in peanuts. Aflatoxins cause liver damage. *Claviceps purpurea* produces ergotoxin that causes ergotism with hallucinations, fever, seizures, abortion and even death in humans. But on the other side, *Penicillium* species produces penicillin, and *Streptomyces* species produces streptomycin. Both products are the basis of potent antimicrobial drugs, the antibiotics. *Aspergillus terreus* produces pravastatin that is used as lipid-lowering

agent. This shows that the fungi are diverse, and many products are used for the benefit of the people. Another example is that fungi are used for the production of insulins. They are used for the degradation of environmental pollutants (e.g. toxic chlorophenols) or for the filtration of metals from wastewater. They produce enzymes for detergents or alcohol as a raw material for synthesis of many hydrocarbons. In the food industry or in the chemical industry, fungal fermentation is used on a large scale. In the nutrition industry, fungi play a major role for the fermentation of wine or beer (*Saccharomyces cerevisiae*) or for the refinement of cheese (*Penicillium roqueforti*).

In the environment, fungi for "fruiting bodies" are commonly perceived as mushrooms. They are composed of chitin and cellulose; thus, they should be enjoyed well cooked. However, fungi are also part of human microflora. In small amounts, the yeast *Candida albicans* is a normal commensal on the skin, mucous membranes and intestines. *Candida albicans* can become pathogenic when local environment on the skin or mucosae is severely damaged or the immune response is vastly impaired.

Mushroom Poisoning

Certain fungi produce fruiting bodies that contain toxins. Eating these mushrooms leads to what is perceived as the classic mushroom poisoning. Therefore, it is important only to collect and eat mushrooms in the forest that are reliably identified. The most serious mushroom poisoning is caused by the toxin of *Amanita phalloides* (death cap) with severe diarrhoea and fulminant hepatic failure within 24 h. Acute liver transplantation only can save the patients. Another well-known poisonous mushroom is the *Amanita muscaria* (fly agaric). Its toxin produces sweating and hallucinations but was used for religious ceremonies in many cultures. There are many more poisonous mushrooms depending on the geographic regions.

17.2 Common Fungal Diseases (Mycoses)

17.2.1 Superficial Fungal Infections

The causative agents of more than 90% of the superficial mycoses are dermatophytes. These are the fungal genera *Epidermophyton*, *Microsporum* and *Trichophyton*. Commonly they are transmitted through skin scales. Infants and small children are particularly affected. Dermatomycoses most often present with sharply defined reddened dry scaly lesions on the skin. Think of tinea and consult a dermatologist for further treatment. The genus *Epidermophyton* is also found on pet dogs and cats. These pets are asymptomatic carriers and the reservoir of treatment-resistant dermatomycoses in children.

Superficial fungal infections caused by dermatophytes are called dermatomycoses or tinea. There are several forms of tinea. The most common ones are tinea intertriginosa (in the skinfolds), tinea manuum (hands), tinea pedis (feet), tinea corporis (on the trunk), tinea capitis (hair) and tinea barbae (beard). Dermatophytes cause onychomycosis (mycoses of the nails). Onychomycosis is very common and contributes to the spread of dermatophyte spores.

The fungus *Malassezia* can cause pityriasis versicolor, a skin disease occurring in only some persons. Pityriasis versicolor is not contagious and presents mainly as itchy scaly lesions. These lesions are whitish on suntanned skin and brownish on untanned skin. This is due to the formation of azelaic acid by the fungus thus damaging the melanocytes of the skin. Pityriasis may be ugly but it is not dangerous.

17.2.2 *Candida* Infections

The most common *Candida* species are *Candida albicans* (more than 80% of all human isolates). There are other species isolated in varying proportion in clinical samples: *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, *Candida krusei*, *Candida lusitaniae* and *Candida pseudotropicalis*. *Candida auris* is an emerging pathogen isolated in outbreak of fungemia in intensive care patients on several contries including South Africa, India, the United States, England and Spain.

The *Candida* species are colonizing the gut and maternal genital tract. During birth *Candida* as part of the maternal microflora is transferred to the infant. *Candida* is the pathogen of superficial mycoses in immunocompetent persons. However, *Candida* may be a serious pathogen in immunocompromised and severely ill patients.

Invasive *Candida* Infection

Invasive *Candida* infection may occur in premature babies. Risk factors for *Candida* infection in these infants are the following: a birth weight <1500 g, moist skin, breakdown of the skin barrier because of the supportive use of vascular catheters for infusions or parenteral nutrition, excessive intestinal colonization, necrotizing enterocolitis and the administration of corticosteroids. The not yet fully developed immune system of premature newborns with a diminished function of the white blood cells (reduced chemotaxis of the neutrophils, decreased lymphocyte function and reduced interferon-gamma production of naive T cells), inadequate formation of complement and sometimes very rare inborn congenital immunodeficiencies enhance susceptibility to *Candida* infections. Except for the congenital syndrome "mucocutaneous *Candida* infection", invasive *Candida* infection is always considered to be a healthcare-associated infection.

Risk factors for invasive *Candida* infections are colonization of skin and mucous membranes with *Candida*, immunosuppression, renal failure, haemodialysis, previous surgery, burns >50%, severe trauma, general serious condition, previous or concomitant infections with bacteria and viruses, use of antibiotics, vascular catheters, urinary catheters, diarrhoea, parenteral nutrition, mechanical ventilation and neoplastic underlying disease.

Superficial *Candida* infections are common and include the following:

- *Intertrigo*. *Candida* may cause intertrigo infection under large skinfolds and buttocks due to skin damage by moisture. Intertrigo presents as bright-red oozing erosions. In children, a special form of intertrigo is the diaper skin rash: The

treatment of choice is to keep dry, frequent diaper changes, accumulation of heat and moisture, skin care with moisture-absorbing pastes and—if necessary—topical antifungal treatment.

- *Candida vaginitis* (vaginal thrush) with severe itching, redness and creamy crumbly discharge of the vagina and the outer genitalia. The *Candida vaginitis* is very common. It is an annoying concomitant disease after antibiotic treatment or during pregnancy. Another risk factor may be diabetes mellitus. *Candida vaginitis* does not lead to premature birth rate but must be treated because of the unpleasant symptoms. The therapy is mostly topical with antifungal troches and creams. Only in exceptional cases is there a need for systemic oral therapy.
- Balanitis (*Candid*a infections of glans penis).
- Oral thrush with dryness, white crumbly films on the oral mucosa and the tongue.
- *Candida* esophagitis with burning pain when swallowing food.
- Paronychia (*Candida* nail bed infection).
- *Candida* folliculitis with bright-red erosions on the skin.
- Perianal *Candida* infection with redness, burning and itching.

Candida auris

Candida auris has been recognized as a new emerging pathogen responsible for nosocomial outbreaks among very vulnerable patients. It has been first reported in Japan in 2009 [1]. Antifungal resistance of *C. auris* and transmission despite enhanced infection prevention and control measures are major concerns when it comes to this pathogen.

Suggested Readings

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Parasites and Parasitic Diseases

18

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Parasitism is a form of existence. Parasitism means "life of an organism ('parasite') at the expense of another organism (host)". If the profit is on both sides, this is called symbiosis. The host may be damaged but not necessarily. Parasites are therefore mono- or multicellular organisms.

18.1 Definitions

- Parasite infestation: Detection of parasites in and on humans without clinical manifestation.
- Parasitosis: Detection of parasites in and on humans with clinical manifestation (= illness).
- Host: Every living organism, in or on which another organism (= parasite) lives, feeds, multiplies and propagates.
- Definitive host: The final host is that host in which the parasite reaches sexual maturity and produces offspring.
- Intermediate host is that host in which the parasite continues its development, but does not reach sexual maturity.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_18

- Accidental host is a host (final or intermediate host), in which the parasite does not develop or exist while maintaining its full functions, e.g. trichinellosis. The parasites get killed sooner or later.

18.2 Classification of Parasites

- Single-cell parasites (protozoa)
  - Trypanosomes
  - *Leishmania*
  - *Trichomonas*
  - *Giardia lamblia*
  - Amoebae
  - *Toxoplasma gondii*
  - *Plasmodium*
  - *Pneumocystis carinii*
- Multicelled parasites (flukes and worms)
  - Trematodes (flukes), e.g. *Fasciola hepatica*, *Clonorchis sinensis*, *Paragonimus* sp., *Schistosoma* sp.
  - Cestodes (tapeworms), e.g. *Taenia* (beef tapeworm, pork tapeworm), *Echinococcus* (dog tapeworm)
  - Nematodes (roundworms), e.g. *Ascaris lumbricoides*, *Enterobius vermicularis*, hookworms (*Ancylostoma* sp., *Necator* sp.), *Trichinella spiralis*, *Toxocara canis*, filaria (*Brugia malayi*, *Onchocerca volvulus*)

18.3 Mechanisms of Transmission

- Orally
  - Water (*Dracunculus medinensis*)
  - Meat (*Taenia* spp.)
  - Fish (*Diphyllobothrium* spp.)
  - Crabs (*Paragonimus* spp.)
- Dirt or smear infection
  - *Toxocara* spp.
- Randomly eating insects
  - *Gongylonema pulchrum*
- Percutaneously
  - Active invasion by the parasite larvae: hookworm, *Schistosoma* spp.
  - Passive acquisition via mosquitoes: filaria
- Via the placenta
  - *Trichinella* spp., toxoplasmosis

18.3.1 Parasitic Worm Infections

Organ localization of worms (helminths) in humans:

- Small intestine: *Fasciolopsis* and other flukes, *Taenia*, *Hymenolepis*, *Strongyloides* (hookworm), *Trichuris*
- Colon: *Enterobius vermicularis*
- Bile duct: *Fasciola*, *Opisthorchis*, *Clonorchis*
- Central nervous system: *Taenia solium*, *Echinococcus*, *Toxocara*, *Angiostrongylus*, *Gnathostoma*
- Eye: *Toxocara*, *Onchocerca*, *Dirofilaria*, *Loa loa*
- Blood vessels: *Schistosoma* spp., filaria
- Lymphatic system: Filaria
- Skin: *Onchocerca*, *Ancylostoma*, *Trichobilharzia*
- Muscles: *Trichinella*, *Taenia solium*
- Liver: *Echinococcus*, *Toxocara*, *Capillaria hepatica*
- Lung: *Echinococcus*, *Paragonimus*

18.3.2 *Ascaris lumbricoides* (Roundworm)

Approximately 1.5–2 billion people are infected with *Ascaris lumbricoides*. The distribution is worldwide, especially in countries with low hygiene level. Deaths are very rare; the mortality is 0.1–1% in patients with severe infestation. The life cycle of *Ascaris lumbricoides* begins with the oral ingestion of the *Ascaris* eggs by smear infection. In the intestine the larva hatches and eventually matures by migration through the liver, bloodstream to the lungs and back through the trachea and oesophagus to intestine as an adult worm. Contaminated food includes vegetables contaminated or even fertilized with human faeces, soil and dust. Prevention: sanitation, sewage and waste water in sewage treatment plants.

