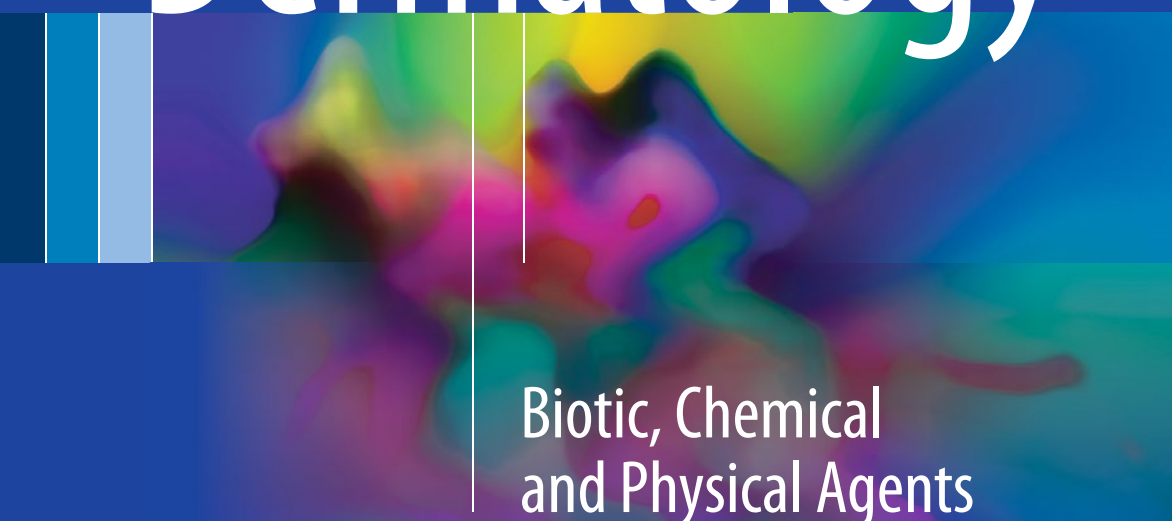
Aquatic Dermatology



Biotic, Chemical and Physical Agents

Second Edition

Domenico Bonamonte
Gianni Angelini
Editors

Springer

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Biotic, Chemical and Physical Agents

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To Davide
Elizabeth
Gianmarco

Preface to Second Edition

The rapid growth of knowledge in the field of skin diseases due to aquatic agents makes publication of this second edition of "*Aquatic Dermatology*" particularly timely. Fourteen years ago, the first edition of the monograph was written with the object of spreading a better knowledge of a somewhat neglected sector of dermatology. But now, thanks to the unlimited spread of aquatic activities for all sorts of purposes (holiday, sport, working activities) and to the advances in the understanding of the biology of marine animals, many elements have become mainstays of the new text. Therefore, this edition reinforces that earlier goal and has the aim of being easily accessible to all those (clinicians, dermatologists, biologists, marine biologists, emergency doctors, beach lifeguards) interested in the clinical and basic science of aquatic dermatology.

Each chapter of the first edition has been extensively revised, and a new chapter on traumatic injuries caused by fish has been added. Diagnostic elements and medical therapeutics sections have been expanded to reflect the importance of the different diseases. Moreover, this edition has been enhanced by the addition of many figures of clinical pictures and aquatic animals, as well as new tables, that offer a faster overview of the key aspects of each topic. Finally, the title of the work has been partly modified in order to highlight the various etiological, biotic, chemical, and physical aspects underlying the manifold clinical-pathogenic pictures that can be induced in fresh and seawaters, as well as artificial pools, household water supplies, and aquaria, in different parts of the globe.

Bari, Italy
May 2016

Gianni Angelini, MD
Domenico Bonamonte, MD, PhD

Preface to First Edition

This updated and extended edition of a work first published in Italian 10 years ago owes its revised production in both Italian and English to a series of factors. Foremost among them is the ever growing number of skin diseases caused by aquatic organisms, affecting the immense population that flocks to the water for holiday, sports, and professional activities. Aquatic skin diseases are no longer only a seasonal affliction but can be observed at any period, thanks to the boom of aquatic holidaymaking throughout the year.

The volume of literature in the field of aquatic dermatology is rapidly expanding. In the USA, one of the nations that is particularly attuned to the problem, a Bulletin, the "Jellyfish Sting Newsletter" has been issued six-monthly for the last 10 years. It is edited by Prof. Joseph W Burnett (Department of Dermatology, University of Maryland School of Medicine, International Consortium for Jellyfish Stings, 405 W Redwood St., 6th floor, Baltimore, Maryland 21201, USA), one of the great pioneers and researchers in the field of skin reactions to marine organisms.

The widespread passion for aquariums filled with tropical saltwater or freshwater animals, together with various pathogenic bacteria, has also contributed to the increase in aquatic skin diseases.

In this new edition of the book, etiological and clinical aspects have been thoroughly updated and the illustrations renewed. Greater attention has also been paid to aquatic biotic agents from tropical countries that can now be observed everywhere as "imported" diseases.

Finally, the book aims to make a modest contribution to the knowledge of some aquatic animals that have only developed a poisonous apparatus for protective purposes. A fuller understanding of these fascinating creatures may help people to better appreciate the beauty of the aquatic environment and to enjoy this enthralling habitat at lesser risk.

Bari, Italy
May 2002

Gianni Angelini, MD
Domenico Bonamonte, MD, PhD

Acknowledgments

This book is a revised and updated version of a monograph published in 2002. Cordial thanks went in the previous edition to all the people who had contributed to it, and for much of the work collected in this volume these thanks are heartily renewed.

This second edition has been enriched by the precious contributions of many colleagues, to whom we are deeply grateful. Professor Vidal Haddad Jr., of the Faculty of Medicine of the University of São Paulo (Botucatu), Brazil, a great specialist and world famous author of books and articles on aquatic dermatology due to biotic agents, and a great friend, has honored us by contributing to this monograph a strong impact topic that complements and completes our book. The young doctors Angela Filoni, Paolo Romita, Pietro Verni, and Michelangelo Vestita, of the Dermatological Clinic of Bari University Hospital, have devoted great enthusiasm and interest to helping us to draw up this monograph; we make them our most sincere compliments and wish them splendid professional careers.

The G.R.O. photoarchive of Catania (Sicily) of Dr. Filippo Massari and Fabrizio Frixa and Dr. Pablo Helman (coauthor with Susanna Volpe of the interesting book on marine biology "Il Quaderno Blu," Provincia di Imperia Ed., 1995) have most generously contributed superb quality photographic material to the present edition. The images of marine fauna and flora marina have made the work both more interesting and extremely attractive.

We would like to thank the publishers Piccin (Padova, Italy), Poletto (Gaggiano, Milano, Italy), Cambridge University Press (Cambridge, UK), and John Libbey Eurotext, Editor of *European Journal of Dermatology* (Montrouge, France) for having kindly authorized the reproduction of various figures.

Finally, we are very grateful to Springer-Verlag for their assiduous commitment to producing this volume.

Gianni Angelini
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Introduction

1

Domenico Bonamonte and Gianni Angelini

The aim of this work is to provide dermatologists, general practitioners, physicians working in emergency settings, biologists and all those concerned with diseases arising due to contact with the aquatic ecosystems, with a comprehensive guide to the cutaneous clinical presentations induced by different types of aetiopathogenic mechanisms, above all biotic but also chemical and physical, in the various types of salt- and freshwater environments. The closest analysis will be devoted to clinical skin pictures induced by biotic agents, owing to the extremely high frequency of these observations worldwide.

Throughout history, man has migrated to try and find places to live near water - the sea, rivers or lakes. Nowadays in particular, in our technologically advanced age offering so vast a choice of leisure activities, "water activities", even just during the short holiday period, have become a must for us all. What is more, they allow us to enjoy two other ingredients that are generally considered to be antidotes to the stresses of everyday life, in other words semi-nudity and exposure to the sun.

In recent decades more than ever, during warmer weather the coasts are literally invaded by millions of holidaymakers attracted by the chance to practice water and underwater sports. However, although these enthusiasts are fascinated by the marine and submarine panorama, they are often entirely ignorant of the flora and fauna that populate the aquatic environment and above all of the lurking dangers it hides.

Diseases and accidents caused by the aquatic environment have therefore increased year by year, giving rise to the rapid development of Aquatic Medicine, now a specialist field in its own right: indeed, close attention is now paid to the

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various professional underwater diving diseases. Instead, Aquatic Dermatology seems to have been comparatively neglected, despite the enormous number of patients that present with aquagenic dermatoses.

Oceans, rivers, lakes, ponds, swimming pools and aquariums all contain innumerable animal and vegetable organisms of variable sizes, including myriads of microscopic organisms. During the course of evolution, many aquatic species have developed natural defense and offense mechanisms against their natural foes and can sting or bite, quite apart from the fact that they frequently possess a venomous apparatus. Unfortunately, these self-protective mechanisms are sometimes turned on chance or involuntary aggressors, such as swimmers, underwater divers and fishermen.

Poisonous bites or stings can induce not only various dermatological pictures but also systemic reactions, often of a serious or even fatal nature. In any case, even when the damage is not serious, the very fact of being attacked in deep water can cause the swimmer to panic, and thus pose a danger in itself. Most fatal accidents, that are fortunately rare, are not in fact due to the toxicity of the poison injected but to the functional impotence it triggers as a secondary symptom, which can paralyze the victim's ability to swim or to resurface correctly from the depths.

From the medical viewpoint, by no means all the complex problems linked to poisonous marine organisms have yet been entirely elucidated, and the various clinical manifestations of toxic aquatic origin are often quite unknown to the public, while even the doctor is barely more conversant with them. To compound the problem, the boom of plane travel and extreme tourist mobility to distant holiday clubs and even submarine safaris, has meant that the onset of afflictions of an aquatic nature may occur even after the tourist's return from far-off waters ("imported" dermatoses). For this reason, an Italian dermatologist may be asked to recognize and treat an unfamiliar disease contracted in the Caribbean or in Polynesia, for instance.

Although many aquatic dermatological diseases resolve spontaneously, their importance must not be underestimated. Immediate, appropriate treatment of these clinical forms can prevent very serious systemic consequences. Clearly, therefore, the clinical suspicion must be followed by a firm diagnosis, especially in the presence of life-threatening reactions. The aim of this work is to furnish the doctor with a knowledge of the innumerable aetiological factors underlying aquatic dermatitis complaints, together with the various clinical pictures observed, and some notions of specific treatments.

Many of the diseases dealt with are skin afflictions caused by Mediterranean flora and fauna, of course, but some aetiological agents from more remote and exotic seas are also referred, with their respective clinical pictures. It should be borne in mind that for reasons linked to the various aquatic human activities, and in particular to global warming, that is particularly evident in the Mediterranean Sea, there have been countless reports in recent years of alterations of the normal balance of flora and fauna, and of their uncontrollable effects on the biodiversity of this closed environment. There can be no doubt, for instance, about the increasing phenomenon of translocation of new animal species through the Gibraltar straits, and

above all the Suez Canal. Owing in particular to fouling by ships keels and the ballast waters inside oil tankers, especially those coming from the Indo-Pacific and the Caribbean, this phenomenon is proceeding apace at a speed that would hitherto have been unimaginable. Various exotic fish species that inhabited the coral reefs of the Red Sea or around the Polynesian islands can be seen swimming, or could be caught, along the Italian coasts. Other less "attractive" species like sharks have also moved in.

It is important, however, to take into account the fact that unlike in other geographical areas, in the Mediterranean Sea there should be no marine species present that are particularly harmful to man. This characteristic sets the Mediterranean apart from all the other seas and oceans on earth. It features a relatively high quantity of dissolved mineral salts (37.7 g/l). Also, it is really, brilliantly blue, again unlike the oceans and the North Sea, and the water is relatively transparent thanks to the hydrodynamism of the strong sea currents and marked thermal variations. However, the lesser frequency and severity of diseases caused by Mediterranean fauna is perhaps the very reason (although no justification) why the biotoxins present in this sea have been so little studied, in comparison with their tropical counterparts, and why so little research has been devoted to the specific antisera.

Diseases caused by aquatic organisms can be of three different types: toxic, toxotraumatic, and traumatic. This volume will focus particularly on the first two types, although it includes a section devoted to various traumatic events (such as an encounter with a shark, for instance), to complete this treatise of a multiforme, multidisciplinary scientific field of study.

Apart from the diseases caused by both large and microscopic biotic agents present in all types of water environments, an ample section of this volume will address non biotic skin conditions induced by direct contact with salt- and freshwater. Aquatic pruritus, aquagenic urticaria, cold aquatic urticaria, and other possible conditions arising during the different aquatic activities will conclude this clinical overview of aquatic dermatology.

The Aquatic Biotic Environment and Its Biotoxins

2

Domenico Bonamonte and Gianni Angelini

The aquatic world, together with its animal kingdom, is renowned for its enchanting beauty (Fig. 2.1). In particular, the vast tropical coral reefs offer a shimmering, glittering underwater panorama featuring an infinite variety of hues, sometimes clashing but always ultimately harmonising. In some cases, however, these beautiful shapes, elegant movements and profusion of colours seem to go hand in hand with disease and death. This is one of the great paradoxes of the aquatic world.

An analysis of the map of the hydrosphere shows that the centre of the world of potentially harmful aquatic animals is the great area of the Indian and Pacific Oceans, although aquatic animals of less aggressive type are present in all the seas. The defence and/or offence mechanisms of marine fauna can be of two different types, physical or chemical (Table 2.1). Some observations of the latter type have unveiled a fascinating sector of marine biology that is still largely a mystery.

Aquatic biotoxicology is the science that studies aquatic biological toxins, and as this book focuses above all on the skin damage that can be wrought by poisonous or venomous aquatic creatures, it seems wise to start off with an overall classification of poisonous aquatic animals [1–5].

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Fig. 2.1 *Hyppocampus guttulatus* (sea horse) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

Table 2.1 Aquatic animals and types of lesions they provoke

1. **Aquatic animals inducing mechanical injuries**
Sharks
Giant manta rays
Barracuda
Moray eels
Giant groupers
Sawfish
Piranhas
Alligators
Crocodiles
Gavials of the Ganges
Seals
Sea lions
Polar bears
Walruses
Killer whales
Giant squid

Table 2.1 (continued)

2. **Venomous aquatic animals: Invertebrates**
Porifera (sponges)
Coelenterates (hydroids, sea anemones, jellyfish, corals)
Annelidae (Polychaeta)
Molluscs (cone shells, cephalopods)
Echinoderms (starfish, sea urchins)
Arthropods (aquatic bugs)
3. **Venomous aquatic animals: Vertebrates**
Venomous fish
Stingrays
Catfish
Moray eels
Weeverfish
Scorpionfish
Surgeonfish
Flying gurnards
Venomous snakes
Sea snakes
Freshwater snakes
Venomous freshwater mammals
Platypus
4. **Poisonous aquatic animals: Invertebrates**
Protozoa
Coelenterates (sea anemones, corals)
Echinoderms (sea urchins, sea cucumbers)
Arthropods (crabs, lobsters)
5. **Poisonous aquatic animals: Vertebrates**
Ichthyosarcotoxic fish
Ciguatoxic fish
Surgeonfish
Triggerfish
Butterflyfish
Dolphins
Wrasses
Mullet
Morays eels
Parrotfish
Mackerel
Porgies
Barracuda
Clupeotoxic fish
Herrings
Anchovies
Scombrotoxic fish
Hallucinogenic fish
Sea chub
Tetrodotoxic fish
Puffer fish
Porcupine fish
Sunfish

(continued)

Table 2.1 (continued)

Ichthyotoxic fish
Sturgeon
Gars
Whitefish
Catfish
Codfish
Ichthyohaemotoxic fish
Freshwater eels
Crabs
Ichthyocrinotoxic fish
Lampreys
Hagfish
Pufferfish
Other poisonous vertebrates
Amphibians
Salamanders
Newts
Frogs
Toads
Reptiles
Turtles
Marine mammals
Dolphins
Porpoises
Whales
Polar bears
Sea lions
Walruses
Seals
6. **Aquatic animals with an electrical mechanism**
Torpedinidae

2.1 Toxic Aquatic Animals

The brief classification of poisonous aquatic animals listed below includes a large number of species living in enormously different geographical areas and habitats [2].

2.1.1 Invertebrates

Invertebrate poisonous aquatic animals, i.e., those with no backbone, can be subdivided into the following groups or phyla.

1. Protozoa

   This group includes single-cell planktonic organisms with which man can come in contact when eating molluscs or fish that feed on Dinoflagellates.

2. Porifera
   Some sponges produce chemical substances that are highly irritant to the skin.
3. Cnidaria (Coelenterata)
   Few species of Coelenterates are poisonous to eat but most of them are venomous.
4. Platyhelminthes
   Various species of Platyhelminthes are considered poisonous to eat.
5. Annelida
   Some Polychaetae worms are equipped with irritant hairs or spines, while others have venomous glands.
6. Mollusca
   Many bivalvular molluscs are transvectors of various toxic substances. The cone shell and the octopus are included in this class of molluscs with a venomous apparatus.
7. Arthropoda
   Some species of Asiatic crabs are poisonous to eat. There are also a few species of poisonous aquatic insects, belonging to five different families of bugs that inhabit freshwater.
8. Echinodermata
   Some species of sea urchins are poisonous because their eggs are toxic, and so are some sea cucumbers.

2.1.2 Vertebrates

1. Poisonous and venomous fishes
   Many fish can cause human bio-intoxication when eaten, due to the presence of toxic substances. This class does not include fish that have been accidentally contaminated by pathogenic bacteria. The largest category is that of ichthysarcotoxic fish, that contain poisonous substances in their muscles, viscera or skin, that obviously cannot be destroyed by heat or gastric juices. The second major category of poisonous fish is that of ichthyocrinotoxic fish, that release toxins through the skin by means of specialised secretory organs. The third category includes the various venomous fish with specialised secretory organs and a wound-producing apparatus, such as spines or teeth.
2. Venomous amphibia
   Some amphibians (salamanders, toads, newts) produce very strong poisons.
3. Poisonous reptiles
   Some species of sea turtles are considered to become poisonous through eating toxic plants, but the precise source of the poison is unknown. Water snakes make up the most numerous reptile category, and some of these contain very potent poisons.
4. Poisonous mammals
   The liver of some whales, polar bears, walruses, seals and sea lions can be toxic.

2.2 The Functions of Biotoxins

Biotoxins, i.e., "poisonous" organic products of bacterial, vegetable or animal origin, are substances that have various different biological actions, of variable severity, when introduced into other organisms. A substance, of animal or vegetable origin, is poisonous if it is harmful to eat (e.g., some mushrooms and some fish are poisonous). Instead, an animal is "venomous" if it produces substances that are harmful when they enter the bloodstream (e.g., the viper and some Coelenterates are venomous, but their secretions are innocuous when eaten). Obviously, the toxic products of a venomous animal can be harmful when injected [5].

As shown above, many species of marine Vertebrates and Invertebrates produce biotoxins. An animal will be described as "poisonous" or "venomous" according to the use it makes of its poison: when it is used as a defence or offence mechanism and to capture prey for food, the animal is said to be "venomous", or actively toxic. Instead, a "poisonous" or passively toxic animal produces or ingests substances that are harmful when the animal is eaten [5].

There are large volumes of data in the literature on the biotoxins of marine animals [6–17]. Some general notions are reported below, while the toxins inherent to each animal species will be dealt with in the relative chapters.

Most marine animal poisons serve to capture prey for food. However, not all marine animals use toxins just to procure food: microphagic animals feed on live or dead organisms and organic waste floating in the water or mingled with the sand, and therefore filter the water or ingest the sand to obtain the nourishing substances. For this reason, some of these animals may be toxin carriers because they act as filters, and so any toxic substances present in the micro-organisms or in the aquatic environment will accumulate in their organs and make them poisonous to eat.

Instead, macrophagic animals need to use defence and offence mechanisms to capture and immobilize their prey. Hence, while the mammalian salivary glands have only a digestive function, in many Invertebrates and some Vertebrates (snakes) these glands secrete substances that are actively toxic to the prey's nervous system or other organs. Cephalopod Molluscs, for instance, immobilize their prey with secretions from their posterior salivary glands, which contain both digestive proteolytic enzymes and biotoxins. Snakes also produce many poisons that are injected with their saliva into victims. Coelenterates capture their prey, such as fish, with their tentacles and immobilize them by injecting toxins through the nematocysts. Not all the action mechanisms of these immobilizing neurotoxins are known: some act on the brain centres or ganglial chains, and others on the peripheral nervous system by impeding the conduction or transmission of nerve impulses at the level of the neuromuscular sheath.

Biotoxins may be used purely as defence mechanisms. The scorpionfish (Scorpaena) defends itself from predators thanks to its venomous dorsal spines. The ray (Dasyatis) has a strong, well-developed sting apparatus in the tail which is thrust into the body of the predator. Not only does this organ provoke a painful, lacerating wound, but it also conveys the secretions of the potent poison glands situated at its base.

In short, when they are produced by the salivary glands, biotoxins serve above all to capture prey for food. The biotoxins in the nematocysts of Coelenterates have the same function. Instead, when they are secreted by glands at the base of the spine or radioles, they have a defensive function against other animals. The role of the toxins present in the muscles or ovaries of many marine animals is difficult to ascertain, but what is certain is that owing to these toxins, such animals are poisonous to other animals and man.

2.3 The Biochemistry of Biotoxins

Up to now, the biochemical make-up of only relatively few biotoxins has been identified, for various reasons: it is difficult to obtain sufficient material for extracting and purifying the poisons, while we have little knowledge of the environmental distribution of many pelagic or deep-sea animals, and no suitable means for capturing them.

The biotoxins whose chemical nature is known are of various types: some are simple amino or phenol derivatives with a low molecular weight, or choline esters, or derivatives of steroid or isoquinoline compounds; others are peptides formed by few amino acids or proteins with a high molecular weight.

Generally, a venomous gland produces various compounds with different functions and chemical structures: the nematocysts of the Coelenterates, for example, contain many active substances with high and low molecular weights.

Research on the synthesis and metabolism of biotoxins is still in its infancy. With a few exceptions, no antidotes to the various poisons have yet been discovered, even for those that can cause mortal epidemics, like mytilotoxin and tetrodotoxin.

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Dermatitis Caused by Coelenterates

3

Domenico Bonamonte, Angela Filoni, Pietro Verni, and Gianni Angelini

Coelenterata, or "Cnidaria" (from the Greek *knidi*, meaning a nettle), are animals with a simple symmetrical radial structure, a mouth that opens out of a single cavity (coelenteron) and a body membrane consisting of two layers of cells (ectoderm and endoderm) separated by an amorphous jelly-like substance (mesoglea, that range from completely acellular, as in Hydrozoans, to richly cellular). Owing to the symptoms they induce, Coelenterates are also known as "sea nettles" (Fig. 3.1).

These organisms are often very beautiful and have remarkably elegant active and passive movements. They appear vulnerable and inoffensive but in actual fact they are equipped with recondite microscopic weapons running all over the body surface, which are used for defensive and offensive purposes.

The Coelenterate phylum has a worldwide distribution, even if it is prevalent in tropical and subtropical seas. The phylum is subdivided into five classes: Scyphozoa (from the Greek *skyρhos* = a cup) (true jellyfish; about 200 species); Anthozoa (from the Greek *anthos*, meaning a flower) (sea anemones, true hard and soft corals and sea pens; about 7300 species); Hydrozoa (physaliae, fire corals: not true corals, and hydroids; about 3300 species); Cubozoa (box jellyfish; 36 species); and Staurozoa (stauromedusae: stalked jellyfish; 50 species) (Table 3.1) [1–16].

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Fig. 3.1 *Cotylorhiza tubercolata* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

The Cnidaria phylum is an ancient lineage currently thought to date back to the Pre-Cambrian late Cryogenian period, about 640 million years ago [17]. Recent mitogenomic analysis of cnidarian mitochondrial genomes indicates that the oldest basal cnidarian clade may be the Anthozoa [18–20]. In fact, Anthozoa have a circular mitochondrial DNA, while Hydrozoa, Scyphozoa and Cubozoa have a linear molecule [12, 21]. Anthozoa are exclusively polypoid; Medusozoa are defined by the presence of a medusa (typically the sexual form) and a polyp stage in their life cycle, although in some, the medusa stage has since been lost, while in others the polyp stage has been lost [15].

All the cnidarian species have in common the same types of offensive organule, the production of toxic substances and a mechanism for injecting these substances in their prey. At least four toxic living classes of cnidarians are currently recognized by most systematists: Anthozoa, Hydrozoa, Scyphozoa and Cubozoa. Although all these species are capable of envenomation, most are harmless to humans, as some do not have nematocyst shafts long enough to deposit toxins sufficiently deep in the epidermis [22, 23], while others produce toxins that do not cause significant harm to humans [24]. Harmful cnidarians include vertebrate feeders or bigger jellyfish that can release large amounts of toxins [21, 25].

Table 3.1 Phylum of cnidarians: families, classes and species. The most common, known, toxic animals are reported

1. Class: *Scyphozoa* (true jellyfish)
A. Family: Cyaneidae
Species: *Cyanea capillata*
Cyanea lamarckii
B. Family: Pelagiidae
Species: *Aurelia aurita*
Chrysaora quinquecirrha
Pelagia noctiluca
Rhizostoma pulmo
2. Class: *Cubozoa* (box jellyfish)
A. Family: Chirodropidae
Species: *Chironex fleckeri*
Chiropsalmus quadrigatus
Chiropsalmus quadrumanus
Chiropsalmus buitendijki
B. Family: Carybdeids
Species: *Carukia shinju*
Carukia barnesi
Carybdea rastoni
Carybdea alata
Carybdea xaymacana
Morbakka fenneri
Malo maxima
3. Class: Anthozoa
Subclass: Zoantharia
A. Order: Actiniaria (sea anemones)
Species: *Anemonia sulcata*
Actinia equina
Adamsia palliata
Aiptasia mutabilis
Calliactis parasitica
Condylactis aurantiaca
Actinodendron plumosum
Triactis producta
B. Order : Sagartida
Species : *Sagartia elegans*
C: Order: Scleractinia (true corals)
4. Class: *Hydrozoa*
A. Order: Siphonophora
Species: *Physalia physalis*
Physalia utriculus
B. Order : Leptomedusa (hydroids)
C. Order: Milleporina
Species: *Millepora alcicornis* (fire corals: not true corals)
Millepora complanata
Millepora squarrosa
5. Class: Staurozoa (Stauromedusae) (stalked jellyfish)

Jellyfish are present in all oceans of the world [25, 26], their stings being most commonly observed in warm tropical marine waters [27, 28], but also in more northern regions, such as the United Kingdom [29], France [30], and Norway [31].

The geographical distribution of jellyfish seems to have been undergoing a considerable increase at global scale in recent decades [32–39]. In actual fact, analysis of several long term (8–100 years) trends in jellyfish populations demonstrates that their abundance varies with the climate, often over decadal time scales [40]. However, the recent time series are still too short to exclude circa-decadal climate cycles, and this makes it difficult to draw definitive conclusions on the status of jellyfish populations. The best indication that the recent increase is not only associated with climate changes is perhaps the huge number of reports, from all parts of the world, of problems caused by jellyfish to man and the environment. There is clearly no single cause of increasing jellyfish blooms; various reasons have been suggested: global warming, eutrophication, overfishing, habitat modification, aquaculture, salinity changes, ocean acidification, and, of course, translocation [37]. All these factors may work in concert, synergically creating the conditions that will benefit jellyfish [33, 41, 42].

As is well known, jellyfish interfere directly with many human activities: specifically, through stings (beach closures, tourism impacts, injuries, deaths), clogging intakes (coastal power and desalination plants, shipping, aquaria), interfering with fishing (clogged and split nets, stung fishermen, damaged gear), aquaculture (fish deaths, pens fouled by polyps), and marine biological surveys (interfering with trawls) [37]. But it is also true that some jellyfish can benefit humans [33] as food [43, 44], and more recently from use in drugs, thanks to the beneficial effects demonstrated against arthritis [45] and immunostimulation [46]. Finally, the discovery, isolation and development of a fluorescent protein from jellyfish led to a revolution in biotechnology [47] and a Nobel Prize [48].

3.1 Coelenterate Nematocytes

Nematocytes (or cnidocytes) are highly specialized cells that account for a restricted taxonomic characteristic of the cnidarians [49, 50]. They are arranged in clustered batteries along the surface of the tentacles and sometimes of the umbrella. In some jellyfish they are located in the outermost layer when in the “fire ready” position, or may be withdrawn by a fibrillary network to an unexposed position. In their cytoplasm they synthesize a unique organule called a nematocyst or cnidocyst/cnida. Nematocysts are used for predation, for location and for defense, and owing to their role in predation, they are localized above all at the level of the tentacles. This allows the animals belonging to this phylum to capture prey efficiently (cnidaria are exclusively carnivorous) even if they lack a sophisticated central nervous system. Some types of nematocysts are associated with venom, and this is the source of jellyfish stings. Thus, a nematocyst is a “stinging capsule” secreted by the Golgi apparatus of the nematocyte that delivers the sting [49].

Nematocysts can be of very different sizes (the length range is about 20–200 μm) and shapes (round to cylindrical), but they all have a common structure, consisting of a wall and an attached tubule, that may be equipped with spines and appendices [51]. At the apical end of the cell, a mechanosensory apparatus called a cnidocil (a central cilium surrounded by shorter stereocilia) points outward [52]. The nematocyst is closely anchored inside the cytoplasm of the nematocyte by a microtubule basket surrounding the capsule [53]. All cnidarians, and only cnidarians, produce nematocysts, and this is the characteristic *sine qua non* of the cnidarian clade [49, 50].

Nematocysts are one of the three categories of intracellular secretion products of cnidarians. The other two are ptychocysts and spirocysts. Ptychocysts are present in Ceriantharia cnidarians, that are bottom dwellers adapted to soft substrates into which they bury their base: the products are ejected into the substrate, guaranteeing the animal a secure hold. Spirocysts are found in some corals and sea anemones, and consist of sticky threads that help the animal both to capture prey and to adhere to surfaces.

Depending on their morphology, nematocysts can be subdivided into 25–30 types [49, 50], and so represent an important taxonomic characteristic of cnidarians. The nematocyst is the product of a complex process of secretion and forms in a large post-Golgi vesicle in the nematocyte cytoplasm. Cnidarians invest a large fraction of their energy in the maintenance of their nematocyst repertoire, that needs to be constantly renewed [54]. In response to an appropriate chemical and/or mechanical stimulus, the nematocyst discharges and the tubule, that is coiled and twisted inside the capsule, everts and is ejected out of one end of the capsule, which opens out [55] (Fig. 3.2). The tubule, tightly coiled inside the capsule matrix, is expelled in a harpoon-like fashion (it is a very slender, flexible, hollow tube that is extruded like the finger of a glove when it is thrust outwards) during a nanosecond discharge process [56, 57]. From the synthesis of poly-gamma-glutamate up to their complete maturation, nematocysts in hydrozoans are charged with an osmotic pressure of about 150 bars [58, 59]. Before the discharge, the capsule volume will have increased by 30 % due to osmotic swelling [56, 60], and the explosive exocytosis will release the kinetic energy stored in the elastically stretched capsule wall, under an extreme acceleration of 5,410,000 g [56]. After discharge, the size of the capsule will be diminished by about 50 % [60, 61].

The nematocyst wall consists of a dense matrix made up largely of minicollagens, a feature that is unique to cnidarians [62]. While minicollagens can account for the high tensile strength required for the capsule wall to withstand a pressure of 150 bars, elastomeric proteins are deputed to provide the energy for the extraordinarily fast discharge kinetics. Cnidoin, a novel elastic protein identified as a structural component of *Hydra* nematocysts, is the molecular factor involved in kinetic energy storage and release during the ultra-fast nematocyst discharge [57].

The "cost" of production of nematocysts for cnidarians is really remarkable: it surely absorbs a significant portion of their energy budget. A polyp of *Hydra magnipapillata*, for example, possesses large quantities of suitable cells; about 30 % of the roughly 11,000 cells are nematocytes and nematoblasts. Obviously, each

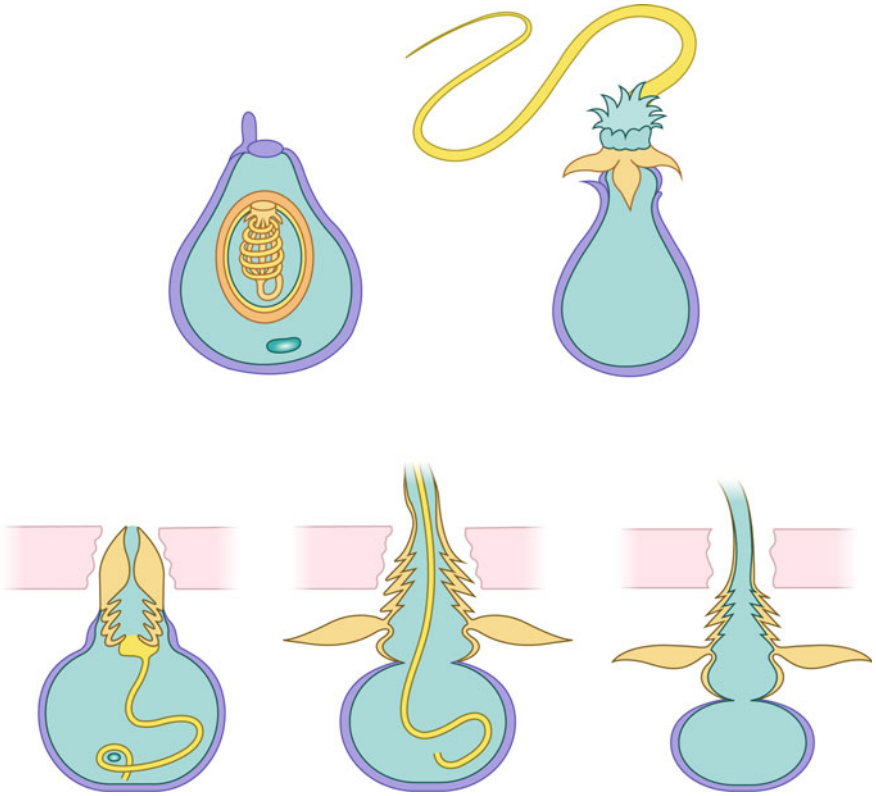

Fig. 3.2 (**a**) Cnidocyte with undischarged nematocyst. (**b**) Discharged nematocyst with evaginated filament. (**c**–**e**) Perforation of the cuticle of a crustacean by a nematocyst, as its wings open a gap for the evaginated filament to pass through

nematocyst is used only once: on the basis of the typically numerous discharges made during an offensive or defensive act, it is estimated that about 25 % of nematocysts (about 7500 cells) are lost from tentacles of *H. attenuata* each day [49].

3.2 Nematocyst Poisons

The nematocysts contain many different biologically active toxic substances, not all of whose chemical structures in the various species are known. In 1902, a French physiologist, Richet, studied the Coelenterate poisons and discovered the anaphylactic phenomenon, which won him the Nobel prize in 1913. Using a glycerinated extract, first of whole tentacles of the *Physalia* and later of the *Actinia,* the author demonstrated its toxic action in some animals, birds and rabbits.

To ascertain the lethal dose, he then injected the extract into dogs, which died after 5–6 days. The animals that had received an insufficient dose of the extract and

survived the experiment were used in further experiments. This led to one of the most important discoveries made in the medical field. A dog that had been administered 0.1 ml of glycerinated extract and had not manifested any symptom, was reinjected with a second dose of 0.1 ml of extract after 22 days. A few seconds after this second injection, the animal went into a coma and died within 25 min. Richet called this phenomenon "anaphylaxis" or, in other words, the reverse of protection [63–65]. Thus, it was discovered that some chemical substances boost, rather than reduce, the organism's sensitivity to their action. From the same tentacles of *Anemonia sulcata*, Richet also isolated three different components: hypnotoxin, thalaxin and congestin. The first induces somnolence followed by respiratory paralysis, the second has an urticarial action on the skin and causes cardiac arrest and the last, which is the one with the anaphylactic action, causes vomiting, diarrhoea and gastrointestinal haemorrhage.

In addition to these components and other proteins, various other substances with a low molecular weight, including tetramethylammonium, adenine, γ-butyrobetaine, histamine and its releasers, imidazyl-acetic acid and 5-hydroxytryptamine, have been isolated in Coelenterates. All these substances and the above proteins are contained in the nematocysts. The substances with a low molecular weight have pharmacological properties but are not harmful in the concentrations present in the organules. Only tetramine, histamine and 5-hydroxytryptamine contribute to the effects on the skin, that consist of burning, erythema and oedema. Instead, the toxic effects are exerted by the protein substances, some of whose amino acid sequences are now known [4].

Some of the cytotoxic and cytolytic effects are caused by damage to the cell membranes, secondary to mitochondrial alterations. In other words, the toxic action exerted by nematocyst poisons has a comparable mechanism to that of calcium-dependent phospholipase [66]. In some species of sea anemones, new protease inhibitors, that act against trypsin and chemotrypsin, have recently been isolated [67, 68]. Some of the toxins present in common sea anemones in the Caribbean seas seem to be able to block the potassium channels or act as antagonists to the glutamate receptor [69]. In reality, even if cnidarian venoms are the subject of intensive study, ascertaining how the venom derives from nematocysts can be very difficult [49, 70, 71]. Although the nematocysts are known to be the source of the venoms, how the latter are obtained is still uncertain [72].

Because they contain the above chemical substances, Coelenterates can be considered venomous and actively toxic, while they are not considered poisonous because they are innocuous when eaten. In fact, in some Italian regions (the Veneto), sea anemones are eaten as raw sea food, or cooked. They are innocuous because their toxins are inactivated by heat, and in any case they are digested by the intestinal proteolytic enzymes.