18.3.3 *Enterobius vermicularis* (Pinworm)

Enterobius vermicularis infests worldwide 300 million people. Symptoms of infestation are a perianal itching, occasional vaginitis and prostates. Children cannot sleep and urinate in the sleep. Sometimes there is abdominal pain and diarrhoea. In children with severe infestation ileus and intussuception with severe abdominal pain can occur. There are very rarely ectopic lesions in the female genital tract and in the peritoneum. The diagnostic test is to stick a transparent tape perianal, put it on a glass slide and examine it in the microscope.

18.3.4 *Trichinella spiralis*

The disease is called trichinellosis. Infection occurs by eating raw pork meat. The pig is the intermediate host, as well as rodents and other wild animals. Definitive hosts are carnivorous predators like wolves and foxes. Man is an accidental host. The cysts in raw meat are ingested, and then the larva develops into the adult worm in the gut. Worm eggs are excreted and eaten by small rodents or wild pigs (wild boar). There, in the intermediate hosts, the larvae develop and form cysts in the muscle.

Signs and symptoms include weakness, abdominal pain, nausea, vomiting and diarrhoea, sometimes rash (hypersensitivity reaction to the worm antigens), fever, muscle pain and oedema around the eyes. Laboratory tests show a distinct eosinophilia.

Prevention: meat inspection (including cadavers of wild animals) and thorough cooking or roasting of the meat

18.3.5 Cestodes (Tapeworms)

- Beef tapeworm (*Taenia saginata*)
- Pork tapeworm (*Taenia solium*)
- Dog tapeworm (*Echinococcus granulosus*)
- Fox tapeworm (*Echinococcus multilocularis*)

18.3.5.1 *Taenia saginata* (Beef Tapeworm)

The distribution is worldwide. The source of infection is raw beef. Man is the final host and houses the adult worms which excrete members or eggs to the ground. These are ingested by cattle or deer with the contaminated grass or by the contaminated environment. These vegetarians are the intermediate hosts. Symptoms include weight loss and abdominal pain. The diagnosis is by seeing tapeworm pieces on the faeces or finding *Taenia* eggs in the microscopic examination of the faeces.

Prevention is by thorough cooking or roasting of the meat. Anthelmintic agents are administered as therapy.

18.3.5.2 *Taenia solium* (Pork Tapeworm)

Taenia solium can occur both as intestinal tapeworm infestation and a generalized disease called cysticercosis. By ingestions of cysts in meat, man is the definitive host of the intestinal tapeworm. But man can also be the intermediate host by ingestion of eggs from contaminated food. The generalized cysticercosis is the generalized disease, where the tapeworm cysts occur anywhere in the body, in the muscles, liver, brain, etc. Depending on localization of the cysts, the host may be asymptomatic or have severe symptoms like cerebral seizures. Infestation in the brains is called neurocysticercosis. Other symptoms comprise headache (migraine), neurocognitive deficits (learning disability, depression, psychosis) and elevated intracranial pressure.

Diagnosis is made by detecting *Taenia* eggs in the faeces when the patient is the final host and with serologic tests in cysticercosis.

The treatment of choice is anthelmintic agent praziquantel. Prevention is by thorough cooking or roasting of the pork meat and vegetables, water and hand hygiene.

18.3.5.3 *Echinococcus granulosus* (Dog Tapeworm)

Echinococcosis is a worldwide parasitosis. Carnivores like dogs, wolves or hyenas are the definitive hosts. The adult worms excrete eggs via the faeces of the dog. These eggs contaminate the environment and are ingested by herbivores. In these herbivores (e.g. sheep but also man), the eggs hatch, and the larvae form cysts throughout the body. These herbivores are resumed by carnivores where the worm reaches its adult stage in the gut and produces eggs. The dog tapeworm is endemic in Austria.

Man is an accidental host. Echinococcus cysts are primarily located in the liver (50–70%), the lungs (15–30%) and also the spleen, kidneys, brain and other organs. In severe cases there may be a generalized distribution of the cysts. Symptoms depend on the location of the cysts. Thus, the host is asymptomatic, but there are headache, seizures, neurocognitive deficits and increased intracranial pressure when the brain is infested.

Cysts in the liver are often asymptomatic and are discovered by chance during ultrasound examinations. Diagnosis is made using CT scan and serology. Cysts can be very large, burst and cause a generalized dissemination of cysts throughout the body. The treatment is both medication with anthelmintic and removal of the cyst without rupture of the cyst. Treatment should be carried out in specialized centres.

18.3.5.4 *Echinococcus multilocularis* (Fox Tapeworm)

The life cycle of the fox tapeworm corresponds to the dog tapeworm. Its final host is the fox. *Echinococcus multilocularis* is endemic in Central Europe. Unlike the dog tapeworm which forms cysts, the fox tapeworm infests the liver forming a tumour-like remodelling, growth of many small cysts and destruction of liver tissue. The anthelmintic treatment of the fox tapeworm is difficult.

For prevention there is a Europe-wide programme for deworming of foxes. Other preventive measures include hand hygiene, washing of wild food (berries, mushrooms) and thorough cooking.

Diagnosis is made with CT scan and serology.

18.3.6 Trematodes (Flukes)

- *Fasciola hepatica* (liver fluke)
- *Clonorchis sinensis* (Chinese liver fluke)
- *Paragonimus* sp. (lung worm)
- *Schistosoma* sp. (fluke)

18.3.6.1 *Fasciola hepatica* (Liver Fluke)

The big liver fluke is most common in marshy pastures. The definitive hosts are herbivores such as cattle and sheep. The eggs hatch to larvae which are ingested by special snail in a humid environment (marshes, pools). Within these intermediate hosts, the larvae develop and excreted as cercariae that form cysts on water plants. When these water plants are ingested by cattle or sheep, the cercaria enters the body and develops to the adult fluke in the bile duct. Man becomes an accidental final host by eating raw watercress or dandelion. In the bile duct, the adult liver fluke obstructs the duct which can lead to cholestatic jaundice. Prevention measures include meat inspection for beef, not drinking water or eating plants or raw snails from ponds and waters with livestock, washing of vegetables and avoiding simultaneous livestock on vegetable fields.

Diagnosis is made by detecting *Fasciola* eggs in the faeces and/or with serologic tests.

18.3.6.2 *Schistosoma* sp. (Bilharzia)

Schistosomiasis is a tropical disease occurring in Africa (from the Nile to equatorial Africa) and Asia. It is a major parasitic disease for more than 250 million people. There are continuous efforts to control schistosomiasis. The three major species are *Schistosoma haematobium*, *S. mansoni* and *S. japonicum*. The life cycle is similar to that of the liver fluke. However, the adult worms live pairwise (male/female) in the small blood vessels (capillaries) of the bladder and the rectum where they produce eggs which are excreted in the urine and in the stool. Without water sanitation and proper sewage, these eggs get into lakes and still parts of the rivers and ponds where they find their intermediate host, a snail. Cercariae actively find their final hosts and enter them through the skin. Man is a final host. Fishermen who fish standing in the low water or women washing the clothes but also people going there for swimming or other leisure activities get infected.

Symptoms are a rash when the cercariae have entered the body (swimmer's itch), fever and buffy eyes (Katayama fever, hypersensitivity reaction to the infestation), muscle pain, diarrhoea, pain and bloody urine and faeces when the adult worms are present. The infection with adult worms leads to scarring in the bladder and the ureters with hydronephrosis and renal failure. *Schistosoma japonicum* may even enter the brain thus causing seizures. Bladder cancer can develop on the grounds of chronic infection. Schistosomiasis can be treated with praziquantel.

Diagnosis is made by detecting *Schistosoma* eggs in the faeces and/or with serologic tests.

Prevention is by avoiding swimming in infested lakes, rivers or ponds.

18.4 Parasitic Infection Caused by Protozoa

The most common protozoa (single-celled parasites) that cause several diseases are:

- *Plasmodium*
- Trypanosomes

- *Leishmania*
- *Trichomonas vaginalis*
- *Lamblia (Giardia)*
- Amoebae
- *Toxoplasma gondii*

Plasmodium, trypanosomes and *Leishmania* are parasitic tropical diseases. Trypanosomes are the agents of sleeping illness. *Leishmania* causes skin ulcers but also severe systemic disease (kala-azar). They are distributed worldwide. *Plasmodium* sp. is the causative agent of malaria.

18.4.1 *Plasmodium* Species (Malaria)

Malaria is serious tropical disease with high and sometimes intermittent fever. More than 200 million people are affected by malaria with more than 400,000 deaths per year. Malaria is transmitted by the *Anopheles* mosquito. *Anopheles* needs to survive a warm climate. Malaria therefore occurs only in the tropics. Malaria was endemic in Europe in mediaeval times, e.g. quartan malaria in swamps around Rome. The life cycle of parasites is within the gut of the *Anopheles* mosquito. The mosquito feeds on humans and delivers the parasites to the human bloodstream. The plasmodia get into liver and multiply in the liver cells. After 14–21 days, they infect the erythrocytes and multiply as merozoites, leading to the burst of the erythrocytes and infection of new erythrocytes. When the mosquito feeds on an infected human, it becomes infested and the cycles close.

There are four major species of *Plasmodium*:

- *Plasmodium falciparum* causing tropical malaria
- *Plasmodium ovale* causing tertian malaria
- *Plasmodium vivax* causing tertian malaria
- *Plasmodium malariae* causing quartan malaria

The designations tertian and quartan relate the periodicity of the fever bouts caused by *P. vivax*, *P. ovale* or *P. malariae*. *P. ovale*, *P. vivax* and *P. malariae* synchronize their propagation cycle so that the fever is induced by bursting of the merozoites every 48 h (the third day, "tertian malaria") for *P. vivax* and *P. ovale* and every 72 h (the fourth day, "quartan malaria") for *P. malariae*. *Plasmodium falciparum* causes the severest form of malaria; the fever is high and irregular. In further course there is organ dysfunction because the small blood vessels are obstructed by dysfunctional parasite-loaded erythrocytes. Without treatment there is further progression to shock and death.

Diagnosis is made by microscopic examination of the blood smears or the thick blood film stained with Giemsa showing ringlike parasites within the parasites.

Malaria is particularly dangerous to pregnant women. Acute malaria may lead to abortion or premature birth. The mortality in pregnant women with malaria tropics is higher than in that of non-pregnant individuals. Small babies develop easily

severe disease leading to organ failure and death. In areas in which malaria is endemic, adults may develop a kind of immunity, however being a reservoir of malaria.

Many measures to eradicate malaria have been taken worldwide. These included drying swamps, mosquito control using insecticides, insect repellents, bed nets, development of vaccines, etc. However, the parasites became resistant to insecticides and antimalarial drugs.

When travelling in the tropics, appropriate advice should be sought. Travellers are advised to take prophylaxis with antimalarial drugs that is tailored to the predominant species and its resistance to antimalarial drugs.

In pregnancy unnecessary travel to tropical destinations is generally not advisable. If it is necessary, prophylaxis is recommended but there may be side effects. All other measures, insect repellents, bed nets and covering bare skin with clothing, should be obeyed.