It is important to bear in mind that not all cnidarian toxins are associated with nematocysts. Some poisonous Coelenterates live among the coral barriers of the Pacific (Tahiti, Hawaii) and the Caribbean (Jamaica): they belong to the *Zoantharia* family and the *Palythoa* genus *(P. toxica, P. caribaeorum, P. tuberculosa, P. mamillata).* Palytoxin, the most poisonous biotoxin in the animal world,

with the most complex chemical structure ever identified ($C_{129}H_{223}N_3O_{54}$) [73–75], was chemically isolated in this genus in 1981. It is a very long chain of carbon atoms with a high content of methyl and hydroxyl groups. These Coelenterates, that are toxic even when ingested by fish and other animals, are very similar to small sea anemones, live in colonies at shallow depths and are shaped like mushrooms about 2–3 cm high. Some fifty tentacles protrude from the apex, forming a crown with a diameter of about 1 cm. The toxin, a non-protein substance, accumulates in the ovary between March and September during the reproductive period and passes into the eggs. It is not known whether palytoxin is present in the nematocysts as well. The toxin exerts its action on the cardiovascular system and especially on the coronary arteries: at the cellular level it increases permeability to sodium and hence induces depolymerization of the cytoplasmic membrane [4]. Palytoxin has also been found in organisms other than cnidarians [76], may be acquired through the food chain [77], and may undergo major concentration changes through the year [78].

3.3 Skin Reactions to Cnidarians: Pathogenic, Pharmaco-Kinetic and Clinical Mechanisms

Nematocyst firing is set off by a set of chemical and tactile factors produced by the victim, whose movements are thus an important factor in controlling the nematocyst discharge [79]. The nematocyst tubule, introduced into human tissues through the epidermis, penetrates the derma and enters or transfixes lymphatic vessels, nerves and capillaries, depositing venom in all these skin structures. In this way, the venom can be injected into the epidermis and/or derma and/or vessels and perhaps even into the hypoderma. For each of these routes of access there is a defined circulation time, that is also influenced by the molecular weight of the venom, by the patient's health conditions, the movements of the affected body part, the patient's perfusion capacity and the site affected by the sting. While the dose of venom depends on the number of nematocysts discharged, the speed of onset and the duration of symptoms will vary in each case according to the various factors that control the circulation span and the interval between the injection of venom and the onset of the symptoms. A further complication is that each harmful molecule attaches to the various receptor sites of the different organ systems, and this also takes some time before the reaction will lead on to manifest symptoms. This prompts two important considerations: the interval spectrum, or incubation time, before the disease becomes manifest will be fairly wide, and the duration and severity of the clinical pictures induced will be equally variable [80].

Injuries caused by cnidarians are of two pathogenic orders, toxic and allergic: most of the reactions will develop through a direct toxic mechanism, while immunological allergic reactions are much more rare; such reactions are usually of immediate type [80–84], less frequently of delayed type [85]. Some delayed reactions, whose onset occurs some days after contact with the animal, are also thought to be induced through immediate and delayed hypersensitivity mechanisms [86–92].

Toxic type reactions, that are the most common, affect any individual who comes in contact with cnidarians, and are directly correlated to the species of coelenterate involved, the venom dose injected and the extension and site of the lesions. Instead, allergic type reactions only affect some individuals, require previous contact, and can manifest as particularly severe clinical pictures; they are not dose-dependent. In the latter forms, skin tests (prick-by-prick, patch tests) with the incriminated animal are positive, and specific IgE can be isolated in the patient's serum, while at histological-immunohistochemical level, infiltrates of lymphocyte cells of various types are found. In the context of allergic type reactions, the possibility of cross-reactions among toxins of cnidarians belonging to different species but of the same class must be remembered [93]. As to the possibility of cross-reactions among toxins from different animals (e.g. jellyfish and bees, wasps, and some snakes) that contain related components (i.e., peptides, hyaluronidase), according to the literature this relationship does not seem to have a clinical relevance, even if it has been demonstrated *in vitro* [80, 94, 95]. In any case, humans do not acquire a clinical resistance or susceptibility to bee stings after exposure to cnidarian venoms or vice versa [80].

3.4 Clinical Eruptions

The various cnidarians envenomation clinical pictures are reported in Table 3.2 [80]. The overall skin pictures and syndromes delineated are common to all toxic Coelenterates. Other particularly specific clinical forms induced by some classes of cnidarians will be described in the sections on the classes in question.

3.4.1 Local Reactions

Toxic Reactions Contact of the skin or mucosa with a jellyfish will induce immediate local pain, that may be due to the reaction of exogenous and endogenous chemical mediators on the sensory nerves of the skin [96]. A special quinine-like mediator present in the poison is likely responsible for inducing the pain, that is perceived instantly, flares to a peak within 5 min and persists for between 30 min and 24 h: it is immediately followed by linear skin eruptions of various shapes. These are urticarial lesions that first appear pale, and then rapidly become erythematous. The lesions last a variable length of time, minutes or hours, but sometimes persist for a longer time depending on the intensity of the skin damage.

Lesions can also be vesicular, blistering, intensely oedematous, haemorrhagic and necrotizing, and may be associated with local, asymmetrical, excessive sweating and subsequent satellite lymphadenopathy.

Cases of contact with the eyes can induce photophobia, intense pain and burning, conjunctivitis, chemosis, corneal ulceration and palpebral oedema. Other possible ophthalmological signs are reduced visual acuity (that returns to normal in all

Table 3.2 Clinical pictures induced by cnidarians

1. Local reactions
Toxic reactions (to skin, mucosa, cornea)
Angioedematous reactions
Recurrent allergic reactions
Persistent delayed reactions
Distant site reactions
Contact dermatitis
Local lymphoadenopathy
Seabather's eruption
2. Local chronic sequelae and reactions
Keloids
Hyperchromia
Hypochromia
Scars
Atrophic subcutaneous fat
Gangrene
Ulceration
Mononeuritis
Vascular spasm
Ataxia
Increased ocular pressure
Eye synechiae
Blurred vision
Glaucoma
Mydriasis
Arthritis
3. Dermatoses following stings
Herpes simplex
Granuloma annulare
4. Systemic reactions
Nausea and vomiting
Diarrhea
Muscle cramps and spasms
Dizziness
Diaphoresis, fainting
Convulsions
Respiratory acidosis
Irukandji syndrome
5. Fatal reactions
Toxin-induced
Immediate cardiac arrest
Rapid respiratory failure
Delayed renal failure
Liver destruction
Allergy-induced
Anaphylaxis
6. Reactions after ingestion
Gastrointestinal symptoms
Urticaria
Ciguatera

Modified from Burnett [80]

cases), iritis, increased intra-ocular pressure (from 32 to 48 mmHg), mydriasis and reduced accommodation. Anterior synechiae and unilateral glaucoma are long term sequelae, and mydriasis, too, can persist for a period ranging from 5 to 24 months. Usually, however, the subjective and objective symptoms regress within 24–48 h [93, 97–99].

Exaggerated Local Reactions A local exaggerated reaction of angio-oedematous type lasting 10–14 days was observed in a subject stung by *Chrysaora quinquecirrha* and *Pelagia noctiluca.* For many years, high levels of specific IgE to species with an affinity to jellyfish were then repeatedly found in the patient's serum; his basophils released abundant quantities of histamine when exposed *in vitro* to the *Chrysaora* antigen. A subject with this type of angio-oedematous reaction could probably develop anaphylaxis in the case of any successive stings [95].

Recurrent Allergic Reactions Various cases of recurrent linear skin eruptions, itchy but not painful, have been described, whose onset occurs after variable times from the first and only sting episode. In the first five cases reported, a single recurrence occurred in four patients and two recurrent episodes in 1 [86, 87, 100–106]. The interval between the first reaction and the recurrence was 7–13 days. In 3 of the 5 patients, the recurrence was clinically more serious than the first reaction. In one case, after about a month from the original sting by *Physalia,* antigen-specific serum antibodies of IgG and IgE type were demonstrated.

In 1987, Fisher reported a case of immediate linear toxic dermatitis that developed on the patient's back and resolved in 5 days; 8 days later, a diffuse erythematous-oedematous eruption appeared in the same site [105]. In 1988, Kokelj and Burnett reported 3 other unusual cases of recurrent eruptions after contact with *Pelagia* [107]. We have observed 2 similar cases, in which there was a recurrence after 20 and 30 days, respectively, from resolution of the first and only sting episode. Finally, other observations of recurrent eruptions after stings from jellyfish and other Coelenterates have been referred, in one of which oral prednisone had suppressed the primary eruption [102].

These recurrent eruptions, that may be of a similar severity but can be accompanied by pruritis rather than pain, are considered to be of an allergic nature because of the increase in specific serum antibodies. The studies conducted in this field have led to the following conclusions: the onset of allergic reactions after jellyfish stings is possible in man; high levels of specific immunoglobulins can persist for many years; recurrences are possible at time intervals ranging from a few days to several months without additional causal contact; a serum cross-reaction to different species of jellyfish is possible; the immune reaction involves both the B and T lymphocyte subclasses.

Persistent Delayed Reactions Some persistent delayed granulomatous reactions have been observed after jellyfish stings [87]. At the moment of contact the patient suffers only local pain but after 4–7 days a delayed eruption starts to appear. This will feature nodular lesions of variable size that may persist for months. Histological

analysis has demonstrated a dense dermal cellular infiltrate, morphologically similar to the one observed in delayed hypersensitivity reactions.

In view of the histological findings and chronic nature of the eruption, this type of reaction is considered to be an example of delayed cell-mediated immune response. The serum levels of specific IgG and IgE are within normal ranges. Eruptions featuring multiple nodular lesions persisting for several weeks have also been reported after contact with other Coelenterates [87, 89, 106–109].
Distant Reactions A subject stung on the ankle and right foot by *Physalia physalis* developed an erythematous-oedematous reaction at the level of the ear, the gingival mucosa and the right cheek a few hours later; the eruption lasted 10 days [110]. Seven years later, no serum anti-*Physalia* IgE or IgG were found in the patient's serum.

Contact Dermatitis Contact dermatitis to the tentacles or nematocysts of Coelenterates is an infrequent but possible observation, that can be confirmed by patch test. Such a reaction has been reported to *Physalia* and other jellyfish [102]. A delayed sensitisation reaction was recently observed after repeated contact with *Olindias sambaquiensis,* a transparent hydromedusa about 10 cm long with 380 tentacles. Its usual habitat is tropical and temperate waters between the 23rd and the 42nd south parallel of latitude [111]. It is particularly common along the coasts of the Mar del Plata and in the Blanca Bay area to the south of Buenos Aires. Patch tests with crude extract of the nematocysts were positive in a subject who had developed a more serious skin reaction only after repeated exposure with slight symptoms. The same patch test was negative in 10 controls [112].

Histological Findings Histological analysis of local skin lesions shows a lymphocyte infiltrate, prevalently in perivasal sites in the superficial derma. These lymphocytes are mainly T helpers (CD4+) and T suppressors (CD8+). In recurrent forms the lesions show a deeper dermal lymphocyte infiltrate, with no complement or IgG deposits at the level of the dermo-epidermic junction or around the blood vessels [93].

3.4.2 Local Chronic Reactions and Sequelae

The local outcome of jellyfish-provoked dermatitis may be keloids, post-inflammatory dyschromia [113], scarring, subcutaneous atrophy [114, 115], gangrene and contracture [107, 116, 117]. We have most often observed scarring after dermatitis from *Anemonia sulcata* [118]. Cases with vasospasm, contracture and gangrene have been reported in the Indo-Pacific area [119]. Two cases of multiple temporary mononeuritis of a nerve near (but not within) the contact area have also been reported: one after a sting from a corallimorphous anemone in Papua New Guinea, that lasted about 5 months and the other after contact with an unidentified

jellyfish in Penang (Malaysia), that also lasted 5 months [120]. Three other cases have been reported, one in Norfolk (Virginia, USA) after contact with an unidentified jellyfish [121], one in Florida after a coral prick [122] and one in Penang (Malaysia) after a jellyfish sting [123]. In all these patients, motor and sensory impairment of peripheral nerves was observed, and involvement of the nerves near the site of contact, but no associated vascular disorders; the complaints resolved spontaneously after several months. Monoarticular arthralgia and reactive arthritis can follow *Physalia physalis* stings [124].

3.4.3 Dermatoses Following Stings

Dermatitis caused by Coelenterates has been followed by a recurrence of herpes simplex in a case of *Chrysaora quinquecirrha* sting [102] and by the onset of a granuloma annulare at the site of a sting by *Physalia utriculus* [125].

3.4.4 Systemic Reactions

These include nausea, vomiting, diarrhoea, muscle cramps and spasms, dizziness, fainting, diaphoresis, convulsions, and respiratory acidosis [126]. Psychiatric symptoms (psychosis, convulsions, stupor and coma) have been reported after *Stomolophus nomurai* stings [127], while fever and muscle spasms can ensue after *Chrysaora quinquecirrha, Physalia physalis* and box-jellyfish envenomation [80].

3.4.5 Fatal Reactions

Death after jellyfish stings can occur through toxic or allergic reactions. A rapidly progressive toxic reaction ending in a fatality is the most common observation, and proceeds through 4 steps according to the venom dose absorbed. Large dosages have cardiac effects, inducing various degrees of heart block, ventricular arrhythmia, disturbances of the Purkinje fiber network and coronary artery vasoconstriction [102, 128, 129]. This cardiotoxic action is mediated by alterations in calcium and/or sodium ionic transfer [80, 102, 130]. Moderate venom dosages depress the respiration through the central nervous system, from a few minutes up to some hours after the sting. Finally, even lower venom dosages can be fatal due to acute renal failure with tubular necrosis [131] or liver failure with cellular necrosis [132].

3.4.6 Reactions after Ingestion

For the reasons described above, it seems reasonably safe to eat Coelenterates: in fact, in various areas in the world, jellyfish are commonly eaten as condiments or hors d'oeuvres [43]. However, cramps and abdominal pain due to these

delicacies have been reported: in one case these symptoms, together with persistent urticaria, followed the ingestion of dry jellyfish [133], while a ciguatera-like outbreak followed a meal of imported frozen jellyfish products coming from the Orient [134].

3.4.7 Indirect Reactions

There are various possibilities of a jellyfish-induced dermatitis developing without there ever having been a direct contact with the animal [105]. Coelenterates can release poisonous antigenic substances into their aquatic environment and these substances can induce sensitisation in swimmers even without any contact with the nematocysts. In any later contact with a jellyfish, the sensitised subject may develop an allergic dermatitis of a serious nature.

When strong storms are blowing, nematocysts detach from the tentacles of jellyfish, in particular, float away and continue to release toxins for several months. Contact with these can cause the development of a "dermatitis caused by nematocysts" without any contact with the Coelenterate. In fact after a storm, "epidemics" of moderately itchy skin eruptions can be observed, that are difficult to diagnose in the absence of linear lesions and a history of contact with a jellyfish (Figs. 3.3, 3.4, 3.5, and 3.6).

Two species of Nudibranchs (Molluscs) (Fig. 3.7), *Glaucus atlanticus* and *G. glaucilla,* feed on the tentacles and nematocysts of *Physalia;* these nematocysts are not digested but migrate and are stored in their dorsal papillae. Swimmers coming in contact with these "armed" Nudibranchs can be stung by the nematocysts. The

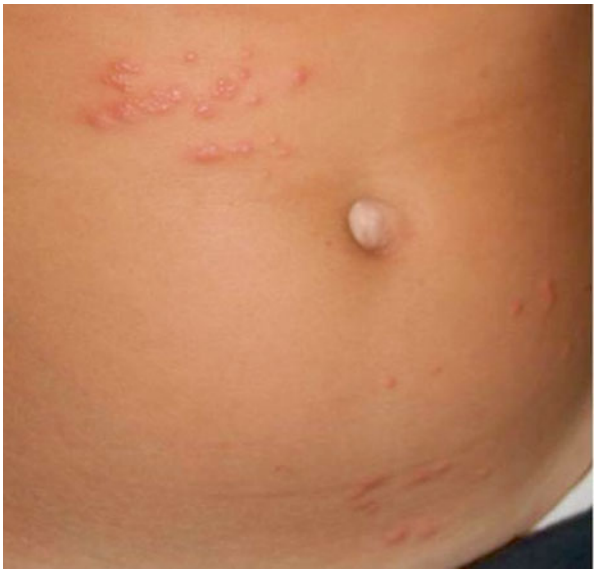

Fig. 3.3 Multiple isolated erythemato-vesicular lesions caused by nematocysts

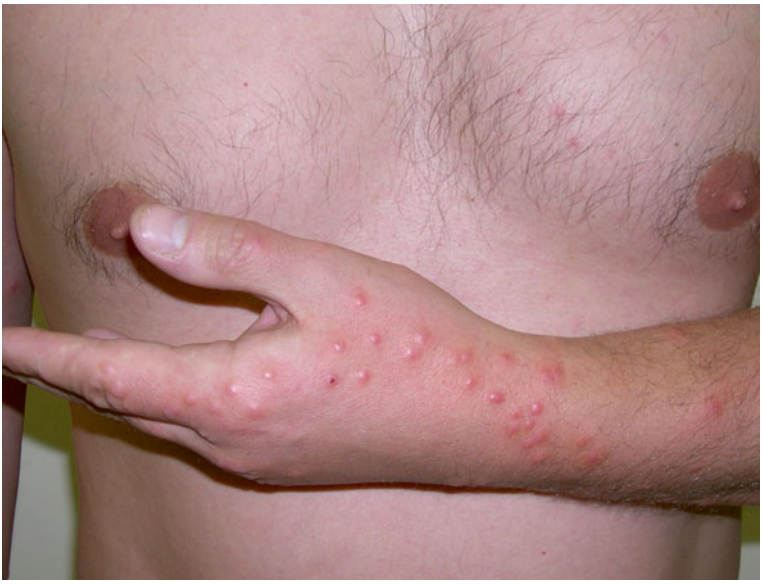

Fig. 3.4 Multiple isolated erythemato-vesicular lesions caused by nematocysts

ensuing reaction, known as "dermatitis caused by Nudibranchs" is actually a dermatitis caused by nematocysts.

3.5 Reactions to Scyphozoa (True Jellyfish)

Scyphozoa, or true jellyfish, cause a large number of accidents in the world, even if these are generally less serious than those induced by other cnidarians, like box jellyfish and *Physalia* species. The most important genera with toxic properties are *Pelagia*, *Chrysaora*, *Stomolophus*, *Cyanea* (lion's mane jellyfish), and *Linuche*. The symptoms induced by contact with these animals are generally of local type but systemic effects, such as malaise, fever, weakness, and muscle spasms are possible (these symptoms are more frequently suffered by children after exposure) (Table 3.3) [14, 118, 135, 136].

Although they have a worldwide distribution, Pelagiidae are more common in warm waters, especially in the Mediterranean Sea (*Pelagia noctiluca*) and African and coastal Brazilian waters (*Chrysaora* species). The habitat of these jellyfish is typically the open sea but they frequently gather in swarms along bays and estuaries.

P. noctiluca is a ubiquitous species, present in tropical seas, as well as the North Atlantic and Pacific Oceans [136]. It is reportedly very common in the Mediterranean Sea [118, 137–139] (Figs. 3.8 and 3.9). This jellyfish has a hemispherical umbrella with a diameter that usually measures about 12 cm, and numerous stinging, wart-like protuberances on its surface. The bell can range from transparent to fluorescent light pink. Sixteen marginal tentacles, 30–40 cm long, stick out from the umbrella,

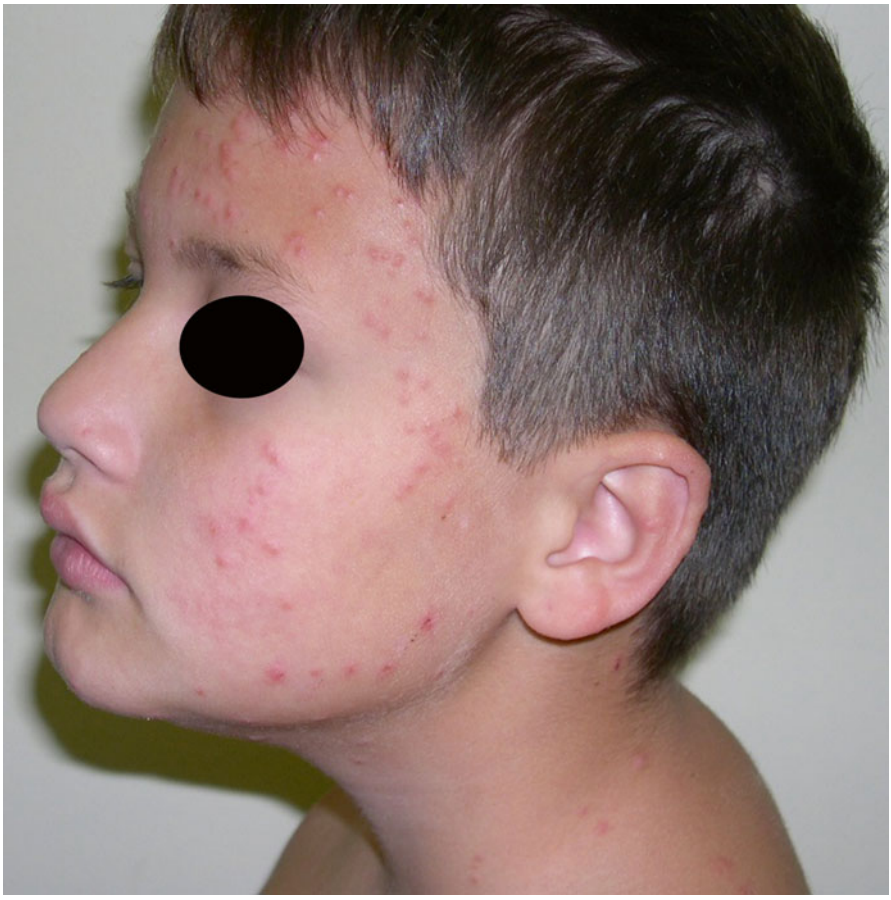

Fig. 3.5 Multiple isolated erythemato-vesicular lesions caused by nematocysts

with mouth arms about five-times the bell height. The tentacles and the mouth arms are normally colourless or red/ magenta [25, 26]. The discharge of *P. noctiluca* nematocysts has been stimulated in the laboratory by anionic solutions, such as Cl^- and especially I^-, whereas the venom release has been blocked by cations, such as Mg^{2+}, Ba^{2+} and above all Ca^{2+}, that can also offset the effect of iodide solutions on venom discharge [139]. Because it has nematocysts all over its surface, not just on the tentacles but also on the bell, this "nocturnal jellyfish" is a severe stinging jellyfish, that generally induces local symptoms (pain, erythema, oedema, blistering). Its stinging capacity is restored after only a few days from the last ejection of nematocysts [139]. Its stings are not usually life-threatening and systemic symptoms are uncommon, although exceptional cases of anaphylaxis have been reported in literature [93, 95, 140]. In recent years there have been seasonal invasions of *P. noctiluca* along the Adriatic coast, especially in the month of September: dense colonies float in to a few meters from the shore, causing obvious problems for bathers.

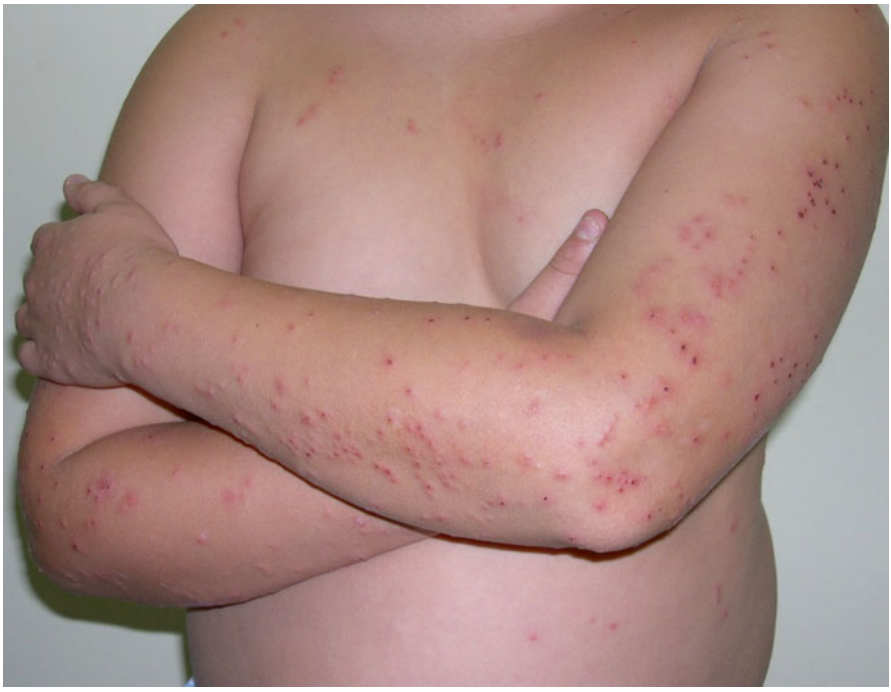

Fig. 3.6 The same case as in Fig. 3.5

Fig. 3.7 *Flabellina ischitana* (nudibranch mollusc) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

Table 3.3 Main stinging cnidarians: geographical distribution and symptoms

Species	Geographic distribution	Symptoms
Pelagia noctiluca	Worldwide, tropical and cold waters. Common in the Mediterrean Sea, North Pacific and North Atlantic Oceans	Immediate severe pain, wheals, vesico-bullae Rare systemic effects
Chrysaora quinquecirrha	Australia, Atlantic, Pacific and Indian Oceans	Intense pain, wheals/rash for days
Cyanea capillata	North Sea, North Atlantic, Arctic Sea, North Pacific	Pain, wheals, erythema
Chironex fleckeri	Australia, Indo-Pacific region	Pain, wheals, blistering for 10 days, scarring Severe hypotension, arrythmias, cardiac failure/arrest, pulmonary hypertension
Chiropsalmus quadrigatus	Australia, Indo-Pacific region	Pain, wheals, swelling for 24 h Bradycardia, asystole, pulmonary hypertension/oedema
Chiropsalmus quadrumanus	North West Atlantic, Caribbean, Brazil	Pain, wheals for 24 h Scarring and dyschromia for 2 months Hypotension, acute cardiac failure, pulmonary hypertension/oedema
Carybdea rastoni	Australia	Delayed moderate pain, wheals, blisters, dyschromia for 2 weeks
Carybdea alata	Tropical/subtropical Pacific waters, Hawaii	Pain, wheals, blisters, dyschromia for 2 weeks Mild Irukandji syndrome, possible allergic reactions
Morbakka	Australia	Wheals, intense pain, vesicles, skin necrosis. Irukandji syndrome
Caruchia barnesi	Australia	Irukandji syndrome
Anemonia sulcata	Mediterrean Sea	Intense pain, burning, erythemato-oedemato-bullous lesions Nausea, vomiting, muscle cramps, bronchospastic crises
Physalia physalis	Worldwide, more common in tropical waters	Acute pain, wheals, skin necrosis after 24 h Muscular spasms, abdominal pain, headache, arrhythmias
Physalia utriculus	Tropical Indo-Pacific Ocean, Australia, South Atlantic	Local pain, wheals Very rare systemic symptoms

P. noctiluca can cause various clinical pictures (Figs. 3.10, 3.11, 3.12, 3.13, 3.14, 3.15, 3.16, 3.17, 3.18, 3.19, 3.20, 3.21, 3.22, and 3.23) induced by both toxic and immunological mechanisms. Kokelj and Burnett observed three emblematic cases of unusual reactions induced by contact with this jellyfish [107]. The first case was an underwater diver who was stung for the first time by *Pelagia* on the right thigh, which gave rise to a local burning erythemato-vesicular lesion, which regressed within a few

Fig. 3.8 *Pelagia noctiluca*

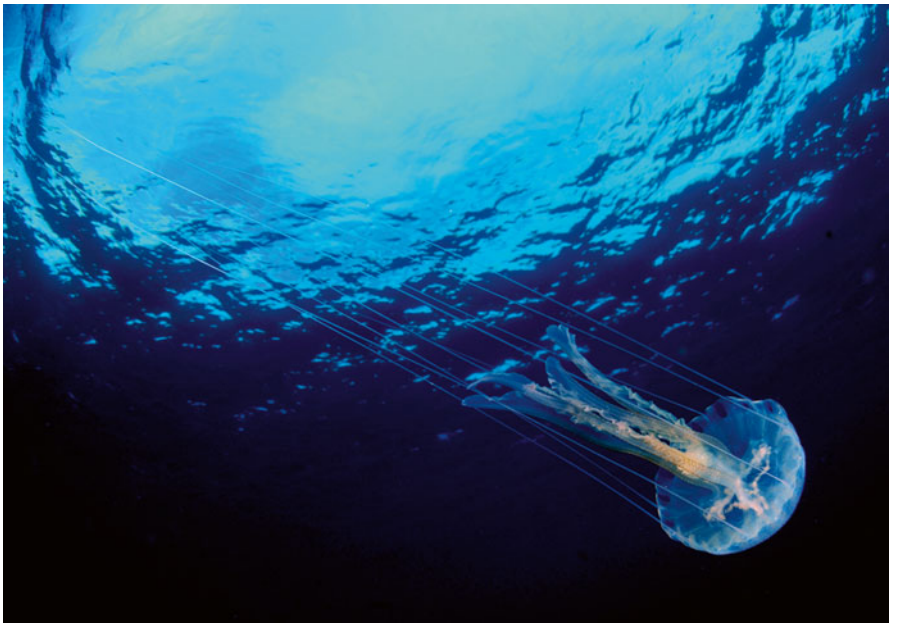

Fig. 3.9 *Pelagia noctiluca* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

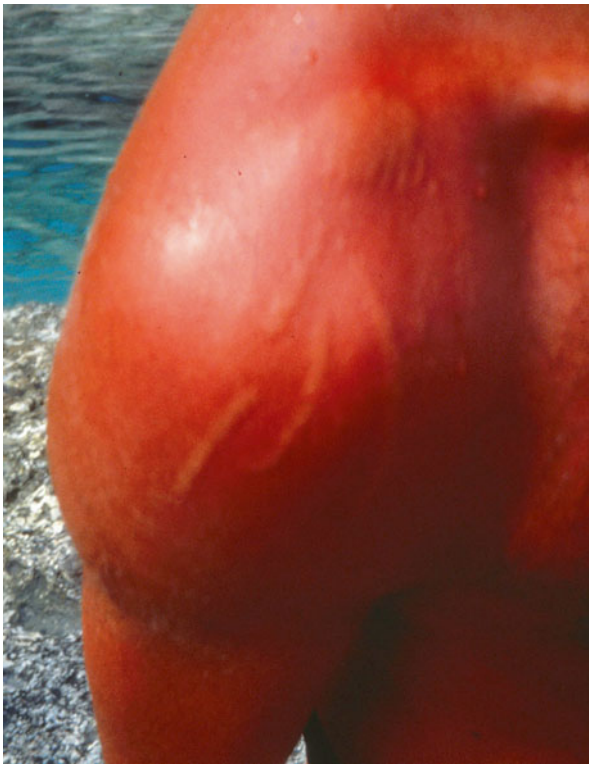

Fig. 3.10 Erythemato-oedematous reaction to jellyfish. The bell and tentacles are reproduced on the skin

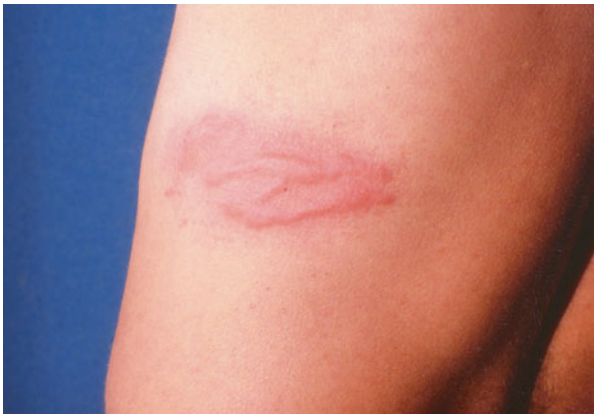

Fig. 3.11 Erythemato-oedematous reaction to jellyfish

weeks. In the following 6 years, the same subject was repeatedly stung on various sites, provoking lesions lasting 10–15 days. Six years after the first episode, a further contact occurred on one side of the face, secondary to a *Pelagia* having entered the mask. This caused not only a local reaction but also the appearance of an intense, burning erythema on the site of the first lesion (the thigh), which resolved within about 10 days.

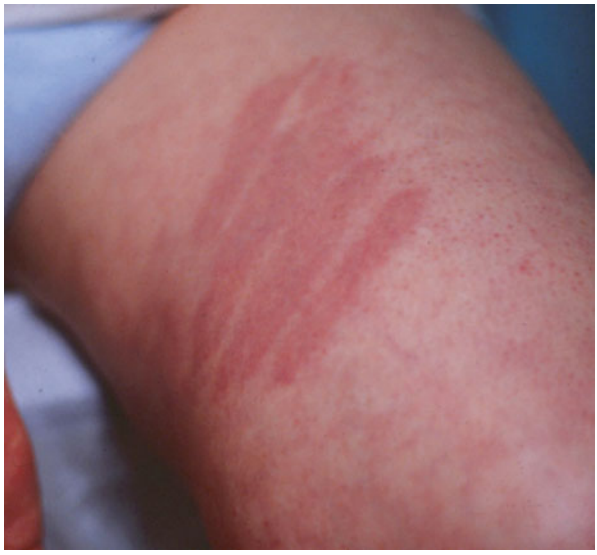

Fig. 3.12 Erythemato-oedematous reaction to jellyfish

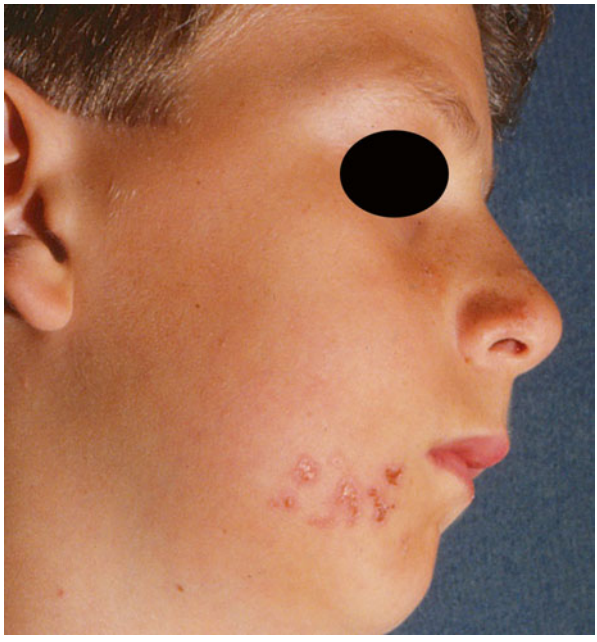

Fig. 3.13 Erythemato-vesicular reaction to jellyfish

The second case was that of a child of 11 who was stung on the left arm by *P. noctiluca.* The lesion resolved after about 1 month, leaving a hypochromic area. In the 2 years after contact, frequent recurrences of the lesion were observed, in concomitance with any episodes of fever or particular emotional stress. The affliction

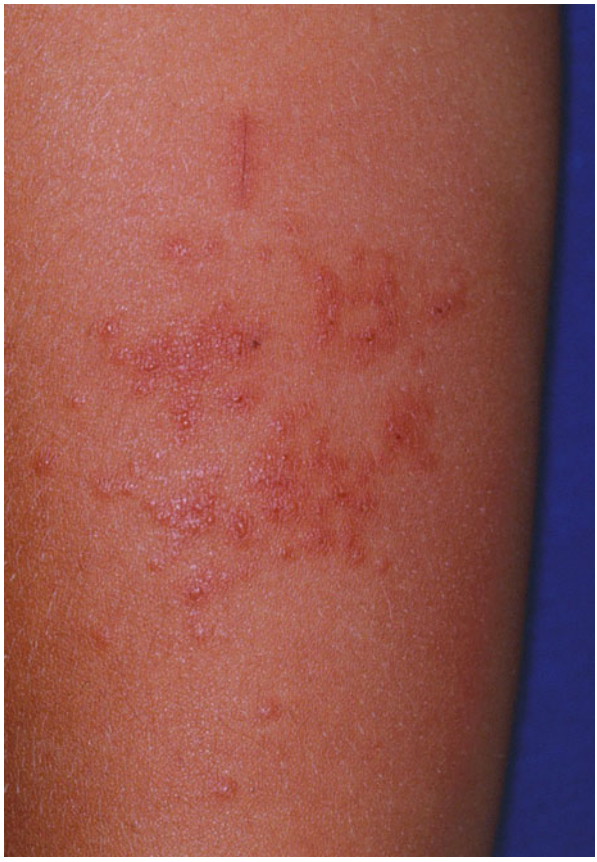

Fig. 3.14 Erythemato-vesicular reaction to jellyfish

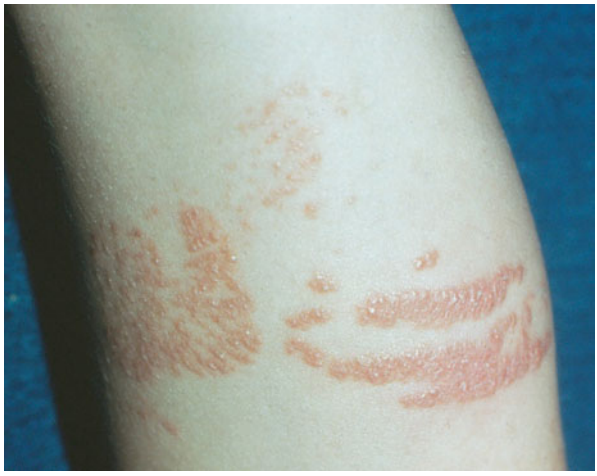

Fig. 3.15 Erythemato-vesicular reaction to jellyfish

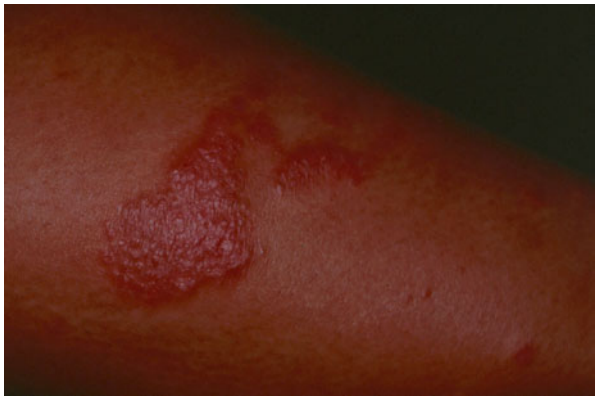

Fig. 3.16 Erythemato-vesicular reaction to jellyfish (Reproduced with permission from Bonamonte and Angelini [12])