18.4.2 *Toxoplasma gondii* (Toxoplasmosis)

The protozoon *Toxoplasma gondii* is an obligate intracellular parasite. Found worldwide, *T. gondii* can infect all mammals, but domestic cats are the only known hosts in which the parasite can undergo sexual reproduction. Transmission of *Toxoplasma gondii* to human is either ingesting oocysts shedding cat faeces or by ingesting tissue cysts in uncooked meat. The third route of infection is spread of *Toxoplasma gondii* to unborn via the placenta during primary infection. When *Toxoplasma gondii* cysts are ingested, it spreads throughout the body and forms the microcysts in many tissues and also in the brain. There is scientific evidence that cerebral toxoplasmosis in small animals like rats alters their behaviour. Man is an accidental host.

Toxoplasmosis is a fairly common disease in Europe, particularly in Austria and France. The toxoplasma serology is positive in up to 60% of the tested persons. When primary infection occurs during the first trimester of pregnancy, there may be an abortion but otherwise serious harm like jaundice and underweight newborn. In the second trimester, the organ formation is nearly finished, but primary toxoplasmosis may cause deformities, encephalitis with hydrocephalus and calcifications. In the third trimester, primary toxoplasmosis may cause chorioretinitis with blindness and seizures. However, the primary infection may be asymptomatic in many cases. Only in 10–20% of immunocompetent infected persons have symptoms with swelling of the lymph nodes, particularly in the neck area, fever, malaise, headache and muscle pain. The disease is self-limiting. The toxoplasma disease is controlled by the immune response. There is very rarely an infestation of the retina, most commonly in children.

Diagnosis is made by serology. Primary toxoplasmosis in pregnancy has to be treated. The toxoplasma treatment has to be continued in the newborn during the first year.

Infection prevention is pivotal for seronegative, and thus pregnant women should be careful and obey the following rules:

- Avoid contact with cats, particularly young cats.
- Avoid working with cats' excreta.
- Do not eat raw meat or raw meat products like cold smoked ham.
- Do not drink raw milk.
- Wash carefully any vegetables and fruits that may be contaminated by cats.
- Perform gardening with gloves.
- Hand hygiene, especially before eating or before preparing food.

18.4.3 *Trichomonas vaginalis* (Trichomoniasis)

Trichomonas vaginalis is a flagellate protozoon. The occurrence is worldwide. The transmission occurs through unprotected sexual intercourse; thus trichomoniasis is a sexually transmitted infection of the vagina.

Many infections are asymptomatic but women are more symptomatic that men. Symptoms are yellowish foul-smelling purulent discharge from the vagina. Chronic trichomoniasis may cause infertility. Men are often asymptomatic (carrier) but may suffer from urethritis or epididymitis.

Therapy during pregnancy is always topical because the treatment of choice, metronidazole, cannot be used. The partner(s) should be always treated too.

18.4.4 *Giardia lamblia* (Giardiasis)

Giardiasis is a zoonosis. *Giardia lamblia* occurs worldwide in animals and humans. Infection occurs when *Giardia* cysts are ingested with contaminated water (surface water). In water, the cysts survive very long and are also resistant to chlorination. *Giardia* growth forms (trophozoites) live in the small bowel. Often the patients are asymptomatic. However, patients may have awkward symptoms like severe bloating, nausea, bulky stools, arthralgia and weight loss.

Diagnosis is made by detecting *Giardia* cysts in the faeces by microscopy.

The therapy of choice is metronidazole.

18.4.5 *Entamoeba histolytica* (Amoebiasis)

Entamoeba histolytica is the pathogen of amoebic dysentery. *Entamoeba histolytica* lives as growth forms (trophozoites) in the gut, but when shedded to the environment environmentally, stable cysts are formed. Transmissions occur with contaminated surface water, fruits and vegetables.

Entamoeba infections are most common in countries with poor water sanitation. Entamoeba infection ranges from bloody, slimy "raspberry jellylike" diarrhoea to bloody colitis (amoebic dysentery) with high fever and colicky abdominal pain. There may be extraintestinal infection manifesting in liver abscesses and peritonitis but sometimes also in the skin, lung and pericardium. Laboratory tests show

significant signs of inflammation with high numbers of leukocytes and a high C-reactive protein. Diagnosis is made by detecting amoebae and/or amoebic cysts in the faeces and/or serology. The treatment of choice is metronidazole (be careful in pregnancy) followed by an antimicrobial that is active against cysts (diloxanide furoate).

Suggested Readings

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Epidemiology

19

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Epidemiology is the study of the occurrence of diseases, their course and their distribution in a population. The term itself is derived from the Greek epi = "upon" and demos = "population".

- "Epidemiology is the science whose object is the distribution and propagation of diseases in human populations" [1].

The origin of epidemiology lies in loimology (study of pestilential diseases and plagues). Among them was understood the doctrine of detection, control and prevention of communicable diseases. The British physician John Snow recognized in 1854, on the occasion of a cholera epidemic in London, that this disease was not spread by fumes (miasmas), as was widely accepted at the time. Almost all sufferers got their water from a certain pump on Broad Street. This well had been contaminated by sewage with microorganisms in an attempt to flush the open, foul-smelling sewers into the Thames. A cholera epidemic with 14,000 dead was the result. John Snow was able to prove that the deaths centred around a water pump on Broad Street. After he put the pump out of operation, it came to a standstill of the epidemic. However, his theory was not recognized during his lifetime by the then scientists and doctors and confirmed only some years after his death [2].

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_19

With the increasing importance of chronic noninfectious diseases, the work of epidemiologists has also changed. Modern epidemiology also includes noninfectious diseases, their causes and risk factors (e.g. obesity, cardiovascular diseases, cancer).

The general aim of epidemiology is to describe/study the distribution of the incidence of diseases in a population by identifying etiological factors, providing data for planning and utilizing the knowledge gained for occupational or population health purposes.

Data Sources
Epidemiology draws its data from different sources:

- *Primary data*: Data collected specifically for examination purposes (e.g. health survey of the German Cardiovascular Prevention Study, Bundesgesundheitssurvey 1998).
- *Secondary data*: Obtained from primary data through modelling or processing steps. The majority of existing health-related data is secondary data (i.e. data on health insurance benefits, such as incapacity to work).
- *Causes of death*: Official statistics based on the death certificate. Only the main cause of death is included in the statistics. The reliability (reliability) of this data depends on care and knowledge of the underlying cause of death.
- *Types of illness*: Social security benefits, in particular incapacity for work, hospital diagnostic statistics and pension benefits due to occupational or occupational disability (only suitable as epidemiological morbidity measures).
- *Collection of notifiable diseases*: Epidemic law; due to various reporting obligations (illness, suspicion), limited data are available, which is also related to the problem of reporting discipline.
- *Disease register*: Registration of all persons suffering from a particular illness or who have died (regionally available for a few diseases in Austria). Examples: cancer registries.

19.1 Methods and Measures of Epidemiology

Descriptive Epidemiology: describes the disease pattern of a population as well as those characteristics that may be related to this distribution pattern. Here, no or only very fundamental statistics are performed; it is the description of the data in the foreground.

Question: Who? Where? What? When?

Analytic Epidemiology: results in hypotheses of disease development, which are being investigated in the population. For this purpose, statistical methods and mathematical models are used to obtain an interpretation from the data obtained. Here one can distinguish between qualitative analysis ("Are there indications of interrelationships between variables?") and quantitative analysis ("How strong are these relationships?"). This allows statements on causality of/between risk factors.

Question: Why? How?

19.2 Measurements of Epidemiology

In epidemiology, numbers are used either as *absolute numbers* (are not very meaningful because the reference value is missing) or as *relative numbers* (rates, the absolute number is related to a constant population, i.e. mortality, lethality, etc.).

The most important measures in epidemiology are:

- Prevalence
- Incidence
- Mortality
- Letality
- Morbidity

Prevalence is the number of all "existing" cases of a particular disease "at a given time". It is a measure of the incidence of disease *in a defined population* at a given time.

$$\text{Prevalence} = \frac{\text{Nr. of all existing cases of a particular disease at a specific point in time}}{\text{Nr. of all persons of the total population at risk at a specific point in time}}$$

Influencing factors:

- Number of new cases
- Disease duration
- Case definition (depending on diagnostics methods)
- Migration (inflow and outflow)
- Causes of disease

Variants:

- Point prevalence
- Period prevalence

Example: how many students of the "X" Faculty have a cold?
Population at risk: students of the "X" Faculty
Given time: today
Population: 40
People with cold: 10

$$\text{Prevalence} = \frac{10}{40} = \mathbf{25}\% \rightarrow \text{Prevalence of cold of the "X" Faculty students today is } 25\%.$$

The calculated measure is an example of descriptive epidemiology: the population and the desired characteristics are merely described, but no statements can be made, e.g. about the onset of the disease or the morbidity rate.

This type of prevalence is also called point prevalence because it is a single point in time. In contrast to:

$$\text{Period prevalence} = \frac{\text{Nr. of all existing cases of a particular disease at a specific period of time}}{\text{Nr. of all persons of the total population at risk at a specific period of time}}$$

Period prevalence measures the number of existing cases in a defined population over a predetermined period.

Incidence is the number of new cases of illness related to a specific number of persons (population) in a given period of time. It measures the new cases within a given period of time in a defined group of individuals who were free of the disease at the beginning of the observation period. The initially disease-free group is also called "population under risk". Within incidence, the cumulative incidence risk is to be distinguished from the incidence density.

$$\text{Incidence} = \frac{\text{Nr. of new cases in a period of time}}{\text{Population exposed to the risk in this period to time}}$$

Example: how many students of the "X" Faculty will have a cold in the next week?

Population at risk: students of the "X" Faculty

Given time: 7 days

Population: 40

People with new cold: 4

$$\text{Incidence} = \frac{4}{40} = 10\% \rightarrow \textbf{Incidence of cold of the "X" Faculty students is 10\% per week}.$$

The incidence rate represents the magnitude of morbidity within a population, as it takes into account the period during which disease-free individuals were "risk-exposed" to a disease.

Morbidity is the frequency with which a disease appears in a population. Morbidity can be an incidence measure (number of persons in a population who become ill (incidence)) or a period prevalence (number of persons who are ill at a given time from the morbidity rate; the disease probability can only be estimated).

Mortality is a measure of the frequency of occurrence of death in a defined population (e.g. 10,000, 100,000 persons) during a specified interval

$$\text{Mortality}(\text{crude death}) = \frac{\text{Nr. all deaths}(\text{year})}{1000 \text{ individuals in the population}}$$

$$\text{Mortality}\left(\text{cause-specific}\right) = \frac{\text{Nr.deaths attributed to a specific cause}\left(\text{year}\right)}{1000\,\text{individuals in the population}}$$

Letality (or *case fatality rate*) is the number of deaths over the number of sick with a specific disease. It is the proportion of cases in a designated population of a particular disease, which die in a specified period of time. Lethality represents a measure of risk. It is a better measure of clinical significance of the disease than mortality, and it is most often used for diseases with discrete, limited time courses, such as outbreaks of acute infections.

19.2.1 Standardization

In order to make a comparison between epidemiological rates, they have first to be standardized. Standardization is intended to "balance" distorting structural differences in the population and may, for instance, be applied for age, gender or other characteristics. Standardization by age is particularly prevalent, as information is usually available and age is important in most health problems.