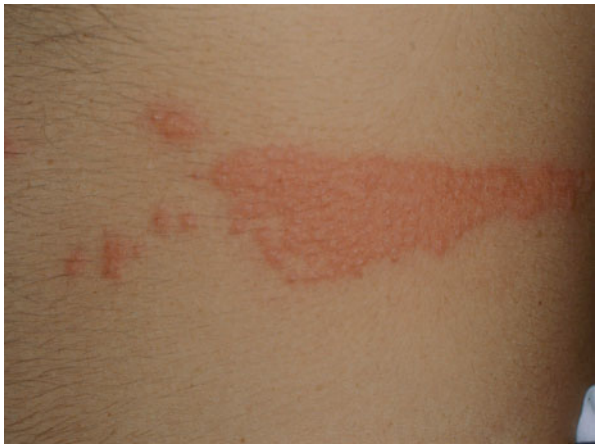

Fig. 3.17 Erythemato-vesicular reaction to jellyfish

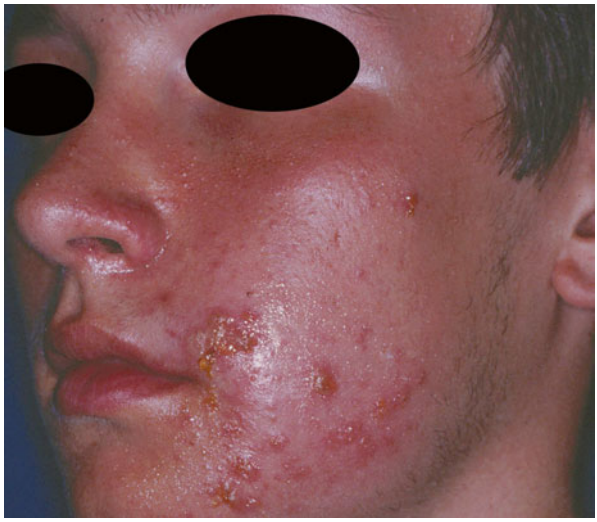

Fig. 3.18 Erythemato-vesico-pustular reaction to jellyfish

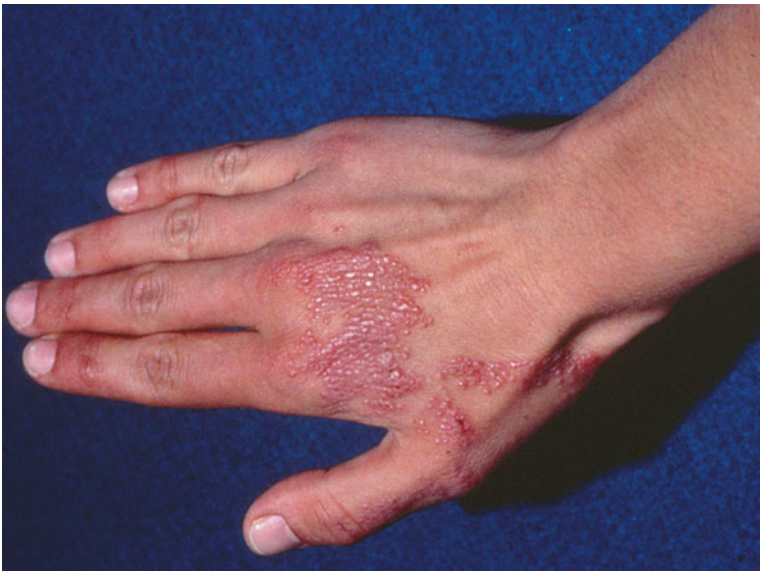

Fig. 3.19 Figured erythemato-vesicular reaction to jellyfish

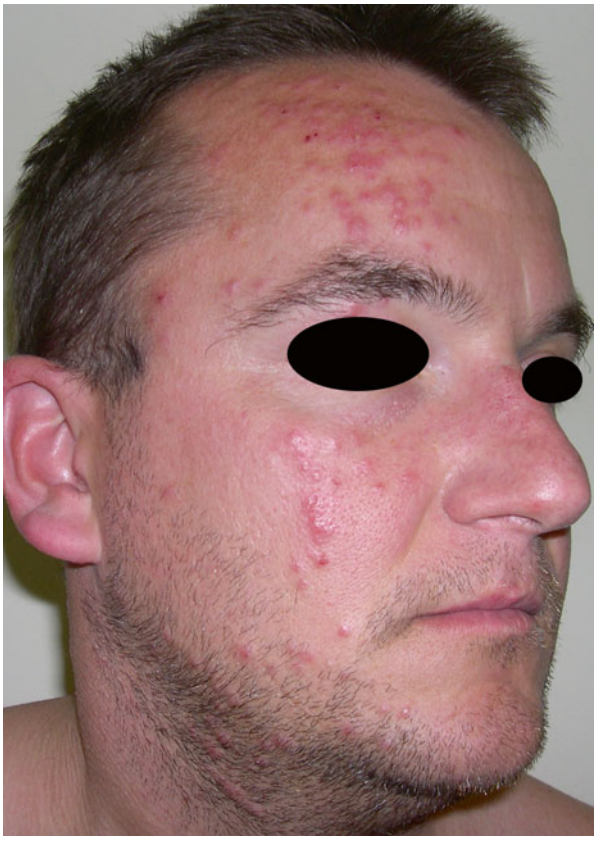

Fig. 3.20 Erythemato-vesicular reation to jellyfish

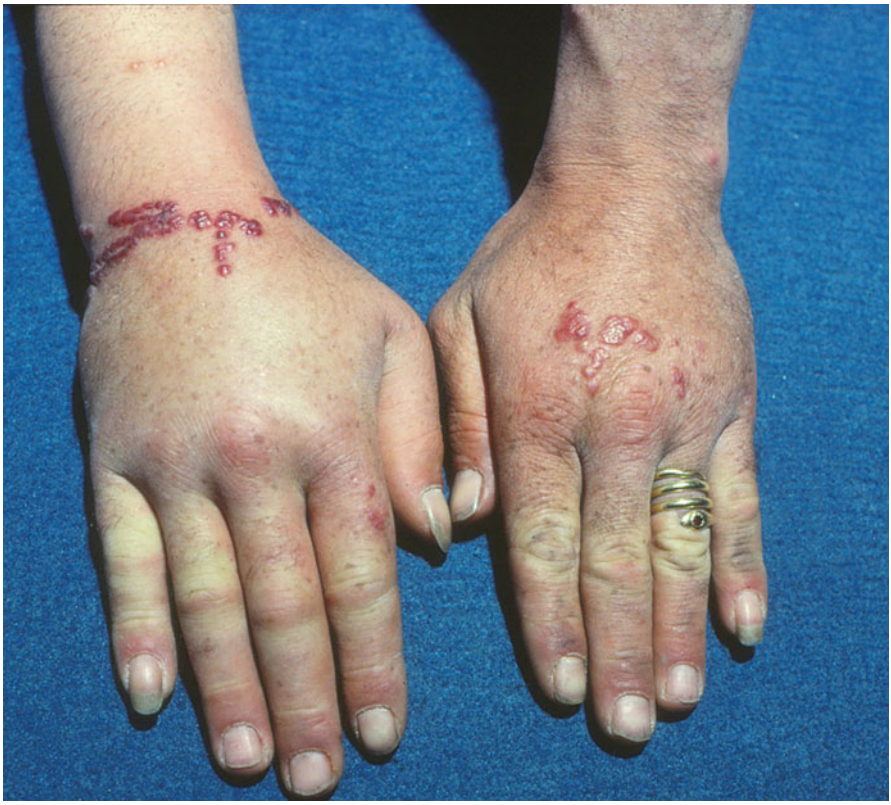

Fig. 3.21 Erythemato-oedemato-vesico-haemorrhagic reaction to jellyfish. The fisherman had plunged his hands into the catch that also contained several jellyfish

then gradually regressed spontaneously. Both this patient and the one described previously had significant IgG antibody titres to the crude extract of nematocysts of *P. noctiluca* and also to toxins from *P. physalis*, of the Hydrozoa class.

The third case was a doctor who was stung on the left thigh and developed a burning, erythemato-vesicular reaction that healed spontaneously in 15 days. One month after recovery, the lesion recurred, with an itching sensation, although there had been no further contact with a jellyfish Unlike the other two patients, this third patient did not have specific circulating antibodies in serum, assayed 19 months after the episode. This means that sensitisation to *P. noctiluca* does not always last long.

Among the other Mediterranean jellyfish, *Rhizostoma pulmo* (Fig. 3.24) can sometimes cause dermatitis [141], while it is not known whether *Aurelia aurita* (the "moon jelly"), one of the most beautiful jellyfish, with a transparent blue body about 25 cm in diameter, is dermotoxic. It is thought to be innocuous but contact can induce a burning sensation that lasts a few minutes. Instead, the toxicity of *Chrysaora hysoscella* [142, 143], *Carybdea marsupialis* [144] and *Rhopilema nomadica* [145,

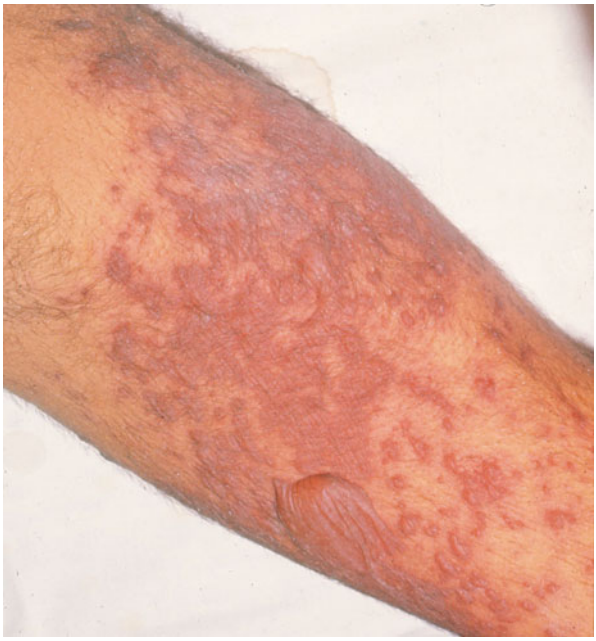

Fig. 3.22 Erythemato-vesico-bullous reaction to jellyfish

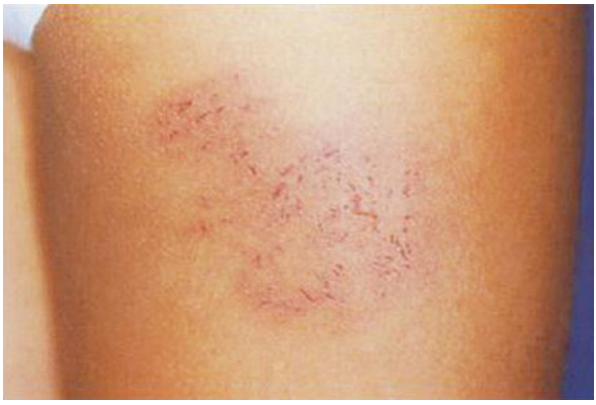

Fig. 3.23 Figured atrophic and dyschromic outcome of reaction to jellyfish

146] has already been demonstrated. This last jellyfish arrived in the Mediterranean in the 1980s, coming from the Red Sea through the Suez Canal. It is also possible to observe jellyfish that have come in from the oceans to the Mediterranean, especially on the west coasts, at some periods of the year.

Chrysaora quinquecirrha ("sea nettle"), present in the Atlantic, Indian and Pacific Oceans, has a bell diameter of about 6–25 cm and a smooth exumbrella; in adults it generally has 40 tentacles that can extend up to 3–4 m [25, 26]. Contact with this jellyfish normally causes mild to moderate pain, wheals and pink spots that may persist for about 1 month [147].

Fig. 3.24 *Rhizostoma pulmo*

Members of the Cyaneidae are ubiquitous, being very common in both warm and cold waters. They are found in shallow waters, and their tentacles are distributed in clusters. The largest *Cyanea* species are present in polar regions. *Cyanea capillata* is widely distributed, being found everywhere in Australia, and most commonly along the Norwegian coast and the North Sea [148]. The colour of its bell varies from pink to reddish-gold or brownish-violet, with purple oral arms and reddish or yellow tentacles (30–50 cm in the length): hence the common name "lion's mane". The umbrella ranges from 30 to 80 cm in diameter, but in some cases can even reach nearly 2 m [148]. Stings from *C. capillata* can cause minor or severe pain; the swelling normally resolves after about 15 min, but erythematous stripes remain for several days [25]. Sometimes systemic symptoms may develop (nausea, sweating, abdominal and muscular cramps). The tentacles are still capable of envenomation even after they have detached.

3.6 Reactions to Cubozoa (Box Jellyfish)

Box jellyfish (Cubozoans species) are among the major toxic marine animals, and envenomation usually poses a medical emergency (Table 3.3). They are almost invisible in the water, having transparent, cube-shaped bodies with underlying tentacles. They are found swarming along coasts, in harbours and shallow waters. Two different orders of cubozoans are known: the large multi-tentacles chirodropida (among the most harmful marine creatures) and the smaller four-tentacled carybdeida [14, 25, 149].

Chironex fleckeri was responsible for several sudden and painful fatalities in Australian waters [149–158]. This box jellyfish can weigh up to 6 kg, and the diameter of its cubic bell measures about 20–30 cm. It is equipped with four bands of 10–15 translucent tentacles stemming from four pedalia; the tentacles of mature species are flat and may extend up to 3 m [25]. They generally come in from the open sea to shallow waters to search for small prawns, in the proximity of beaches where most stings will then occur. It has never been found off-shore around coral reefs.

C. fleckeri is almost impossible to see, even after it has stung. Although most stings are minor, eliciting local pain and skin changes, a massive envenomation may cause severe systemic symptoms and sometimes even death, usually within few minutes [159]. Local signs include intense skin pain, with oedemato-erythematous lesions measuring 0.5–1.0 cm in diameter on the affected site. These wheals resemble whip marks. They will be followed by blisters formation, that leave full-thickness areas of skin necrosis after the healing process, that generally takes about 10 days. Permanent scars with dyspigmented areas are common sequelae. The severity of the stings depends on the size of the bell.

Systemic reactions include: dyspnoea, hypotension, unconsciousness, arrhythmias and cardiopulmonary arrest [160]. The venom is also cardiotoxic (the lethal component has yet to be identified) [160], having a direct effect on the heart muscle and vascular tissue [161]. Massive contact with these animals can cause loss of consciousness in a few seconds, and death may ensue after 5–20 min [154–162]. Severe signs and death can follow even after lesser skin contact [159], in particular in children with a lower body mass [162]. Death is generally the result of cardiac asystole [162, 163].

C. fleckeri anti-venom, obtained by hyperimmunization from sheep, has been widely available since the 1970s and is produced by the Commonwealth Serum Laboratory (Melbourne, Australia) [153, 161]. However, it must be administered very soon after the event. Indications for anti-venom include cardiorespiratory arrest, arrhythmias, and difficulty in breathing, severe pain, or extensive skin lesions.

Chiropsalmus quadrigatus is very common in Australia, the Philippines, Japan, the Indo-Pacific Ocean, North America and the Caribbean seas [26]. It is rather difficult to identify this jellyfish, and in fact, many jellyfish in the Western Pacific Region are incorrectly classified as *C. quadrigatus* [164]. The latter species swims on the sea surface and is often found in shallow coastal waters. It is smaller than *C. fleckeri*, has a bell measuring 7–10 cm, and a pedalium extends from the four lower corners of its cubic bell, with 9–15 rounded tentacles about 3 m long.

C. quadrigatus envenomation is generally milder than that of *C. fleckeri*. The immediate local symptoms include intense pain and redness and swelling, that can last from some minutes up to 24 h. Systemic symptoms have been reported along the Pacific coastal areas but not in Australia, and include hypertension, bradycardia, cardiac asystole, respiratory failure, shock and death [164]. The administration of *C. fleckeri* anti-venom in mice exposed to *C. quadrigatus* prevents lethal and haemolytic effects, as well as myotoxic and neurotoxic effects *in vitro*, but not the cardiovascular effects of the venom [164]. However, clinical evidence for the use of *C. fleckeri* antivenom in *C. quadrigatus* envenomations is still lacking [159].

Chiropsalmus quadrumanus is found in warmer waters of the Atlantic Ocean, from North Carolina to Brazil [165]. Its transparent cubic bell has a diameter of up

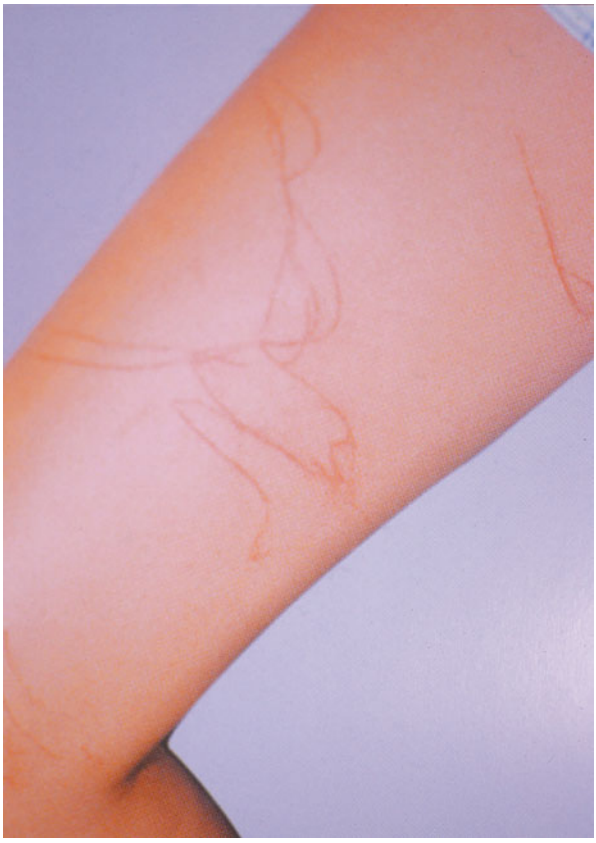

Fig. 3.25 Erythemato-oedematous linear lesions from *Chiropsalmus quadrumanus* (Courtesy of Prof. Vidal Haddad Jr, Department of Dermatology, Botucatu, University of São Paulo, Brazil)

to 14 cm, and 7–9 pale mauve tentacles originate from the 4 palmate pedalia and extend for 3–4 cm [26]. Contact with this jellyfish produces skin lesions and can even be potentially lethal to children [25] (Figs. 3.25 and 3.26).