Age standardizations based on a standard population are often used in cancer registries to compare morbidity or mortality rates. If different age structures are present in populations of different regions or in the population of an area over time, their mortality or morbidity rates are only limitedly comparable. For interregional or intertemporal comparisons, age standardization is necessary. Here, the reference population is the age structure of a reference population, the so-called standard population assumed. The age-specific mortality or morbidity rates of the reference population are weighted according to the age structure of the standard population. After age standardization, data from different years or regions can be compared with each other without causing any distortion due to different age structures. When interpreting age-standardized morbidity or mortality rates, it should be noted that they do not represent real (in the sense of empirically observable) information. Rather, they describe what the mortality or morbidity rates in the considered population would be if the reference population corresponded to the standard population, i.e. was abstracted from age structure-related effects.

19.3 Epidemiologic Studies

19.3.1 Cross-Sectional Studies

Indicators: the frequency of diseases (prevalence) and the simultaneous occurrence of risk factors or exposure parameters are recorded in one population at a time, so that—in contrast to the following case-control study—generally valid statements on the association between the diseases and the exposure, also expressed as relative risks, are possible. Relative risk is the factor by which the probability of disease increases (or decreases) under exposure. The statement of a cross-sectional study is descriptive.

Period: the duration of the study is relatively short; a time sequence (exposure → illness) cannot be proven. Especially with smaller populations, possible selection effects (i.e. avoidance behaviour of particularly sensitive persons in relation to hazardous substances or also the withdrawal from the region particularly affected) must be taken into account when interpreting the results.

Population: in contrast to the ecological study, individuals are directly measured so that the relationship between the diseases and the exposure to other factors can be controlled.

19.3.2 Case-Control Studies

Indicators/Population: in this type of study, a group of previously identified patients is retrospectively examined for the presence of the risk factors and the exposure compared to a non-affected control group. From the relative frequency of exposure in patients or non-sufferers, the so-called odds ratio can be taken as an estimate of the relative risk of the disease under the exposure. This type of study allows for evidence of causality.

Period: defined period (prospective or retrospective).

Especially in cancer epidemiology, this type of study is very often used, because the studies provide relatively fast results compared to the long latency of the diseases; furthermore case-control studies should be conducted with huge observational numbers in order to ensure statistically proved statements. However, a serious disadvantage of these studies lies in the information about the true exposure status of cases and the control persons in the past, which is often distorted by various factors.

19.3.3 Cohort Studies

While in the case-control study the direction of the disease is exposure, in the cohort study, it is always exposure to the disease.

Period: In a (prospective) cohort study, a population that differs in the exposure status of individuals is monitored over a defined period of time, for example, to detect the onset of disease as a function of exposure status.

Indicators: Incidence (the incidence of new diseases) and mortality from a particular disease (for subgroups of the population, e.g. for “heavily exposed”). From the possibilities of statement, this type of study, in which parallel exposure status and disease probability are considered, is the most versatile, provided that the observation periods are sufficiently large enough to be able to show effects at all.

Special case retrospective cohort study: data on the course of exposure development and the target diseases for the study population are already available and will be analysed retrospectively. However, this type of study is not flexible in the study design; it is not possible to easily incorporate new exposure parameters, disturbance

variables or target diseases into the observation phase (since the data were collected in the past), so this study type also requires suitable exposure and registry data. The statements of a cohort study are mostly incidence and causal statements.

Population: A defined population (e.g. groups, families, villages, regions) is subdivided into exposed and nonexposed, and both groups are compared for the proportion of already "ill" and "not ill".

While in the case-control study the direction of the disease is to the exposure, in the cohort study, it is always from the exposure to the disease.

19.3.4 Intervention Studies

The starting point of an intervention study is a cohort study, whereby in a subpopulation the exposure status has changed due to an external intervention in the observation period, so that the effect of this intervention on the development of the target diseases can be observed (e.g. comparative studies between real drug and placebo). This type of study comes closest to an experimental study (control and control of key exposure parameters).

19.4 Analytical Measures

19.4.1 Relative Risk

Relative risk (RR) can be calculated from cohort studies showing the disease incidences of exposed and unexposed persons. For this purpose, a contingency table is created with the absolute values of the respective group.

	Disease		
Exposure	Yes	No	
Yes	a	b	a + b
No	c	d	c + d
	a + c	b + d	

The risk of the exposed cased is R(EX) = a/a + b (cumulative incidence in the exposure group).

The risk of the not exposed cases is R(NEX) = c/c + d.

If both values are divided, one obtains a measure indicating the probability of an event occurring in an exposed group to the probability of the event occurring in a comparison, nonexposed group.

The relative risk is:

$$\mathrm{RR} = \mathrm{R}\left(\mathrm{EX}\right) / \mathrm{R}\left(\mathrm{NEX}\right) = \left(\mathrm{a} / \mathrm{a} + \mathrm{b}\right) / \left(\mathrm{c} / \mathrm{c} + \mathrm{d}\right)$$

Exercise: do people with hypertension have an increased risk of coronary heart disease? This involves comparing a control group with an experimental group and investigating whether there is any effect to the study group. This effect is called "relative risk".

	Coronary heart disease		
Exposure	Yes	No	
Yes	43	1475	1518
No	69	11,635	11,635
	112	13,153	

19.4.2 Odds Ratio

Odds ratio (OR) is defined as the ratio of the probabilities (odds, chances) of an event occurring in one group to the probabilities of it occurring in another group. Odd ratios show the correlations between exposure and disease in case-control studies.

Odds = "Chances"; Odds Ratio = "relative Chances"

OR is very similar to the relative risk, but does not include any incidence, but rather prevalence differences between exposed and nonexposed persons. It is used to figure out if a particular exposure is a risk factor for a particular outcome and to compare the various risk factors for that outcome.

	Disease		
Exposure	Yes	No	
Yes	a	b	a + b
No	c	d	c + d
	a + c	b + d	

$$OR = a^{*}\, d / c^{*}\, b$$

(Measure of the strength of a difference between groups → sets a relation between odds of exposed and not exposed groups)

- Relation between ill and not ill under exposure
- Relation between ill and not ill with no exposure

Odds ratios can therefore be interpreted as a measure of interrelation:

- OR = 1 means that there is no difference in odds.
- OR > 1 means that odds of the exposed group are higher.
- OR < 1 means that odds of the exposed group are lower.

19.5 Outbreak Management and Basic Epidemiology

By definition, an outbreak is the cumulative occurrence of infectious diseases where an epidemic link is likely or suspected. Outbreaks can occur in the form of:

- *Pandemic*: limited in time, spatially unlimited (e.g. influenza during the winter months)
- *Endemic*: unlimited in time, spatially limited (e.g. norovirus within a nursery)
- *Epidemic*: temporally and spatially limited (e.g. cholera within several neighbourhoods)

Sporadic individual cases of illness (for instance, individual norovirus sufferers in some hospital wards) are not an outbreak.

The goal of an outbreak investigation is to quickly identify the cause(s) and prevent further transmissions. Outbreaks are usually recognized by meticulous healthcare workers. Eighty percent of all reported outbreaks are no outbreaks, but 80% of all outbreaks are only detected by scrupulous reporting and tracking!

The basis of outbreak management is to determine whether, in the event of an outbreak, the cases have a common cause or source. The "tools" of outbreak management are descriptive and analytical epidemiology, microbiological examinations and, last but not least, the use of common sense. An outbreak investigation must be structured and conscientious. The steps of such an outbreak investigation are generally structured as follows as soon as the notification of an unusual incidence of disease cases or MDRO comes in:

1. Prompt general control measures.
2. Confirm outbreak.
3. Form outbreak team.
4. Site visit.
5. Case definition (secure diagnosis).
6. Determine cases (line list).
7. Collect data (time/place/person).
8. Hypothesis formulation.
9. Analytical study on hypothesis.
10. Targeted control and prevention measures (detection of infection source).
11. Create a report.
12. Surveillance.

The creation of an epidemic curve is an instrument for the visualization of the temporal-/spatial-/population-related relationships of the outbreak. Such a curve is a visual aid to document and track the course of an outbreak. The curve can be easily created by pen and paper, and no complicated technical tools are necessary.

Special outbreak programs are available, which are a useful tool, especially in pandemics, and the creation of a Microsoft Excel document to track the progression of increased prevalence of infection is often used (see Example).

				x				x	10 cases
				x					
				x					
			x	x					
			x	x					
	1	2	3	4	5	6			
	2017								

Example: episodes of *Staphylococcus epidermidis* isolated in blood cultures from Ward X (January to June 2017)

On the basis of the distribution pattern of the epidemic curve, the nature of the outbreak can sometimes already be recognized as in Fig. 19.1.

19.5.1 Case Definition

A case in an outbreak is defined by:

- *Place* (ward, OP, ICU, etc.)
- *Time* (day, month, admission, microorganisms, etc.)
- *Person* (gender, age, disease, etc.)

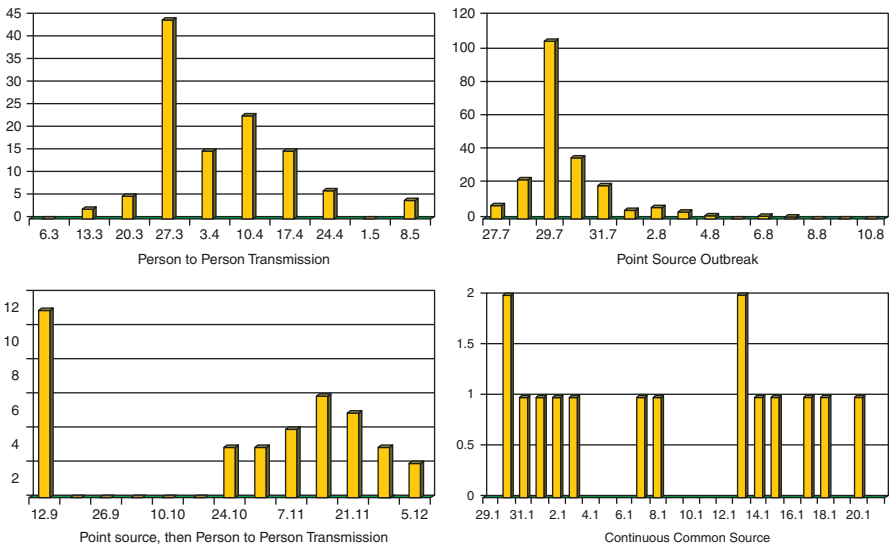

Fig. 19.1 Possible distribution pattern of the epidemic curve

19.5.1.1 Time-Person-Place

At the end of an outbreak investigation, the event is analysed retrospectively by the outbreak management team. Gained information should be used to implement control and prevention measures or to complement existing measures. An *outbreak report* should be prepared in which the case and the procedure for examination, diagnostics, evaluation, etc. are described in detail. The final evaluation should include deficit analysis and definition of future prevention strategies.

Appropriate questions are as follows:

- Was a timely detection of the outbreak ensured?
- Did the breakout management team and communication chains work efficiently?
- Were the immediate targeted measures correctly taken?
- Have any further illnesses occurred despite the measures taken?
- Was an efficient cause clarification ensured by hygienic, microbiological and epidemiological investigations?
- Was a causal clarification of the sources of infection and chains of infection ensured?
- Which prevention strategies have been proven effective?
- Which prevention strategies had to be modified or newly established?