Carybdea rastoni has a small bell (3 cm wide and 5 cm long; tentacles from 5 up to 30 cm long); this carybdeid jellyfish is very common in all Australian waters and Western Pacific. Stings produce 4 wheal marks 3–12 mm wide, delayed moderate pain lasting for 2 h, swelling and erythema lasting for 2–3 days, while pigmentary changes may persist for 2 weeks [22].

Carybdea alata (also known as *Alatina moseri*) is a tropical animal that is very common in Hawaiian and Eastern Pacific waters [25, 166, 167]. The bell, that is higher than it is wide, has a diameter of about 230 mm and a blunt, flat head. The 4 pink tentacles are longer than the milky white umbrella diameter. Stings are not generally lethal. The pain is moderate to severe and lasts about 2 h. Skin signs are 4 wheals of about 10–20 cm in length and 3–12 cm in width; subsequent vesicles and pigmentary changes may persist for up 2 weeks after the accident [22, 25]. Cases of anaphylaxis or anaphylactoid syndromes have been reported [168]. Unlike *C. rastoni*, *C. alata* can induce the Irukandji syndrome [168].

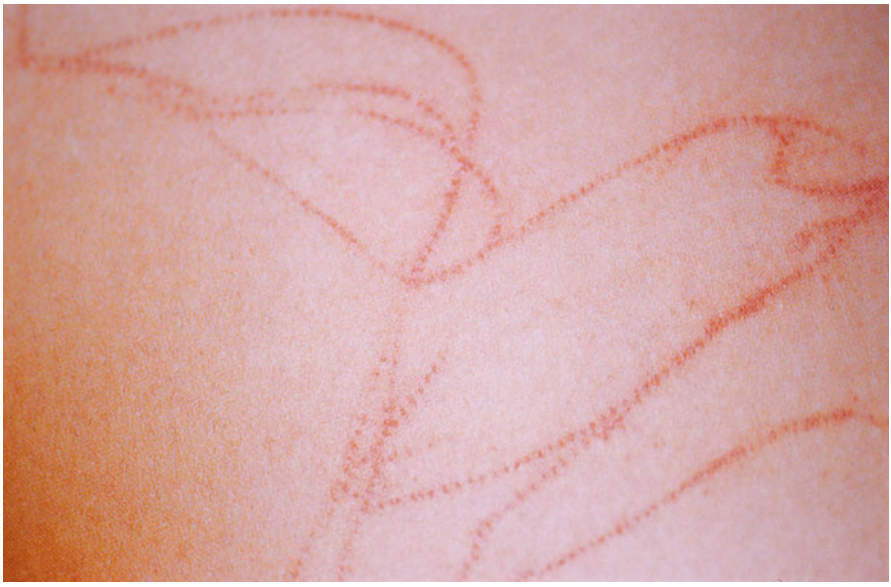

Fig. 3.26 The same case as in Fig. 3.25 (Courtesy of Prof. Vidal Haddad Jr, Department of Dermatology, Botucatu, University of São Paulo, Brazil)

Morbakka ("fire jelly") is a large carybdeid jellyfish found in Queensland, Australia. Its transparent bell is 10 cm high and 6 cm large [169]. Stings with its tentacles cause immediate burning pain lasting about 24 h and wheals 20 mm wide [25]. In approximately 10% of stings, *Morbakka* may induce Irukandji-syndrome-type symptoms, although these are far less intense than the classic Irukandji syndrome [169].

3.6.1 Irukandji Syndrome

This syndrome, named after an Aboriginal tribe that formerly populated the area north of Cairns (Queensland, Australia) [170], is mostly induced by a carybdeid jellyfish, namely *Carukia barnesi*, present throughout all Australian waters, but particularly in Queensland and the Northern Territories [152, 153, 168]. This small, transparent jellyfish has a cubic bell 2 cm wide and 2.5 cm long; its four tentacles vary in length from a few mm to 35 cm [25]. In summer, it inhabits shallow coastal waters as well as the deep sea off the Greater Barrier Reef.

The syndrome was given its name by Flecker in 1952 [168]. In 1961, Barnes identified the jellyfish responsible and then Southcott, by combining the words "carybdeida" and "Irukandji" coined the terms "Carukia", and "barnesi" commemorating Barnes [14, 170–174].

C. barnesi stings are usually mild and can go unnoticed, also because the jellyfish is hard to see. About 20 min after the sting, an oval erythematous area of 4–7 cm develops on the affected area, with a cluster of surrounding vesicles about 2 mm in size ("goose-pimple effect"). This local reaction persists for about 30 min but may

Table 3.4 Signs and symptoms of Irukandji syndrome

Sequelae	Symptoms
Pain	Lower backache, muscle cramps in all limbs
	Abdominal and chest pain
	Pins and needles
Catecholamine response	Sweating
	Piloerection
	Anxiety, feeling of "impeding doom"
	Restlessness
	Severe headache
	Nausea, vomiting
	Peripheral tremor
	Pallor or peripheral cyanosis
	Tachycardia
	Hypertension
	Cerebral edema (not frequent)
Cardiac effects	Cardiac failure
	Pulmonary oedema (≤15 h after the sting)
	ECG changes
	Troponin leaks

Modified from Nickson and Coll. [173]

not be noticed. After about 30 min–1 h after the sting, the onset of severe systemic symptoms occurs. Williamson and Coll. compared the symptoms of Irukandji syndrome with the envenomation by the scorpion and funnel web spider, and concluded that any of these may result in the excessive release of catecholamines into the bloodstream, with similar presenting signs and symptoms [25].

The syndrome follows a pattern that has up to three documented sequelae. Signs and symptoms include pain, catecholamine response (epinephrine-like effects), and cardiac effects (Table 3.4) [172–176]. Apart from severe muscle cramps, that are always present, various combinations of these symptoms can be observed, and at different times, although they will invariably manifest in sequence. Irukandji syndrome can consist of severe low back pain, tremors, muscle cramps in all 4 limbs, abdominal and chest pain, anxiety, sweating, nausea, vomiting, headache and palpitations [168, 172, 173]. Life-threatening hypertension (up to 300/150 mmHg), tachycardia, pulmonary oedema and toxic global heart dilatation require admission to the intensive care unit. Depending on the species responsible, there may be pain but no hypertension [177]. Death due to intracerebral haemorrhage secondary to severe hypertension has been reported [178]. According to some authors, cardiac dysfunction may be linked to myotoxin [179], while others attribute it to the release of high quantities of noradrenalin [180]. It has been suggested that the syndrome could be caused by venom disruption of the sodium ions, generating massive catecholamine release [180]. It can be associated with a calcitonin gene-related peptide, endogenous catecholamines and stress cardiomyopathy [180, 181].

Irukandji syndrome has also been reported in other zones, such as Thailand [182], Guadaloupe [183], Florida [27], Malaysia [28], and Torres Strait Islands (between the northeast of Australia and Papua New Guinea) [184].

Various other species of carybdeid jellyfish have recently been associated with Irukandji syndrome: *Carybdea xaymacana, Carybdea shinju, Malo maxima, Alatina moseri, Alatina mordens, Malo kingi, Gerongia rifkinae*, and *Morbakka fenneri* [168, 185, 186]. The Australian multi-tentacled *Physalia* species also seems to be implicated in an Irukandji-like syndrome, that features less severe symptoms, such as back pain, dyspnea and anxiety [168].

A great media interest in stings by *C. barnesi* has recently arisen, owing to their Viagra-like action [187]. Actually, priapism had already been reported in the Irukandji syndrome [188], as well as in other envenomation syndromes (from scorpion stings, spider bites, and Brazilian banana spiders), that have in common a "catecholamine storm" and involve neuroexcitatory toxins. It is possible that in these syndromes priapism occurs as a result of sodium channel activating, toxin-mediated release of nitric oxide, the most important factor in promoting smooth muscle relaxation of the corpus cavernosum [188].

3.7 Reactions to Anthozoa

The *Anthozoa* (from the Greek *anthos*=flower and *zoan*=animal, as sea anemones resemble flowers) class includes sea anemones and other anemone-like groups, with skeletons (such as the "stony" scleractinian corals), and without skeletons (such as tube anemones), as well as sea pens, sea fans, blue corals, and black corals (Table 3.1). Sea anemones and corals only exist as polyps. Sea anemones (order: Actiniaria) always bear more than eight tentacles. Many sea anemone species are burrowers in mud and sands, but most dwell on hard substrates, cemented permanently or temporarily by secretions from a well differentiated disk. Their sexual reproduction occurs by budding, break-up or fission, or involving either internal or external fertilization of gametes.

Subclass Zoantharia also includes the hard (stony) corals (order: Madreporaria) whose polyps are encased in a rigid, calcium carbonate skeleton. The great majority of hard corals live in colonies composed of vast numbers of small polyps (5 mm), but the less abundant, solitary forms may be large (up to 50 cm). In colonial forms the polyps form a superficial living sheet overlying the skeleton, which is itself secreted from the lower outer (ectodermal) layer.

Corals exhibit a great diversity of growth forms, ranging from delicately branching species to those whose massive skeletal deposits form the building blocks of coral reefs.

3.7.1 Reactions to Sea Anemones

All species have nematocysts. Owing to their great profusion of colours, these animals often resemble anemone flowers, which is why they are commonly called "sea anemones", or "sea roses", or "sea daisies" (Fig. 3.27).

The common species of sea anemones in the Italian seas are *Actinia equina, Condylactis aurantiaca* (Fig. 3.28)*, Adamsia palliata, Aiptasia mutabilis, Calliactis parasitica,* and above all *Anemonia sulcata* (Figs. 3.29 and 3.30). These various sea

Fig. 3.27 *Parazoanthus axinellae* (sea daisies) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

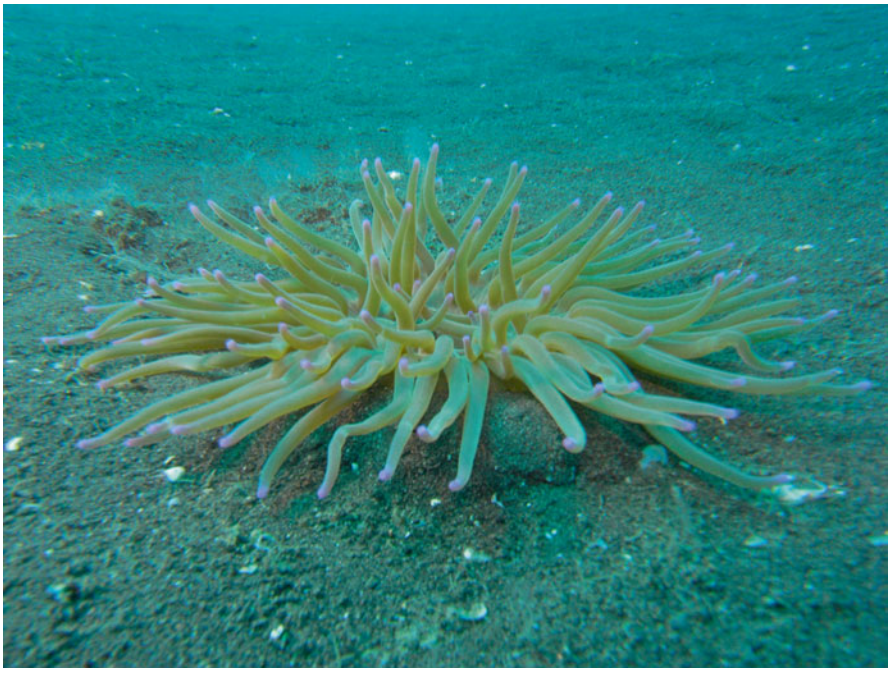

Fig. 3.28 *Condylactis aurantiaca* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Fig. 3.29 *Anemonia sulcata* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

anemones cover the sea bed with their tentacles and display iridescent colours ranging from red through orange to purple. *Anemonia sulcata* ("wax rose sea anemone") is common in shallow waters and up to depths of 10 m; younger examples can frequently be found in pools and under the tide-line where they expand to cover the submerged rocks completely. As they grow bigger they creep slowly out towards deeper waters.

Like jellyfish, sea anemones have a transparent body due to a very high water content, accounting for over 95 % of their body weight. They generally live attached to the sea bed, and outside the water they lose their shape and appear as a jelly-like blob. Sea anemones have a highly variable morphology, looking rather like fleshy flowers on a thick stem, with a crown of brightly coloured tentacles issuing from the apex. The tentacles are long and slender and arch downwards like water from a fountain; they wave gently in the water drawing very elegant figures and fantastic arabesques. In fact, sea anemones offer lovers of underwater diving a sight of rare and incomparable beauty.

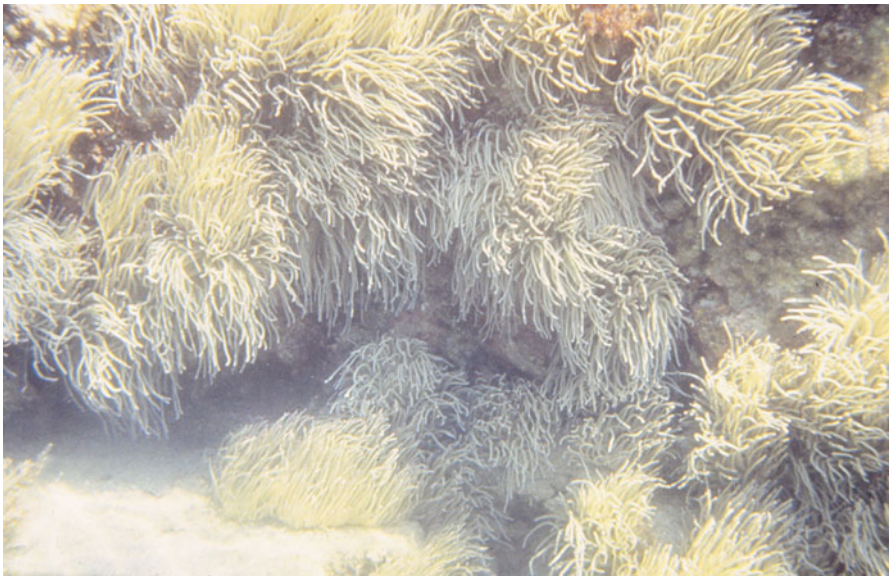

Fig. 3.30 *Anemonia sulcata* (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

From the biopharmacological point of view, sea anemones toxins are relatively stable compared to other cnidarian toxins [189–197]. Most sea anemones toxins belong to one of three classes: 20-kDa pore-forming cytolysins inhibited by sphingomyelin [193], 3–5-kDa neurotoxins acting on voltage-gated sodium channels [192], and 3.5–6.5-kDa neurotoxins acting on voltage-gated kv1 potassium channels [194]. Besides these well characterized peptide toxins, structurally and/or functionally novel peptide toxins which seem to be promising pharmacological reagents have recently been isolated from some species of sea anemones [195, 196].

Although the great majority of sea anemones is harmless, some sea anemones can cause cutaneous reactions. Unlike contact reactions to jellyfish, those to sea anemones have rarely been reported in the literature, even if they are well known to occur [1, 6, 9–11, 82, 118, 198, 199]. We have observed many cases of reactions to *Anemonia sulcata*, some of which show a spontaneous onset after accidental contact with the animal, while others are provoked. The latter pictures are commonly observed in children and young people who, despite being aware of the urticant properties of the sea anemone, like to play at throwing them at one another.

From the clinical point of view, sea anemones can induce the same clinical pictures as those described above for jellyfish. Along the Italian coasts, sea anemones reactions, that are most commonly toxic in nature, generally presented in our experience with much more marked symptoms than those due to local reactions to jellyfish (Table 3.5). In fact, they are commonly observed after close contact with the animal when sitting or lying on the rocks, to which sea anemones are attached, in shallow waters. For this reason, the lesions tend to be more extensive and can take

Table 3.5 Differential characteristics between reactions to jellyfish and sea anemones generally observed along the Italian coasts

	Reactions to jellyfish	Reactions to sea anemones
Incidence	Frequent	Less frequent
Age	All ages	All ages, especially children
Provoked reactions	Exceptional	Frequent in young people (sea anemones are easily picked up)
Type of contact	Generally superficial	Generally very close
Method of contact	Generally brushing against animal while swimming	Generally close when sitting or lying on the rocks
Sites	All sites	All sites, especially posterior face of the thighs and back for above reasons
Extension of dermatitis	Generally slight	Extensive (contact with various areas) for above reasons
Clinical picture	Generally slight	Generally severe
Morphology of lesions	Mainly linear figures	More bizarre and arabesque-like figures
Clinical lesions	Erythema, oedema, rarely blisters and necrosis	Erythema, severe oedema, frequent blisters and necrosis
Local subjective symptoms	Generally pain and slight burning sensations	Generally intolerable pain and burning sensations
Systemic symptoms	Possible, generally slight	Virtually constant and severe
Clinical course	Few days	15–30 days
Sequelae	Infrequent	Frequent
Allergic reactions	Possible	Possible

on bizarre pathognomic pictures, notably elegant arabesque-like stripes. Morphologically, in addition to the erythemato-oedematous aspect, the lesions are most often vesicular or blistering and sometimes necrotizing (Figs. 3.31, 3.32, 3.33, 3.34, 3.35, 3.36, 3.37, 3.38, 3.39, 3.40, 3.41, 3.42, 3.43, 3.44, 3.45, 3.46, and 3.47). The oedema is often serious enough to create an angio-edematous picture (Figs 3.48 and 3.49). Owing to this greater clinical severity of the lesions, the course of the complaint lasts from 15 days to 20–30 days and may be accompanied by very severe subjective and systemic symptoms. The local pain and burning are sometimes intolerable and systemic reactions, such as malaise, weakness and muscular cramps, are nearly always present. Dyschromic or scarring sequelae are much more common after reactions to sea anemones than to jellyfish [118] (Table 3.5) (Figs. 3.50, 3.51, 3.52, and 3.53).