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Basic Immunology

20

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The human body's defences against microbes consist of the barrier function of the surface (skin), normal organ function (respiratory, intestinal) and immune system. The immune system is a very complex defence systems consisting of multiple components that are redundant and have sophisticated pathways of activation and regulation to ensure a rapid and effective immune response to any invading enemy. It is daily confronted by hundreds of invading organisms.

The immune system consists of a cellular and a humoral component. There is an innate and acquired immunity and specific and non-specific immunity. For cellular immunity including the white blood cells (leukocytes), subgroups are granulocytes, lymphocytes and monocytes. Granulocytes are a type of white blood cells with granules in their cytoplasma, these help to "eat" invading or damaged cells and their subsequent lysis. There are three types of granulocytes: neutrophil, eosinophil and basophil.

Lymphocytes differentiate to T-lymphocytes and B-lymphocytes. The lymphocytes are matured in the thymus. The T-lymphocytes have several subsets (T helper ("CD-4"), T-suppressor, natural killer cells etc,,,) with distinct functions. The B-lymphocytes are matured in the bursa near the appendix. When confronted with a foreign antigen, B cells mutate to plasma cells. Plasma cells then produce antigen-specific antibodies called immunoglobulins. They are part of the humoral immune response. The humoral immune response is done by immunoglobulins.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_20

Immunoglobulins (Ig) are classified into IgG, IgM, IgA, IgD and IgE. Immunoglobulins consist of a fixed component and a variable region that is antigen specific. The primary antibody response follows the inclusion of the antigen by formation of IgM in the first week. After approximately 7–14 days, the production of IgG antibodies starts.

Macrophages (monocytes) are eater cells. Their function is the recognition, presentation and elimination of microbes. Thus, macrophages contribute to the more effective recognition of antigens by T-lymphocytes and improve immune response and the memory function. There is a special form of macrophages, the dendritic cells of the skin that are masters of antigen recognition and presentation. Macrophages migrate in the body. They are degraded, especially in the spleen. Macrophages are part of the non-specific immune response.

The unspecific immune response is carried out by eater cells ("phagocytes"). Granulocytes, macrophages and monocytes have also phagocytic function. Additionally, there is another component of the immune system contributing to better antigen recognition, the so-called serum complement. The complement consists of many different protein components that prepare invading pathogens for detection and efficient eliminations by the other components of the immune system.

Innate immunity has been explored only in the last decades. This is a non-specific immune response. It is carried out by the so-called toll-like receptors (TLR 1–12) that recognize microbial structures and activate the immune function.

Immunizations

21

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Definition
Immunizing serves to induce a specific immune response or immune modulation to protect against a disease-causing agent.

21.1 What Can Be Achieved Through Vaccination?

- Individual protection: Protection of the vaccine from illness.
- Herd immunity: Protection of the unvaccinated by reduced pathogen load in vaccinated persons, e.g. influenza or pneumococcal vaccination in children also reduces the incidence rates in adults and the elderly, as they are less frequently infected by vaccinated children.
- Prevention of high-penetration epidemics: Conversely, epidemics may occur with a decrease in vaccination coverage, e.g. measles epidemics in Europe in recent years due to vaccination rates below 90%.
- Eradication of infectious diseases: An example of global eradication of disease through global vaccination programmes is the smallpox disease that has been eradicated worldwide since 1980.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_21

21.2 Active and Passive Immunization

In principle, defence processes as a result of contact with a pathogen in which it comes to a protective immune response can be described as active immunization:

Disease (immunity + risk of secondary disease/damage, e.g. encephalitis after measles infection 1:1000, testicular inflammation postpubertal after mumps infection 20–50 per 100 cases)

Vaccination = application of a vaccine (= preparation in which the pathogen is so altered/attenuated that it is no longer pathogenic but leads to immunity) with the development of a specific immunity.

Active immunization in terms of vaccination leads to:

- Stimulation of own antibody production
- Start of protection after a few weeks
- Duration of protection mostly long (years)
- Mostly immunological memory
- Examples: measles, polio, tetanus, etc.

Passive immunization (*not* a vaccine!):

- Application of preformed antibody
- Homologous or heterologous, diaplacental
- Immediate protection after exposure (e.g. rabies, measles, varicella)
- Duration of protection limited by degradation of the antibodies

21.2.1 Simultaneous Immunization (Active/Passive)

Simultaneous application of vaccine and antibody preparation is only possible with inactivated vaccines; attenuated vaccines are inactivated by antibody preparations. This method combines advantages of active and passive immunization. Examples of vaccines: tetanus simultaneous, rabies.

A distinction is made between attenuated vaccines and inactivated vaccines.

21.2.2 Attenuated Vaccines

In contrast to the inactivated vaccine, an attenuated vaccine contains small amounts of living and reproducible pathogens. The pathogens are attenuated so that they still multiply, but can no longer trigger the disease in immunocompetent persons. Attenuated vaccines can be administered as a vaccine or as an oral vaccine. An advantage of these vaccines is that protection after a primary immunization usually lasts for life. For immunocompromised persons, however, attenuated vaccines are not or only very limited suitable. Pregnancy is a

contraindication for these vaccines (measles, mumps, rubella, varicella). Furthermore, a reliable conception protection is recommended for 3 months after the vaccination.

Viral	Bacterial
Measles	Typhus
Mumps	Cholera
Rubella	BCG (Bacillus Calmette-Guérin)
Varicella	
Rotavirus	
Yellow fever	
Polio (oral)	

21.2.3 Inactivated Vaccines

There are several subgroups of these vaccines, all of which are either whole or killed pathogens or parts of them, but in any case no more fertile material is present. Subgroups include toxoids (diphtheria, tetanus), whole cell vaccines (polio, hepatitis A, TBE), subunit vaccines (hepatitis B, influenza, pertussis) and polysaccharides (meningococci, pneumococci, haemophilus, typhus).

Viral	Bacterial
Hepatitis A	Pertussis
Hepatitis B	Meningococcus
Influenza	Pneumococcus
FSME	Haemophilus influenza
Rabies	Cholera
Polio “Salk”	
Japan encephalitis	

21.3 What Does Vaccine Success Depend Upon?

- Immunization scheme/immunization intervals
- Type of vaccine (attenuated/inactivated)
- Safe storage (temperature control)
- Safe administration (single use materials)
- Vaccination technique
- Type of application: i.m. vs. s.c. or orally (note the package insert)
- Inactivated vaccines: i.m. or s.c.; attenuated vaccines, mostly s.c.
- Application site:
- Adults: Regio deltoidea
- Children: M. vastus lateralis

21.4 Contraindications

Not considered as contraindication (=go ahead with vaccination):

- Mild illness with subfebrile temperatures (up to 38 °C), mild diarrhoea in an otherwise healthy child, skin diseases (e.g. eczema)
- Chronic diseases of the heart, liver, lung and kidney, stable neurological diseases
- Antimicrobial therapy (antibiotics) or administration of low doses of corticosteroids or locally
- Applied steroid-containing preparations, anticoagulant drugs
- Convalescence phase after illness

Vaccination also possible in the case of:

- Preterm birth (<37th week of gestation: vaccination by chronological age)
- Possible or known exposure of the vaccine with infectious diseases
- Allergies, asthma, other atopic diseases or allergies in the relationship
- Penicillin allergy (no vaccine manufacturer currently uses penicillin for production)
- Sudden infant death syndrome (SIDS) in the family history

Postponable contraindications (=should not be vaccinated at the given time):

- Patient has high fever (over 38 °C).
- Severe inflammation (bout of a rheumatic disease).
- Patient has an unspecified immune system disorder. Severe disruption of the haematopoietic/immunological system (e.g. shortly after the chemotherapy cycle).
- Patients taking medications contraindicated for vaccination (e.g. cortisone depending on the dose: up to 20 mg cortisone per day is not expected to have a significant effect on vaccinations).

21.5 Immunizations During Pregnancy

Inactivated vaccines may be administered during pregnancy; however, postponing vaccinations to the second or third trimester is advisable as a general precautionary measure.

Attenuated vaccines should not be used deliberately during pregnancy (the risk of vaccination is more theoretical—there is no teratogenic risk).

21.6 Control of Vaccine Success

Possible	Not routinely possible
Measles	Pneumococcus
Mumps	Meningococcus
Rubella	Influenza
Polio	Japan B encephalitis
Salk	Pertussis
Tick-borne encephalitis	Tuberculosis
Hepatitis A, B	Typhus
Rabies	Cholera
Diphtheria	
Tetanus	

21.7 Vaccine Side Effects

Vaccination reactions: (harmless) complaints that occur in the context of the immune response and have no pathological significance.

Vaccine side effects are differentiated into:

- Caused unwanted reaction (direct vaccine side effect)
- Triggered adverse reaction (triggering of "latent" diseases)
- Unwanted reaction due to product error
- Accidentally coincident diseases without causal relation to vaccination

Vaccination reaction: possibly vaccine disease (harmless complaints in the context of the immune response) is in the percentage range and is easily detectable and quantifiable in clinical trials.

Examples: Local reaction in the injection site, such as swelling, redness and muscle pain.

Vaccination complication: temporarily in need of therapy; lasting damage is in the tenth range (1:1 million), and they are detectable only in very large clinical trials or occasionally not detectable.

Examples: Paresis after OPV vaccination.

21.8 Onset of Vaccine Reactions and Symptoms

Attenuated vaccines (e.g. MMR, varicella)

- Since the vaccine antigens are viable, attenuated pathogens, the timing of the vaccine reaction is delayed and depends on the incubation period of the pathogen. The symptoms correspond to the "original disease" but are greatly attenuated.

  Inactivated vaccines (e.g. diphtheria, tetanus, pertussis, TBE, hepatitis)

- The vaccine antigens are inactivated pathogens or toxoids or single antigens. The vaccination reaction occurs already after 6–48 h depending on the application. It presents as local reactions, general malaise and fever.

More information about immunization protocols can be found online at http://www.who.int/topics/immunization/en/. Each country sets its own vaccination protocol that is subject to ongoing revision and updates. The WHO "Question and Answer" pages which also dispel myths on vaccinations to help HCWs educate patients and parents of the importance of vaccination is worth reading: http://www.who.int/features/qa/84/en/.

Household Hygiene

22

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Not only hospitals are at increased risk of infection, but also the home environment can serve as a source of (cross) infections. In order to minimize the risk of infection at home, it is crucial to identify the critical hygienic issues and to know which steps and measures can disrupt the spread of harmful bacteria.

> Household hygiene is the sum of all measures to prevent infections/communicable diseases and their transmission in the home environment.

For proper household hygiene, it is important to identify and eliminate the sources of infection in order to reduce the number of living microorganisms to a level that is no longer harmful to health.

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_22

22.1 Kitchen Hygiene

Much of the case of food poisoning in Europe occurs in the home environment. Often, cross-contamination via the hands or preparation surfaces is causally involved. Appropriate measures should be taken in all areas of food production and processing in the kitchen to enable hygienic work. A close attention should be paid by purchasing the food (i.e. damaged packaging, unclear or missing labels); however most cases of infections can be attributed to inadequate preparation and incorrect food storage. The basic requirement for good kitchen hygiene is to be aware of the possible sources of infection and pathways in order to be able to interrupt contamination cycles. One differentiates between primary and secondary contaminations. Different pathogens have different reservoirs, especially raw foods such as unpasteurized milk or raw meat. Primary contaminations are usually not sufficient for a disease. Only by improper storage (i.e. without cooling) can it come to massive microorganism contamination of the food.

Food should not be cleaned with detergents, as residues can remain on them, which are then eaten. Here, the cleaning under running drinking water is sufficient, whereby dirt is removed and the number of microorganisms is reduced. In areas with unclear hygienic conditions (e.g. on vacation), fruit, but also vegetables that are eaten raw, should be peeled or boiled. Also food of animal origin (e.g. poultry or fresh fish) should be cleaned under running water before preparation.

Through basic cleaning, dirt particles (especially fat and protein) are normally solved. Over 90% of all surface microorganisms are removed. However, caution is advised when using special cleaner concentrates in the sanitary sector. A mixture of acidic and alkaline detergents is dangerous because of possible gas formation. Warnings regarding the formation of toxic gases or corrosive effects must be strictly observe.

An addition of disinfectants is not necessary when cleaning the kitchen. In an average household, the largest source of microorganisms is the refrigerator with over 11 million microorganisms per cm^2, followed by the flush sponges with 4 million microorganisms per millilitre of wetting water (of which 2500 can cause diarrhoea). The kitchen floor has 10,000 microorganisms/cm^2 and the toilet only 100 microorganisms/cm^2. The kitchen thus offers optimal conditions for the spread of microorganisms.

In the kitchen, the cleaning must be done carefully and immediately after handling food. Used work boards and kitchen tools should—if possible—be cleaned in the dishwasher. Wooden boards should be regularly embedded with nourishing oil to avoid microlacerations. The cleaning of work surfaces with hot water and commercial household cleaning products is sufficient.

Wooden Board Wood is not a closed, dense material. It can absorb and release water like a sponge. Wood is constantly moving and the dimensions are getting bigger and smaller. This leads to cracks in the wood. In addition, long-lasting high humidity damages the wood. On this basis, fungi and other microorganisms thrive very well and decompose the wood over time (which is why wood rots over time on

damp forest soil). The cleaning of wooden boards in the kitchen should be done with warm water. In order to protect the wood from permanent moisture, boards should be regularly embedded with nourishing oil to prevent swelling of the material. Care can reduce the occurrence of scratches, cracks and imperfections, which can easily penetrate microorganisms.

Perishable foods must be cooled or frozen immediately. The refrigerator should be set to a temperature as low as possible below 7–8 °C, the freezer (or chest) to −18 to −20 °C. The main propagation range of bacteria between 10 and 60 °C must be crossed as quickly as possible.

If poultry or meats are processed, it would be advisable to wash the soiled dishes at higher temperatures (above 60 °C). If it is necessary to dry, paper towels should be used. The available for cleaning purposes, often even heavily soiled dishes or sponge cloths, are to be regarded as more hygienic vulnerabilities in dealing with food.

22.2 Hand Hygiene

In addition to a basic cleaning of surfaces, good hand hygiene is also a major factor in maintaining cleanliness at home. If regular hand disinfection can be avoided at home, hand washing with soap plays a central role in domestic hygiene because it can strongly reduce the risk of microorganisms' transmission.

Handwashing should be executed:

- After using the toilet
- After contact with pets and their utensils
- After contact with other people
- Before the meal
- Before contact with food and during the preparation of food
- After contact with body fluids
- Visible pollution
- Before administering medication
- Before and after changing federations
- Before inserting contact lenses
- After activities involving contamination (i.e. cleaning the toilet, preparation of raw meat and eggs)
- After playing on the floor or outdoors

22.3 Breast Milk, Milk and Formula Nutrition

Germs can grow quickly in breast milk, breast milk residue remaining on pump parts as well as milk formulas. Both products replacing mother's milk (infant formula from birth onwards and follow-up formula over the age of 6 month) are not sterile. Although infections from formula or breast milk are rare, powdered feed

Table 22.1 Actions to be implemented in order to avoid milk contamination

Step	Action
Milk preparation	Only use cold, fresh tap water which has to be boiled at least at 70 °C[a]. Do not leave water cooling more than 30 min
Storage[b]	Store the milk for a maximum of 2 h at room temperature, 4 h in bags with cooling elements or 24 h in the refrigerator at ≤4 °C[c]
Bottle and teat preparation	Clean both the empty bottle and the teat with tap water immediately after the meal. Any milk residue left has to be thrown away. Dry bottle and teat on a clean cloth placing them upside down

[a]Warm water can promote microorganisms' proliferation
[b]A high hygienic standard can be maintained only by preparing the milk immediately before the meal. Although storage of prepared milk meal is possible, the risk of infection is lower when the milk meal is freshly prepared
[c]A rapid refrigeration can minimize the risk of activation of any bacterial spores

products as well as milk pumps can be contaminated with bacteria such as *Salmonella* spp., *Enterobacter sakazakii* and *Bacillus cereus*. *Cronobacter* spp. may also form biofilms on feeding equipment which can inhibit cleaning as well as being source of contamination. This can be especially serious in the first 2 months of life and in preterm, immunocompromised or low birth weight infants (Table 22.1).

The risk of infection can be reduced by:

- Milk products should not be frozen as freezing may cause irreversible physical changes.
- Milk pump parts that come in contact with breast or breast milk should be separated and cleaned as soon as possible after pumping.
- For risk group babies (i.e. neonates <3 months, preterm infants or immunecompromised children), an extra germ sanitation (5 min boiling water or dishwasher with heating drying cycle or sanitizing setting) is recommendable at least once a day.
- Although pasteurization of infants' feeds is a matter of debate in the scientific community, this is carried out only in some healthcare setting and for specific risk group of patients. Literature does however support the use of pasteurized donor breast milk especially for preterm infants.

Pasteurization is the brief heating of liquid foodstuffs to temperatures of at least 75 °C (classic Pasteur method) to 100 °C (high pasteurization) to kill microorganisms. It serves to extend the shelf life of food. In the pasteurization, milk is heated for 15–30 s at 72–75 °C and then immediately cooled again. Pasteurized milk remains stored unopened at 6–7 °C for about 6–10 days almost unchanged.

22.4 Toilet and Bathroom

Normal, commercial cleaning products are completely sufficient to ensure adequate cleanliness. Washbasin, bath, shower cubicle, toilet basin, toilet seat and lid, toilet brush should be cleaned more often. Towels should often be replaced and hung up

to dry quickly. In a 95 °C wash, any microorganisms that have settled in the washing drum can be killed.

If a family member suffers from a bowel or fungal disease, its textiles should be washed at high temperatures (above 60 °C) and separately. Personal items like towels, washcloths or hair ornaments should not be shared.

22.5 Housing Space Hygiene

The indoor air should be free from doors and pathogens. Bacteria, yeasts, moulds and fungi are spread by sneezing or coughing but present a low risk of infection in healthy people. The contamination with microorganisms can be avoided by good ventilation and wet cleaning.

22.6 Risks Groups

For persons with a wreaked immune system, special attention should be given to home hygiene. Due to their defensive weakness, they are exposed to a higher risk of disease due to environmental microorganisms. People who fall into this group are:

- Newborns
- Babies
- Old people
- Pregnant women
- Persons with weakened immune systems
- Asthmatics
- Allergics
- HIV carriers

Approximately 20% of the population falls into this risk group. For babies, dishes, cooking spoons, vials and teats must be well cleaned and boiled. Many mothers lick the pacifier before giving it to the baby. This can be transmitted to the mother's existing oral thrush (fungal disease caused by *Candida albicans*) on the child.

Factors such as age and certain underlying diseases associated with changes in the immune system, but also problems such as incontinence expose individuals to an increased risk of infection. Incontinence requires careful laundry hygiene to prevent cross-contamination. Around 850,000 Austrians and 150,000 Austrians are affected by urinary incontinence. Older women are twice as likely to be affected by urinary incontinence as older men. Cancer patients are at increased risk of infection due to their disease. Individuals who have just been discharged from the hospital (especially transplant patients) also need special care in terms of the hygiene of their environment.

Even if *pets* are healthy, they can act as transmitters of *Salmonella*, *Campylobacter*, MRSA and *Toxoplasma gondii*. Especially cats and dogs can haul pathogens into

the house with their paws and contaminate surfaces for food preparation and the floor in the kitchen. Infection (such as *Listeria*) with a pathogen can lead to irreversible damage to the unborn foetus, damage to maternal health or abortion in *pregnant women*. Particularly dangerous for pregnant women are pets (e.g. cat), which can be carriers of toxoplasmosis. Meat and fish dishes are good to cook. Crude milk should be boiled and not minced meat (such as *Campylobacter*, *Salmonella*). In addition, pregnant women should refrain from consuming raw milk products such as soft cheese and the consumption of cheese rind (*Listeria*).

22.6.1 Moulds

Moulds are simple microorganisms that thrive almost everywhere, provided the climatic conditions are met. Among the best known representatives are the *Penicillium* and *Aspergillus* species. Mushrooms propagate via spores, which release them into the atmosphere as fine, usually invisible dust. They are taken via the respiratory tract and can lead to infections or allergic reactions. A mould allergy is a hypersensitivity to the spores of mould or their metabolic by-products. The allergenic effect of mould spores depends on the individual predisposition as well as the allergenic potential of the spores. The mould-related allergies include:

- Allergic rhinitis
- Chronic rhinosinusitis (CRS)
- Allergic fungal sinusitis (AFS)
- Asthma, exogenous allergic alveolitis (EAA)
- Allergic bronchopulmonary aspergillosis

Under the influence of mould-containing aerosols, short-term *irritations* of the skin, conjunctiva and mucous membranes are described. Skin irritations such as skin dehydration, itching and rash have been reported as a result of mould exposure (allergic dermatitis). Irritation and inflammation of the eyes can also occur as a result of mould contamination (keratitis, conjunctivitis). Additional symptoms include hoarseness, coughing, difficulty breathing and symptoms of lower respiratory tract mucous membranes associated with flulike general symptoms such as fever, chills, headache and body aches.

Mycoses (infectious diseases caused by fungi) are rare and are most likely to be inhaled. Local infections are limited to the portal of entry; systemic infections spread from there to the bloodstream in other organ systems. The infectious effect plays a role especially in immunocompromised humans:

- After organ transplantation
- Cytostatic treatment of tumours
- For chronic lung diseases, diabetes and serious infections

Moulds, as well as decay products, from their cell wall on the skin and mucous membranes by the release of inflammatory mediators from epithelial cells and

macrophages have *toxic effects. Mycotoxins*, e.g. aflatoxins, are a common cause of food poisoning when mouldy foods are consumed (nuts, cereals, etc.). However, they can also cause nonspecific health problems such as headaches and body aches, irritation of the mucous membranes and increased susceptibility to infection via the indoor air.