No cases of fatal reactions to sea anemones have been reported in the literature. We have observed two cases of systemic reactions. The first was a 9-year-old boy, who presented an erythemato-oedematous dermatitis with configured lesions on the flexural surface of the right thigh (Figs. 3.54 and 3.55) [199]. The lesions were an agglomerate of erythematous, oedematous and vesico-bullous stripes; the erythema, which was bright red with a purpuric imprint, had fairly distinct outlines. The stripes varied in length from 2 to 7 cm and were interwoven, creating an elegant abstract design with a central core and branches spreading out in various directions, rather like pseudopods. Identical lesions with a more elementary design were present on

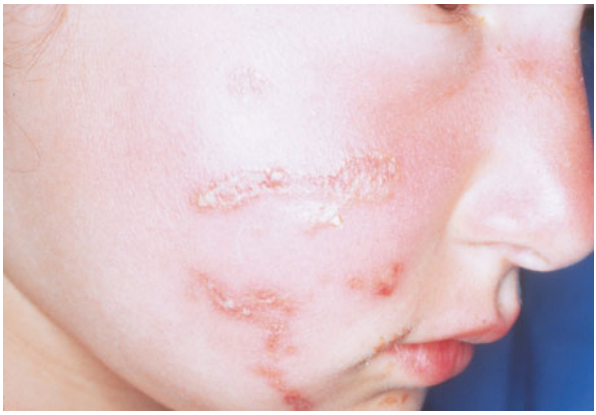

Fig. 3.31 Figured erythemato-vesicular reaction to sea anemone

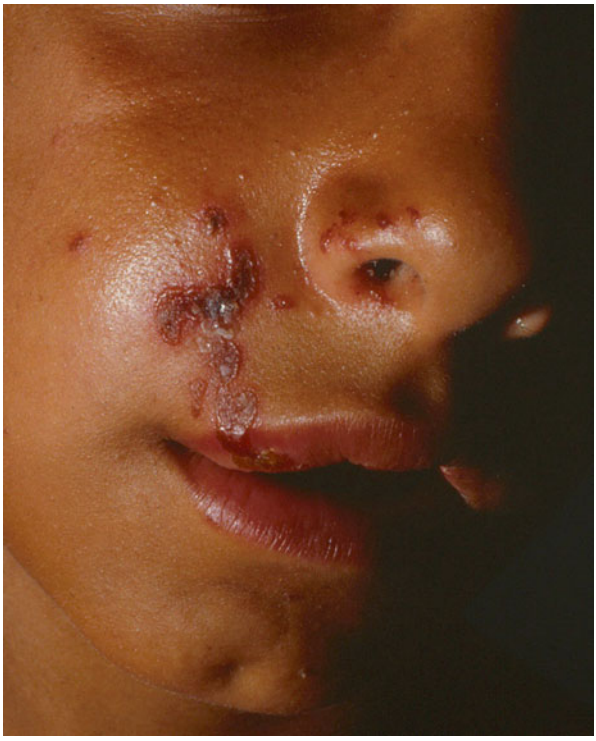

Fig. 3.32 Necrotizing reaction to sea anemone

the volar surface of the right wrist. The skin complaint provoked intense pain and burning and was associated with headache, nausea, vomiting, bronchospastic crises and muscle cramps. The onset of the skin complaint and subjective and systemic symptoms had occurred at the seaside near Bari, a few minutes after the child had sat down on a partly submerged rock. On examination of the place, we collected (with gloved hands) the jelly-like bodies of a few sea anemones that were identified

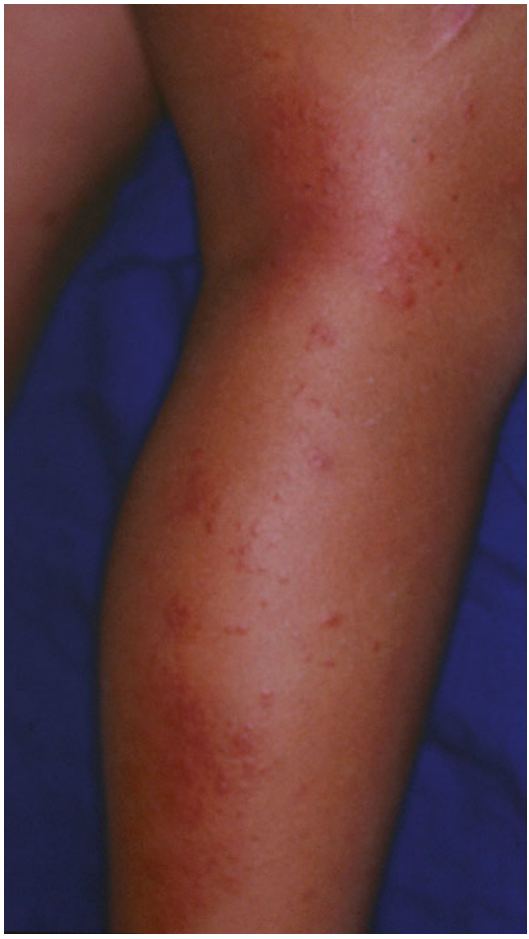

Fig. 3.33 Erythemato-vesicular reaction to sea anemone on a typical site

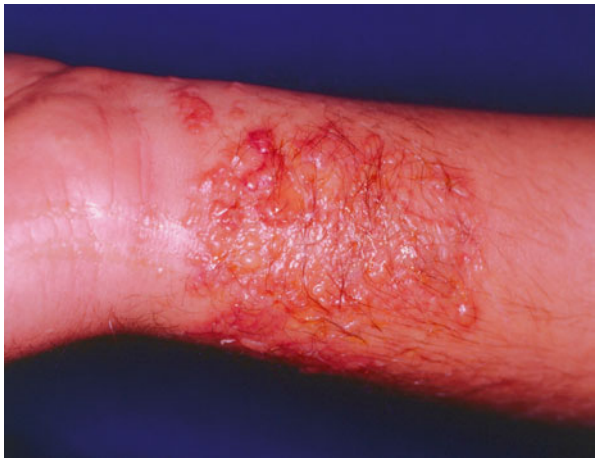

Fig. 3.34 Erythemato-bullous reaction to sea anemone on a typical site

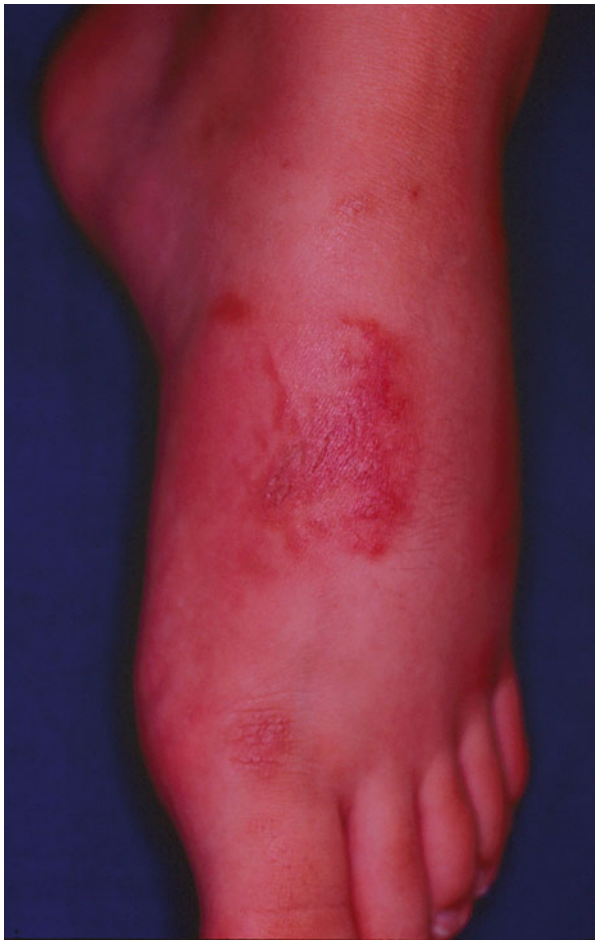

Fig. 3.35 Figured erythemato-vesicular reaction to sea anemone after wading in a pool with open strip sandals

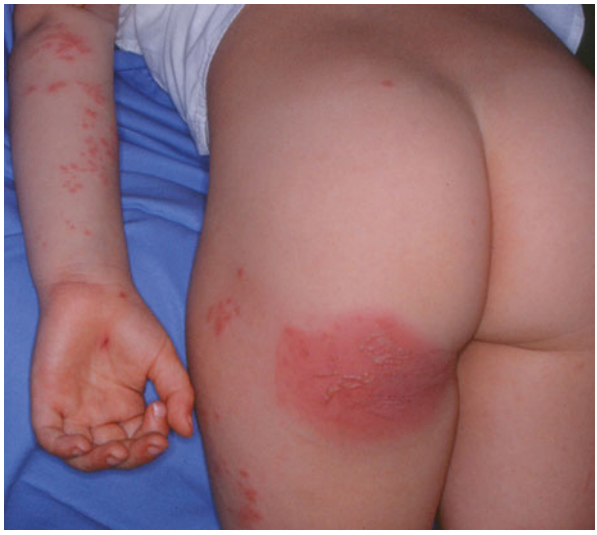

Fig. 3.36 Erythemato-oedemato-vesicular reaction with multiple foci on typical sites. The child had sat on a submerged rock covered in sea anemones

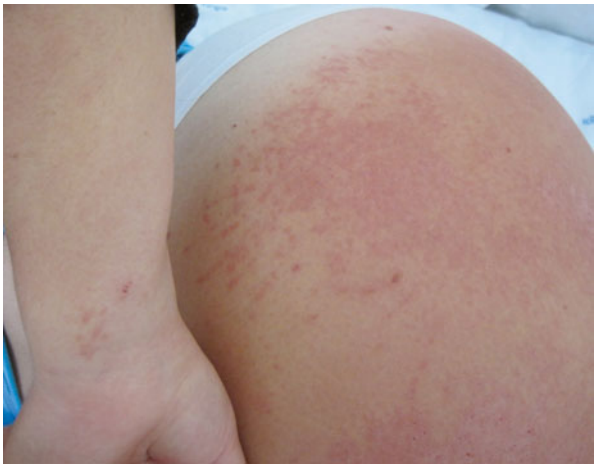

Fig. 3.37 Erythemato-oedemato-vesicular reaction to sea anemone with multiple foci on typical sites

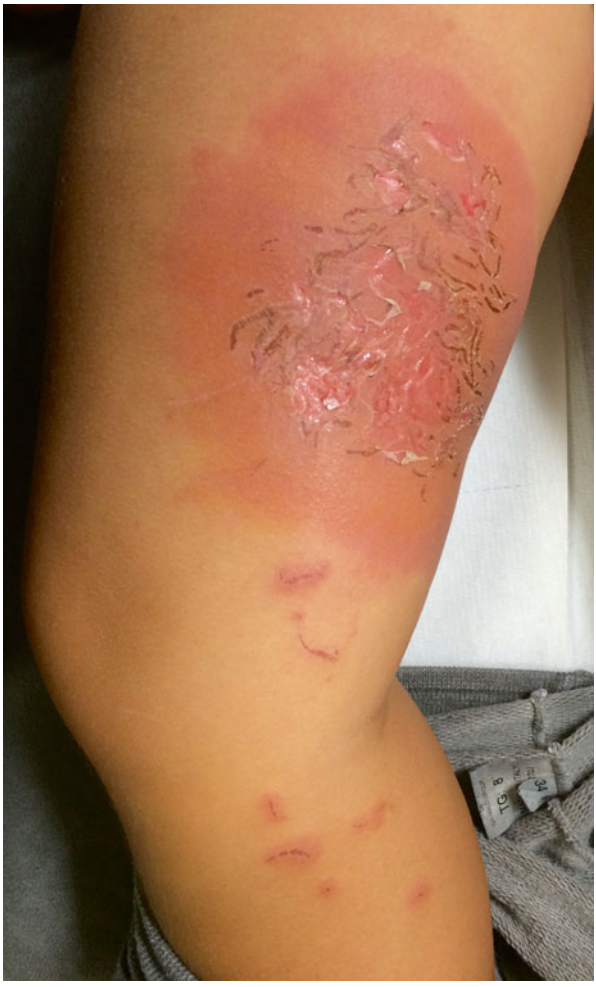

Fig. 3.38 Erythemato-oedemato-erosive reaction to sea anemone on typical site

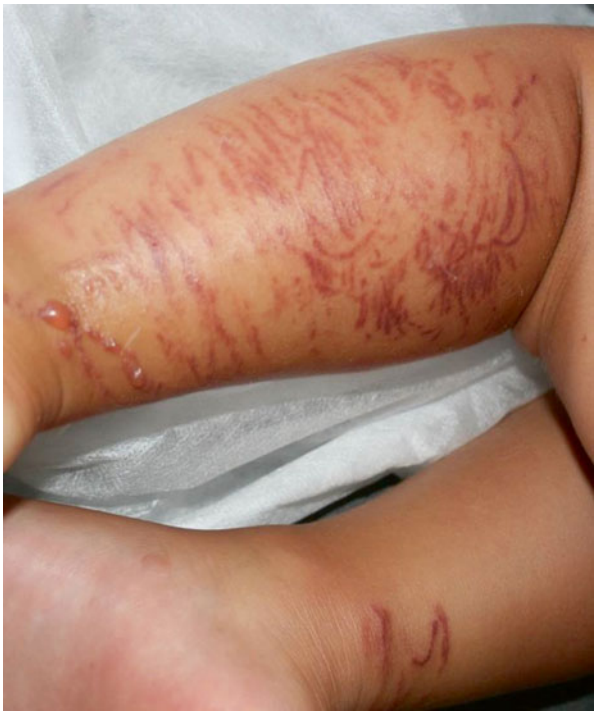

Fig. 3.39 Figured erythemato-vesico-bullous reaction to sea anemones on typical sites

by the Laboratory of Marine Biology of Bari University as members of the *A. sulcata* species.

The second case was a girl aged 12 years (Figs. 3.56 and 3.57). She presented with an extensive erythemato-oedemato-bullous figured dermatitis on the posterior face of the right thigh. The complaint was associated with intense pain at the affected part, nausea, vomiting, headache, muscular cramps and bronchospastic crises. The skin complaint and systemic symptoms were again due to brief contact with the *A. sulcata* species. In both recorded cases, the dermatitis resolved in about 25–30 days.

Clinical manifestations of dermatitis caused by sea anemones depend to a large extent on the extent of the sites affected. Very serious local reactions, such as ulcerations lasting several months, have been reported from the sea anemones *Actinodendron plumosum* and *Triactis producta* [195]. The sea anemone *Phyllodiscus semoni* (one of the most dangerous sea anemones, commonly called "night sea anemone", common in the Western Pacific Ocean) can induce acute renal failure with predominant glomerular endothelial damage in humans [196]. *Haloclava producta* (the “ghost anemone”), a burrowing sea anemone in estuarine sediments of the US East Coast and Gulf of Mexico, was the cause of various cases of the so/called “ghost anemone dermatitis” in residents in Long Island, New York [197].

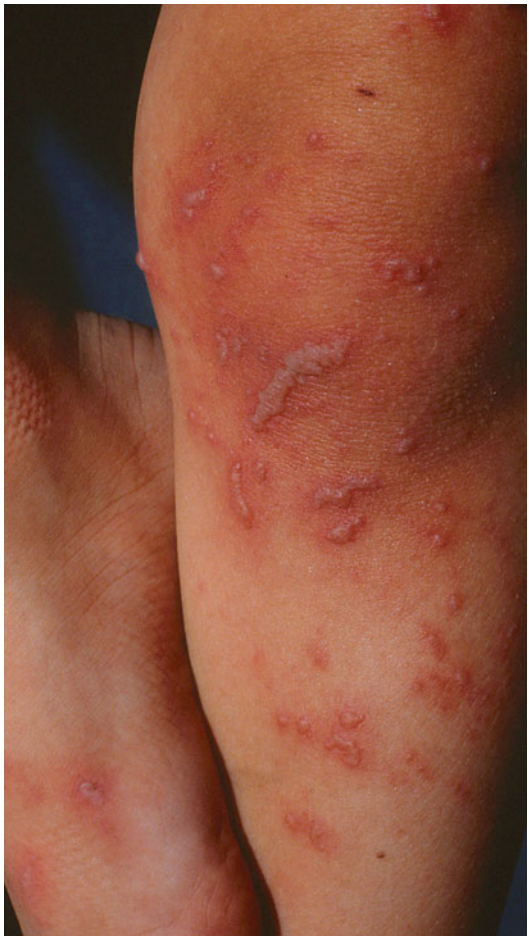

Fig. 3.40 Figured vesiculo-bullous and pustular reaction to sea anemone. The patient had knelt on a submerged rock covered in sea anemones

3.7.2 Sagartia's Dermatitis

One of the most common reactions to sea anemones is dermatitis from *Sagartia elegans*, also known as "sponge fishermen's disease" or "maladie des pêcheurs d'éponges nus", as it is called in some parts of the Mediterranean. *Sagartidae* are very common Coelenterates that live symbiotically at the base of sponges, and are to be found from Iceland right down to the southern Mediterranean. They are shaped like flowers about 1–4 cm long and have a cylindrical polypoid body with two rows of tentacles arranged radially.