Sick Building Syndrome (SBS): those affected feel ill due to a "pathogenic building". Around 10–20% of the employees of a building have nonspecific complaints (e.g. respiratory complaints, mucosal irritation, hoarseness, headache, fatigue, difficulty concentrating, depressive states, allergic skin reactions diminished efficiency, general discomfort, inhalation allergies such as constant cold and asthmatic complaints), which quickly return after leaving the building ease up. Possible causes may be pollutants that occur in the indoor air.

Suggested Readings

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Disinfestation

23

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Disinfestation is the control or destruction of pests on an abiotic basis, i.e. by mechanical, physical or chemical procedure methods. The term "pests" primarily comprises all ectoparasites found in humans or domestic and farm animals. The term systematically covers various animals (e.g. lice, cockroaches, moths, rats). The relevant pests cause harmful effects on health or property. In hospitals, pests like head lice and itch mites can by themselves be responsible for disease, but they can also act as vector for pathogenic microorganisms (flies, cockroaches, pharaoh ants). Combat usually requires the use of chemical agents, but a basic knowledge of the biology of pathogens and carriers is essential to ensure the success of effective prophylactic measures.

Pests are classified into different groups:

- *Hygiene pests*: Transmitting diseases via various contacts (vector characteristic) causes allergies (e.g. rats, mice, flies).
- *Storage pests*: Cause damage to food that becomes inedible (e.g. flour moth, black and weevil).
- *Material pests*: Infestation of wood, leather, textiles, etc. (i.e. clothes moth, termites).

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_23

- *Nuisance pests*: Insects that are not hazardous to health or harmful to humans but whose presence is perceived as a nuisance (i.e. ants, silverfish, hornets, spiders, woodlice).
- *Bloodsucking pests*: Term for insects that sting humans and pets and feed on their blood (e.g. fleas, lice, bedbugs, ticks).

Zooanthroponoses: The infection is only transmitted from animal to humans.

Anthropozoonoses: The infection is almost exclusively transmitted from humans to animals.

23.1 Overview of Important Types of Parasites Found in Hospitals

23.1.1 Lice

Three species of the louse parasitize on humans: louse (*Pediculus humanus humanus*), head louse (*Pediculus humanus capitis*) and pubic louse (*Phthirus pubis*). The occurrence of the clothes louse has become rarer in the past decades, but head and *pubic louse* louse are still widespread. All lice stay on the host during their developmental phase (about 3 weeks) as they depend on regular blood uptake. The clothes louse lives mainly between the body and underwear, as it deposits its eggs (nits) on fabric fibres. Head and pubic lice lay their eggs in the hair: the head lice are sitting in the hair of the head as well as (rarely) in the beard and armpit hair. The *pubic louse* lives almost exclusively in the pubic hair and is transmitted almost exclusively during sexual intercourse.

23.1.1.1 Disease Transmission

Lice can transmit pathogenic microorganisms (i.e. *Rickettsia*, *Borrelia*), but today they no longer play a role in Central Europe as vectors. Their medical relevance lies in the changes in the skin, which can lead to secondary infections in case of heavy infestation. (And lice infestation often brings a psychological burden with it.) The bacteria pass the blood sucking on the saliva of the louse in the bloodstream of humans. The louse, through its legs and body, can also excite human sources of infection from one infected source of skin to another. The diseases transmitted by lice include typhus (*Rickettsia prowazekii*), relapsing fever (*Borrelia recurrentis*) and Wolhynian fever (*B. quintana*).

23.1.1.2 Control

Combating the clothes louse is based primarily on regular linen change and on garment laundry at least 60 °C. These temperatures kill both lice and nits as they are almost entirely in the wash. Lice can only survive 2 days without blood meal at temperatures between 25 and 30 °C, and even at cooler temperatures of 10–20 °C, they survive up to 7 days in starvation. Thus, there is no need to keep the rooms empty if the rooms are briefly overheated or blocked. Warm, dry air of 45 °C kills lice within an hour, as well as freezing at −10 to −15 °C over a day. For chemical disinfection pyrethrum or pyrethroid preparations in the form of pump sprays are suitable, with which clothes, bedding, etc. are treated. In the case of ambulatory patients (especially homeless people) who are being deloused, a chemical delousing must be carried out if a complete change of clothing (including shoes) is not possible.

Control of the head and pubic louse (and their nits) can be done mechanically (lice comb), chemically (shampoos) or medicinal (oral). Simple shampooing is not enough to remove lice and nits. For a successful mechanical removal using a louse comb, the hair must be combed out 2–3 times a week (over a period of several weeks). Local lice products (e.g. shampoos) have a toxic effect on the lice nervous system and are classified as insecticides. There are several possible drug classes to achieve effective delousing. In a single hair wash with special louse shampoos, usually up to 80% of lice are already killed. However, since these substances do not affect the louses, the treatment must be repeated several times. After 8–10 days, all lice have hatched; at the latest then, the treatment should be repeated.

23.1.2 Flies

Various representatives of the real flies (Muscidae), blowflies (Calliphoridae), flies (Sarcophagidae), fruit flies (Drosophilidae), and horseflies (Tabanidae) are classified as hygiene pests.

23.1.2.1 Disease Transmission

Flies can carry pathogenic microorganisms by staying on excrements, wounds, spoiled food and (animal) corpses. During food intake, they often vomit parts of the intestinal contents or expel droppings. The females of some types of fly deposit their eggs or first larvae in wounds or in the genital and anal areas and can cause venom (myiasis). The fly maggots penetrate into the wounds or body cavities and feed on necrotic tissue. Maybe even healthy tissue can be affected.

23.1.2.2 Control

Since flies always enter the room from outside, the possibilities of entry must be prevented. Where windows must be opened, a fly net has to be attached. This is

especially true for hospitals (especially intensive care units and infection departments), kitchens and prospect rooms. All materials that attract flies (faeces, waste, contaminated dressing) must be removed. Since flies can also develop in the soil of potted plants, they are prohibited in areas with high-risk patients (burn victims, postoperative patients, ICUs). The chemical control is carried out with insecticides in spray form (active ingredient pyrethroids), the effectiveness of which is considered very high. It is important to ensure that the spray does not lead to contamination of food!

23.1.3 Rodents

The main representatives of the rodents are the house mouse (*Mus musculus*), the brown rat (*Rattus norvegicus*) and the house rat (*Rattus rattus*). One third of all mammals are rodents. Among the rodents, some species have become serious pests. The teeth of the rodents grow permanently and are kept short and sharpened by gnawing hard objects. They can cause serious health and economic damage. Rats are usually attracted to food (including high-smelling garbage) but are also known as omnivores (paper, soap). Due to their high adaptability, rats are very resistant to pathogens and other pests. For this reason, their propagation is very rapid and becomes a big problem in a short time. The hygiene and health damage arise primarily by the contamination with body secretions (faeces, etc.) of the pests, which leads to a high risk of infection. *On the one hand, they serve as a reservoir for the stable preservation of a pathogen, but on the other hand, depending on the pathogen and its geographical distribution, they are carriers of pathogens*.

23.1.3.1 Disease Transmission

Rats can transmit about 120 infectious diseases. Altogether, 42 important human pathogens or pathogen subtypes associated with rodents are currently known worldwide without the diverse hantavirus species. In summary, the great importance of rodents is they act as a reservoir for salmonella and as a carrier of, e.g. SARS, hantavirus typhoid (*Salmonella typhi*), paratyphoid, leptospirosis (bacteria of the genus *Leptospira*), tularaemia (anthropozoonosis caused by *Francisella tularensis*), toxoplasmosis, trichinosis (larvae of *Trichinella spiralis*), dysentery (*Entamoeba histolytica*, *Shigellosis*), cholera (*Vibrio cholerae*) and pest (*Yersinia pestis*).

Furthermore, rats are also reservoirs of pathogens in the field. These pathogens can be transmitted to humans and animals through ticks and fleas (i.e. Lyme disease caused by *Borrelia burgdorferi*).

23.1.3.2 Control

The damage caused by rodents is considerable. Food losses are not primarily caused by consumption but by destruction and gnawing of the packaging and by contamination with faeces and urine. As soon as damage traces or faeces is determined on an estate, measures for the elimination of the pest infestation are to be introduced. Here, individual measures are meaningless; the infestation must be combated

systemically. Mostly baits are used with an anticoagulant agent. As a result, the animals die under the signs of natural ageing, without feeling pain and without warning the conspecifics. Baits are to be interpreted where rats are seen or suspected, e.g. on rat changes, on tracks and at fouling or entrances to rat constructions. When fighting outdoor, only bait boxes may be used. An open design of bait is prohibited in order not to endanger humans and animals. Rats go back to the bait places, as long as they find something to eat there. Therefore, supplement the baits until nothing is eaten. This assumes that the baits are constantly controlled.

Further measures:

- Close entrance opportunities in the basement and attic.
- Close wall openings and unused drains.
- Close windows with tight meshes.
- Use only closed garbage containers.
- Do not leave food scraps and animal waste on home compost.
- Do not leave animal food open.
- Clean food bowls after feeding the pets.
- If there is a mouse or rat infestation, there are signs of feeding, gnawing and droppings as well as rodent hair.
- Locate nests.
- Setting up traps: falling traps break the animal's back.
- Live traps: Animals are exposed after catching at some distance. Several traps are needed to catch an animal.
- Mice baits may be peanut butter, pumpernickel, cheese; for rats, sweet mashed potatoes.
- In order for the fight to be successful, it should be done at least twice, and above all, in a professional manner to induce infestation. Frequent, non-professional execution can develop resistance.
- To expel the mice, put a cloth soaked in turpentine into the mouse hole or dried, finely crushed oleander flowers or peppermint herb mixed with dry sand deep in the mouse holes.

23.1.4 Cockroaches

Cockroaches (also known as roaches) have existed on Earth for 200 million years. The introduction is usually carried out by packaging, food or consumer goods. Within a few weeks, a strong infestation has developed. Cockroaches lay off so-called egg packets, which are protected by a chitin shell and are thus hardly attacked by pesticides. In an egg package, up to 40 individual cells can be present, which allows a rapid cockroach infestation. In this capsule the eggs are relatively well protected from environmental influences. The preferred temperature of the cockroaches is between 25 and 30 °C. It prefers moist and warm rooms such as commercial kitchens, bakeries, canteens, hospitals, swimming pools and greenhouses.

23.1.4.1 Disease Transmission

Due to their way of life, they can spread human and veterinary significant microorganisms. Documented is the transmission of tuberculosis (*Mycobacterium tuberculosis*), dysentery (*shigellosis*), typhoid fever (*Typhus abdominalis*, *Salmonella typhi*), cholera, polio and hepatitis B by cockroaches. Added to this is the spread of mould spores. It could be determined experimentally that disease microorganisms can adhere to the body of the cadaver for up to 72 h. In addition, cockroaches excrete previously recorded pathogens via the digestive tract. Cockroaches also play a significant role as the cause of allergies. So cockroach allergens come as a cause of house dust allergy into consideration. The contamination of the food is carried out either by faeces or excretions from salivary glands. Food contaminants and the foul odour that cockroaches spread on contaminated food make them unsuitable for human consumption. Cockroaches are not only considered as health and hygiene hazard but are also regarded as material hazards. In particular, technical systems are affected here, as cockroaches like to penetrate into electronic devices and can cause malfunction in this way. On farms, losses of meat and milk yield occur due to the transmission of microorganisms by cockroaches to livestock.

23.1.4.2 Control

Only a systematic control of *cockroaches* leads to success. In general, combating cockroaches requires stamina and patience. A one-time action will not lead to success, as the cockroaches are very resistant. Cockroach control often lasts for several weeks, sometimes even months, no matter how many cockroach traps were spread at the same time.

- Timely detection of infestation.
- Avoidance of garbage accumulation.
- Do not leave food open.
- Keep the kitchen and cooking facilities clean.
- Sticky trap with scent.
- Feeding bait traps.
- Scrupulous *cleanliness*!!

In principle, a professional pest control company should be consulted in case of heavy cockroach infestation. Chemical cockroach control agents comprise several classes of drugs. It may happen that the cockroach population to be controlled develops resistance to the means used. Most of the control takes place through a combination of drug groups and measures.

23.1.5 Ant

The pharaoh ant (*Monomorium pharaonis*) is widespread worldwide and can also live in houses with consistently high temperature (at least 26 °C). Therefore, hospitals are perfect for the living conditions of the ant. A nest consists of several queens

and many thousands of workers. The establishment of a pharaoh ant colony is only possible if at least one queen and several workers are present. The ants never infest buildings by active immigration but are introduced. This is possible because the queens, accompanied by workers, can leave the nest and get into cargo (i.e. laundry, food, packaging material). The nests are often found in pipelines with insulating material or various electrical equipment (heat sources).

23.1.5.1 Disease Transmission

The ant is clinically relevant because of the possibility of carryover of pathogens. Due to their small size, ants can invade almost anywhere. They have already been found in infusion tubes, storage, Petri dishes with bacterial cultures and tightly sealed medication containers. In contrast to cockroaches, ants gnaw particularly aggressively and are a particular danger for patients with mobility impairments. Even in patients with open wounds or gypsum, they get under the dressing material or under the plaster and eat there on the sore tissue. Therefore, pharaoh ants also lead to psychological stress on patients and staff in health facilities.

23.1.5.2 Control

It is difficult to combat the pharaoh ant, which is why all measures to prevent the introduction of a pharaoh should be considered in advance. The most common route of introduction is likely to be via laundries. Fresh, warm, slightly damp laundry is attractive for ants (as well as dirty laundry with organic residues). A bait can be laid out to confirm ants presence: pieces of bloody liver (moist, not dry) lure hidden pharaoh ants within a short time (sometimes minutes). When fighting, it must first be determined in which parts of the building the ants occur and where the nests are located. Detected nests are treated with insecticide spray (preferably phosphoric acid ester). If the nests are hidden in piping or in the masonry, poisoned baits are used, with which excellent control results are listed. The workers not only take the bait themselves but bring it to feed the queens in the nest. In principle, an experienced company should be commissioned to combat the pharaoh ant, so as not to waste money and time unnecessarily.

23.1.6 Mite

Mites have great medical importance as carriers of pathogenic microorganisms. The infestation may be due to contact with outdoor vegetation (e.g. autumnal mite), contact with animals (many types of mites causing skin lesions) or contact with afflicted individuals (e.g. itch mites). As itchy mites parasitize in the skin, strictly speaking, they are not classified as pests but as endoparasites.

23.1.6.1 Disease Transmission

The causative agent of (real) human scabies or scabies is *Sarcoptes scabies* var. *hominis*, the human itch mite. Female mites, after contact with the skin, soon dig into the layer of the cornea and immediately begin oviposition. The excavations

reach about 1 cm in length; the females can leave this one again and drill a new one—in this situation they can be transmitted very easily through contact! Larvae hatch after 3–7 days and soon dig themselves out through the wall of the existing corridor, where they live in small folds of skin and hair follicles until maturation. After mating between male and female mites on the skin surface, the females dig into the skin again for oviposition and the males die off.

In the first few weeks, the infection usually remains unrecognized, itching only with increasing multiplication of the mites, and the passages under the skin are visible and palpable. Scratching can trigger a bacterial secondary infection. In immunogenic dogs, the number of mites decreases by itself after a few months (after reaching a population of several hundred females), and the infection can go away spontaneously. In immunocompromised individuals (HIV, while receiving cortisone or chemotherapy), untreated scabies can reach excessive levels of several thousand (or even one million) mites. The transmission takes place exclusively from person to person. Close physical contact is a prerequisite, which is why scabies is also classified as a venereal disease. In principle, it can also come through hand areas or fleeting skin contacts to a transmission. Outside the body, itch mites cannot survive; depending on the temperature, they die within hours to a maximum of 2 days.

23.1.6.2 Control

During therapy it is essential to ensure that all contact persons are treated at the same time! There are several effective preparations available (often, hexachlorocyclohexane), which are applied almost exclusively in topical-local application (cream; obsolete, powder). As in lice, the antibiotic ivermectin in oral form is a treatment option but as a last resort (exception: in immunocompromised patients, it is the first choice!). Treatment failure is attributed to continuous reinfection (e.g. if partner is not co-treated). Clothing and bed linen are very rarely sources of infection and only if used in direct succession by several people. Even normal washing temperatures above 40 °C kill mites.

Mange

The equivalent of the human scabies is called mange in the animal. In mammals, there are many subspecies of *Sarcoptes scabiei*, which causes in humans especially itching and a papular scablike appearance of the skin (pseudocabbage) but cannot multiply on it like scabies mites. The existence of the skin symptoms is therefore dependent on the health of existing contact with the infected animal. Also, pets should be kept away from healthcare facilities.

Environmental Medicine

24

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Over the last decades, the effects of the physical environment have proved to be increasingly relevant on the healing process and well-being of people/patients. Factors such as noise play an important role in health maintenance and physical recovery after disease. The World Health Organization (WHO) has published guidelines for community noise with reference values for noise management in different settings (WHO guidelines for community noise, 1999). We therefore decided to include a chapter on environmental medicine, focusing on noise and air pollution in particular mold, in our book.

The field of environmental medicine has developed from various disciplines. Observations in the workplace have shown that certain diseases occur more frequently in certain occupational groups:

- Soot-related testicular cancer in chimney sweeps
- Quartz dust with miners and stonemasons

Since then, more and more toxicological occupational diseases have been listed and recognized.

Environmental medicine is the study of the prevention, diagnosis, and treatment of diseases associated with environmental factors, such as:

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E. Presterl et al. (eds.), *Basic Microbiology and Infection Control for Midwives*,
https://doi.org/10.1007/978-3-030-02026-2_24

- Noise
- Air pollutants
- Mold
- Light
- Odor
- Waste

24.1 Noise

Noise has become one of the most important problem areas in environmental medicine, especially in large cities. Excessive noise is not only disturbing but can also seriously harm human health and interfere with people's daily activities and resting periods. Long-term exposure to noise can lead to sleep disturbance and can cause cardiovascular and psychophysiological effects with influences on social behavior. Noise is unwanted, disturbing sound. A sound event can be clearly described as a purely physical phenomenon by a measurement; the value of the sound pressure level is given in decibels (dB). The sound pressure level (often referred to as the sound level) indicates how loud a sound is. In order to take account of the different sensitivities of the human ear for different high tones, the so-called A-weighted sound pressure level is formed from the sound pressure level. The A rating can be performed automatically by the meter. In practice, therefore, the description and measurement of noise take into account the fact that the human ear perceives volume differently depending on the frequency and the A-weighted sound pressure level is the noise level adapted to the human ear.

A-weighted sound pressure level dB (A):

- Sounds (noises) are caused by mechanical vibrations of elastic materials.
- Airborne sound is sound that spreads in the air.
- Our ears perceive these pressure fluctuations (sound pressure) in the air.

However, possible effects of sound on humans depend very much on subjective and situational factors.

Types of noise:

- Environmental noise
  - Aircraft noise
  - Road transport
  - Hospitality, etc.
  - Noise at the workplace

Limit for health hazard 85 dB >> here soundproofing measures (headphones) are mandatory according to employee protection.

24.2 Noise and Health

Damage to health due to noise can be manifold. Noise and sound not only affect the ear itself but also influence the entire organism via central nervous impulses. For the time being, it can only lead to temporary complaints if the noise pollution persists but also to permanent illnesses. The effects of noise on the organism are distinguished from two types of health effects, those that directly affect the auditory organ (aural) and those that affect the rest of the organism (extraaural).

24.2.1 Auric Effects

Acute acoustic trauma (140–160 dB):

- This refers to the damage of the hearing organ by a single, brief but violent sound event (blast trauma is a damage to the inner ear alone or explosion trauma with additional damage to the eardrum).

Chronic sonic trauma:

- In the case of continuous noise with sound pressure levels above 85 dB, a reversible hearing impairment first appears; if persistent noise persists, irreversible inner ear hearing loss (frequent occupational disease) occurs.

24.2.2 Extra Auric Effects

On the central nervous system (CNS):

- Arousal
- Sleep disorders
- EEG changes

On the psyche:

- Power
- Concentration
- Irritability

On the autonomic nervous system:

- Blood pressure, heart rate, breathing
- Gastrointestinal tract
- Metabolism

At elevated noise levels of over 85 dB (A), the body reacts with an increased release of adrenaline. This speeds up the heartbeat and raises blood pressure. The risk of developing cardiovascular disease is high in areas exposed to noise, such as in the vicinity of airports.

An important noise impairment is the disruption of communication. This very often affects older people who have problems understanding speech in a noisy environment. So noise can lead to increased isolation.

24.3 Mold and Health Effects

Fungi can be found ubiquitous in nature and can survive in hostile environments. From an infection control point of view, we will concentrate in this chapter on molds; they occur in filaments, the so-called hyphae, and grow by apical extension. Natural outdoor levels of environmental fungal spores depend greatly on weather conditions and vary seasonally, whereas indoor, concentration of mold is influenced by factors such as existing ventilation systems and their maintenance state, indoor activity, and cleaning frequency. Water damage of any kind increases the likelihood of indoor fungal growth. It is estimated that humidity remaining for more than 48 h supports mold growth. Therefore the early start of remediation work is essential in order to prevent exposure to mold and resulting mold-related health effects. There is no dose-dependent relationship for mold and occurring health effects; some people have no symptoms upon exposure to mold, whereas for others symptoms can range from nasal congestion and throat irritation to coughing or wheezing and in some cases to eye and skin irritation. People with mold allergies may have more severe reactions. People at increased risk are immune-compromised people and people with chronic lung illnesses; they may get serious infections when they are exposed to mold. From a preventive medical point of view, mold should be avoided in the living and working indoor environment and of course in the hospital environment.

The WHO Air Quality Guidelines (2005) provide an assessment and evaluation of the impact of different other ambient air pollutants on human health and describe possible interventions to reduce air pollution. An update of these guidelines is not yet available, but the WHO Expert Consultation report from 2016 describes available evidence for the future update of the WHO Global Air Quality Guidelines (AQGs).

Suggested Reading

WHO. Air quality guidelines. Global update 2005. Particulate matter, ozone, nitrogen dioxide and sulphur dioxide. Geneva: WHO; 2005. ISBN 92 890 2192 6.