Fishermen harvest these sponges with their bare hands, remove stones and other encrustations from their base and put them in a net slung round their necks. During these manoeuvres the fishermen come in contact with the *Sagartia*'s tentacles and after a few minutes they feel burning and itching sensations, which are followed by erythema and blisters. The erythema is bright red at first but then turns purple. The dermatitis may be associated with systemic symptoms, including headache, nausea,

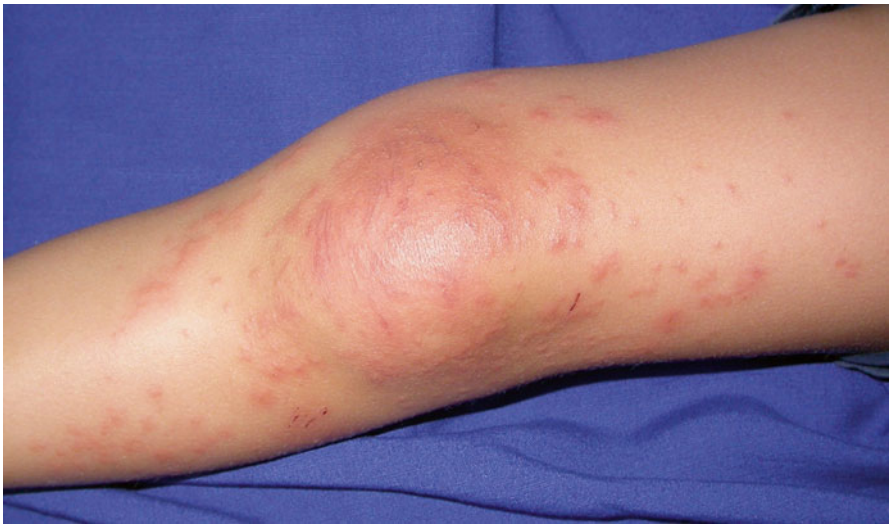

Fig. 3.41 Figured erythemato-vesicular reaction to sea anemone. The patient had knelt on a submerged rock covered in sea anemones

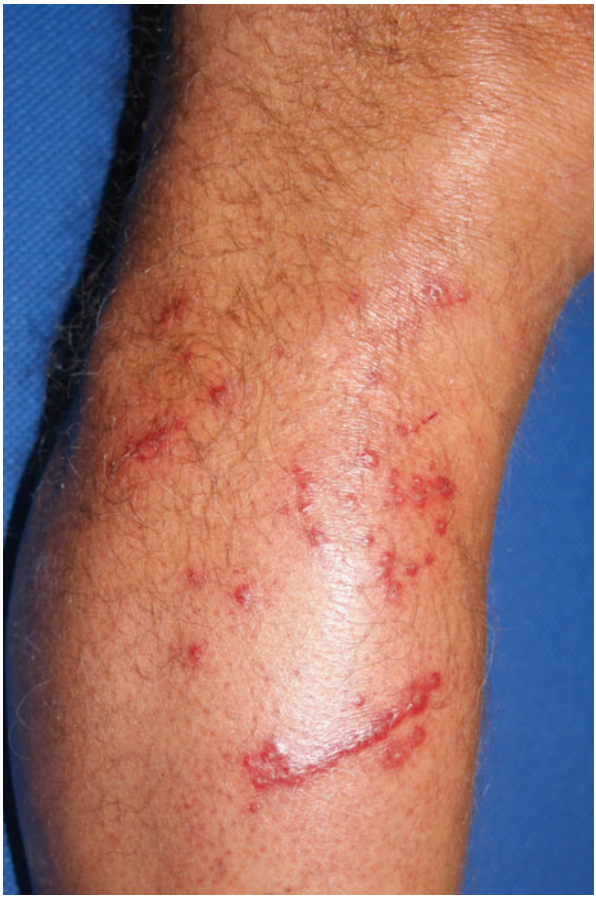

Fig. 3.42 Figured erythemato-vesicular reaction to sea anemone. The patient had knelt on a submerged rock covered in sea anemones

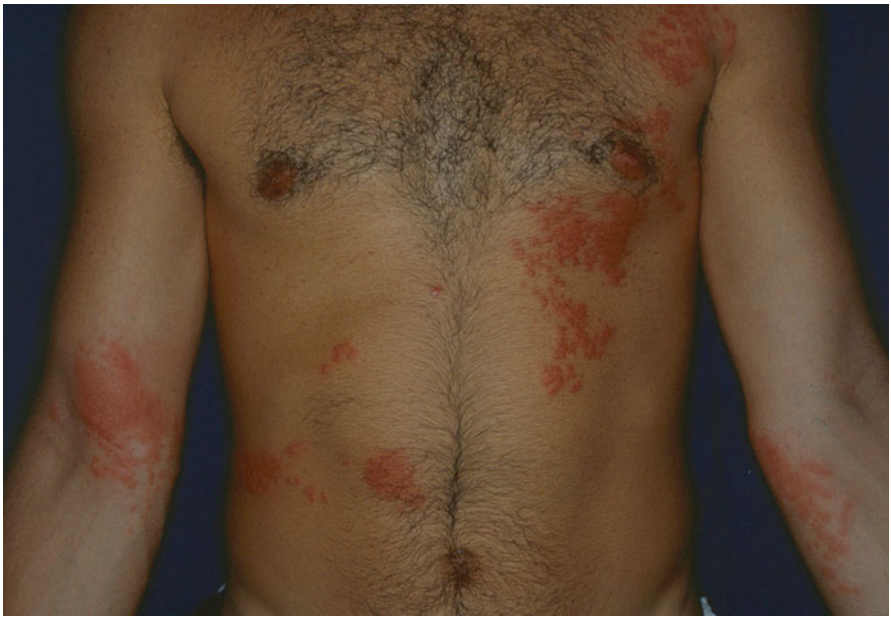

Fig. 3.43 Erythemato-vesicular dermatitis with foci disseminated all over the body in a skin diver who had swum through a field of sea anemones

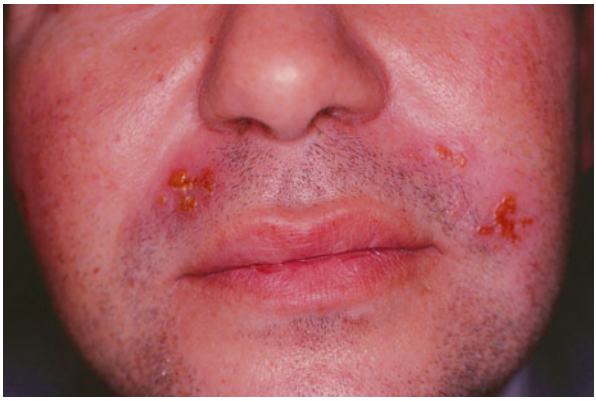

Fig. 3.44 The same case as in Fig. 3.43. Erythemato-vesicular foci of herpes simplex type

vomiting, fever, shivering, muscle spasms and collapse. The skin complaint takes quite a time to resolve and sometimes multiple abscesses develop, which may evolve into ulcers [1, 200].

3.7.3 Seabather's Eruption

The first description of the sea bather's eruption was of a papulous, intensely itchy complaint (Figs. 3.58 and 3.59) on skin areas covered by the costume or wetsuit, affecting bathers swimming on the south-eastern coasts of Florida [201]. The

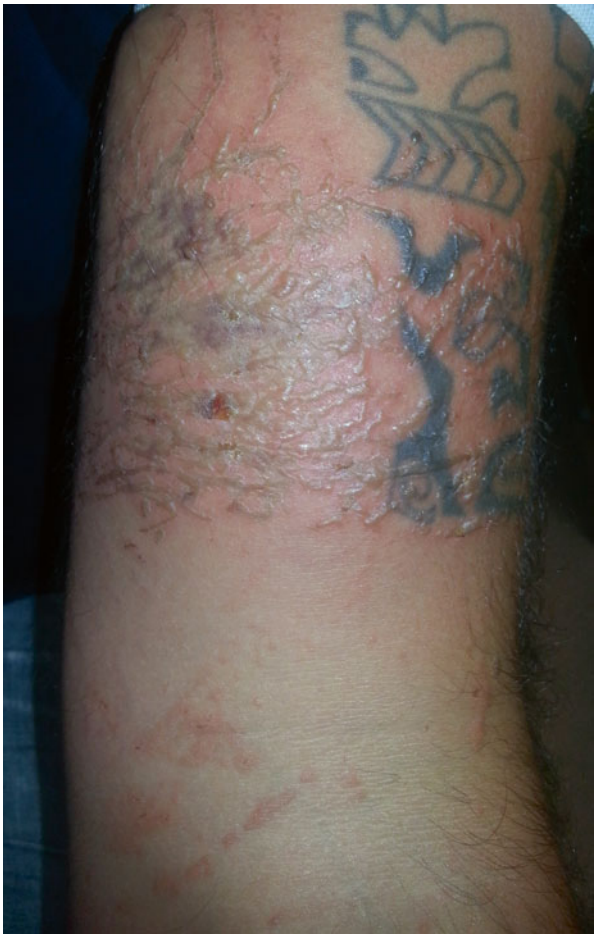

Fig. 3.45 Figured erythemato-vesicular reaction to sea anemones in a skin diver

dermatitis has also been inappropriately labelled "sea lice", a name that should correctly be used for the metazoal parasites of fish [202].

The eruption has been attributed to the nematocysts of Cnidaria (jellyfish, Portuguese man-o'-war, sea anemones, hydroids and corals). It has been reported periodically in Florida [203–205], Cuba [206, 207], the Caribbean and Mexico [208]. Freudenthal reported cases of seabather's eruption along the coasts of Long Island, New York, due to the larvae of the *Edwardsiella lineata* sea anemone [209]. Recently, there have been a number of cases reported also in Brazil [210, 211].

Wong and Coll. [212] conducted an interesting aetiological and clinical-histological study of this dermatitis during the spring and summer of 1992, when episodes of epidemic proportions occurred in south-east Florida. The authors observed 70 subjects (36 male and 34 female) who were resident or holidaying in south-east Florida during the period between April and June 1992. It was the first experience of dermatitis for 76% of them, while the remaining cases had a positive history. Quite severe symptoms were present in 22 patients. Most of them had been swimming at the time of the

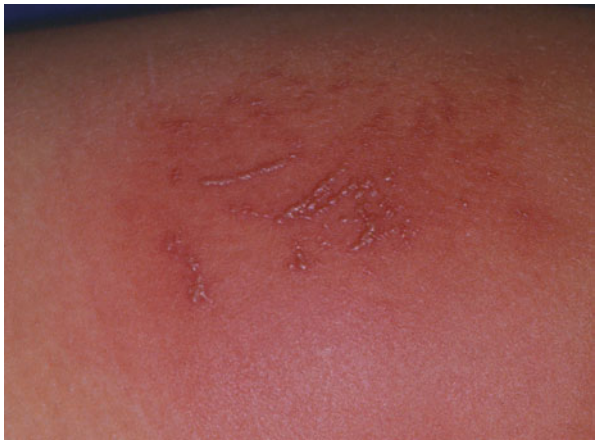

Fig. 3.46 Rounded erythemato-oedematous patch with central figured vesiculation typical of reactions to sea anemones (Reproduced with permission from Foti and Coll. [82])

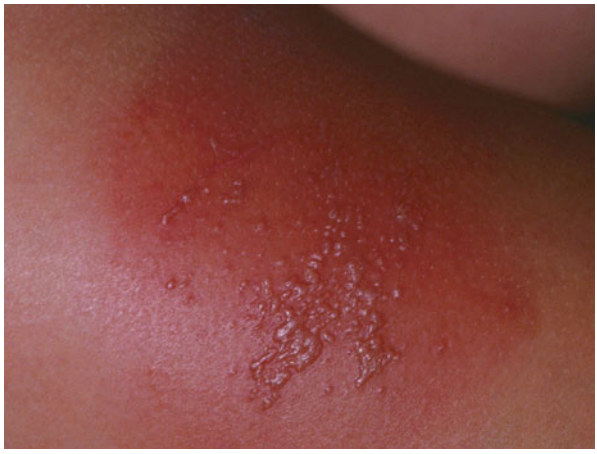

Fig. 3.47 Rounded erythemato-oedematous patch with central figured vesiculation typical of reactions to sea anemones

event (78.6%), while the others were engaged in underwater diving (8.6%), surfing (7.1%) or boating (7.1%). About 25% of the patients developed the symptoms as they came out of the water, while in the others the clinical signs appeared after a mean interval of 12 h. Itching, generally intense, was present in 69 subjects. Other subjective symptoms included malaise and fatigue (23%), fever (18.6%), shivering, headache, nausea, coughing, abdominal pain and diarrhoea.

The objective lesions consisted of many erythematous papules very near together, that sometimes evolved into pustules or blisters. Other lesions had a follicular distribution. In 11% of the cases there were also urticarial lesions. The eruption was prevalently monomorphous and lasted about 3 days. Regional adenopathy developed in 10% of patients. The papules were more numerous and inflamed in those who had not taken off their bathing costumes after coming out of the water. In 68% of subjects, the lesions were confined to covered sites, while the others developed lesions on both covered and uncovered sites. In all cases, the lesions were

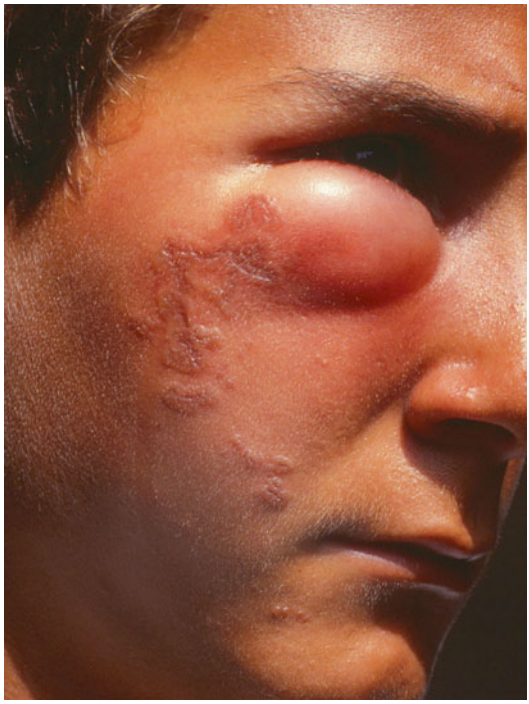

Fig. 3.48 Figured vesicular reaction with severe palpebral oedema from *Anemonia sulcata*

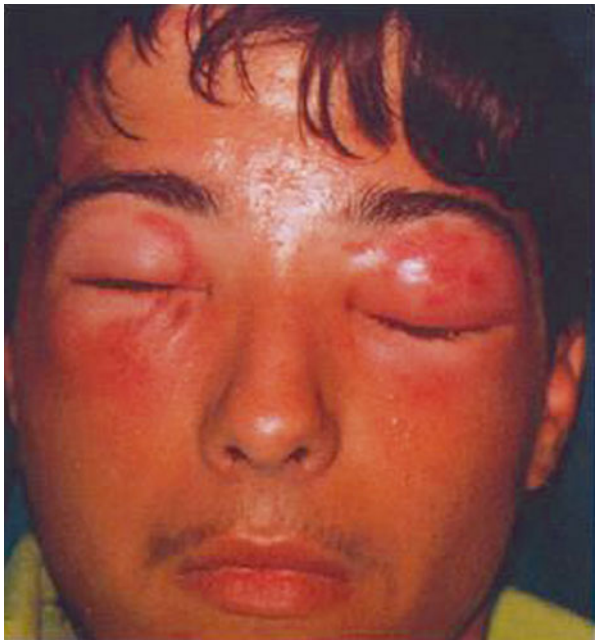

Fig. 3.49 Angioedematous contact reaction to *Anemonia sulcata* from swimming through a field of sea anemones

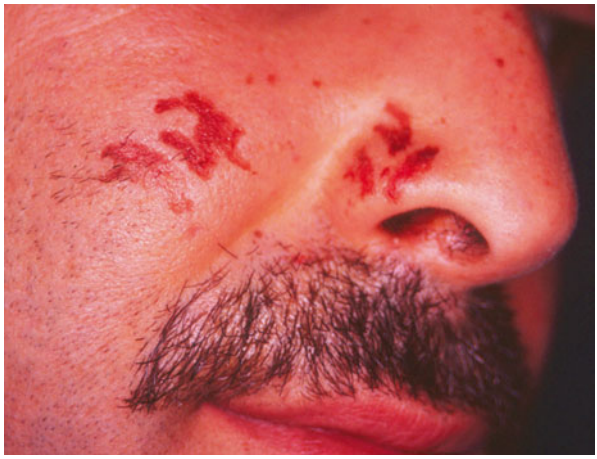

Fig. 3.50 Figured scabs and atrophic outcome of reaction to sea anemone

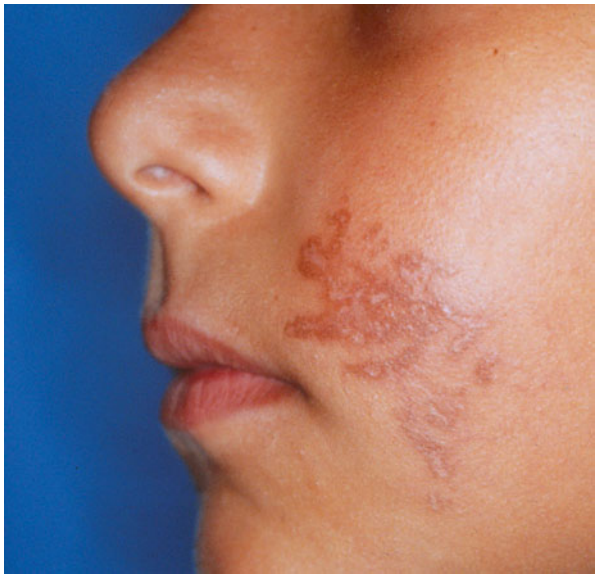

Fig. 3.51 Figured atrophic and dyschromic outcome of reaction to sea anemone (Reproduced with permission from Foti and Coll. [82])

concentrated under the swimming costume, in the skin folds and in sites where the costume hugs closely to the skin. The eruption lasted from 1 to 4 weeks (a mean of 12.5 days). The histological findings were not diagnostic: the most common picture was that of a superficial or deep infiltrate, prevalently perivasal, of lymphocytes, eosinophils and neutrophils. In some cases suppurating folliculitis or subcorneal pustules were evident; there was no spongiosis, necrosis or alteration of the subepidermal membrane.

Analysis of the waters showed that the cause of the eruption was larvae of the *Linuche unguiculata* jellyfish ("thimble jellyfish"). The serum of three patients

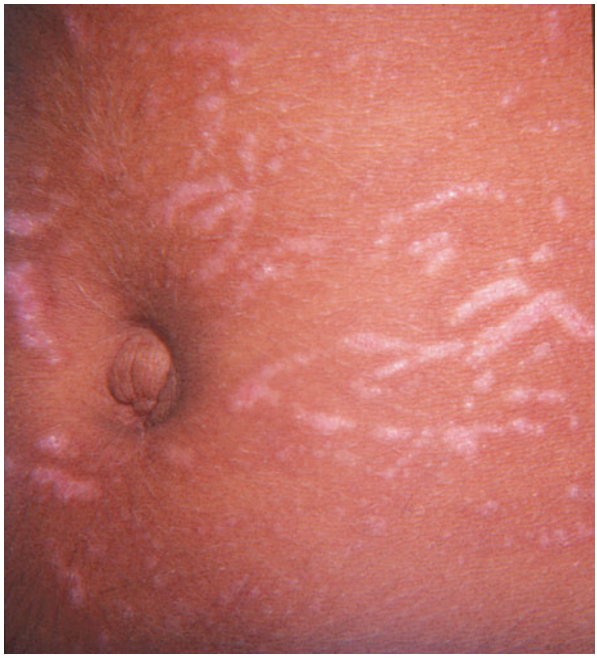

Fig. 3.52 Figured atrophic and hypochromic outcome of reaction to sea anemone

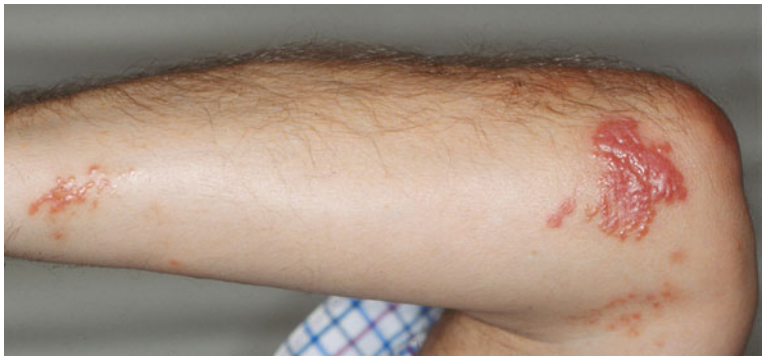

Fig. 3.53 Cheloid outcome of reaction to sea anemone (Reproduced with permission from Foti and Coll. [82])

showed high titres of specific IgG to this jellyfish. General and topical treatment was not very effective, although in some cases partially successful results were obtained with corticosteroids administered topically or systemically.

Other authors have also reported afflictions in which *Linuche unguiculata* was the causal agent [204, 213, 214]. It is not known why the episodes in south-east Florida are periodical but it seems likely that they may be caused by the Gulf Stream: the particularly high temperature of the water in these zones in some periods, such as summer 1992, might offer optimal reproductive conditions for this

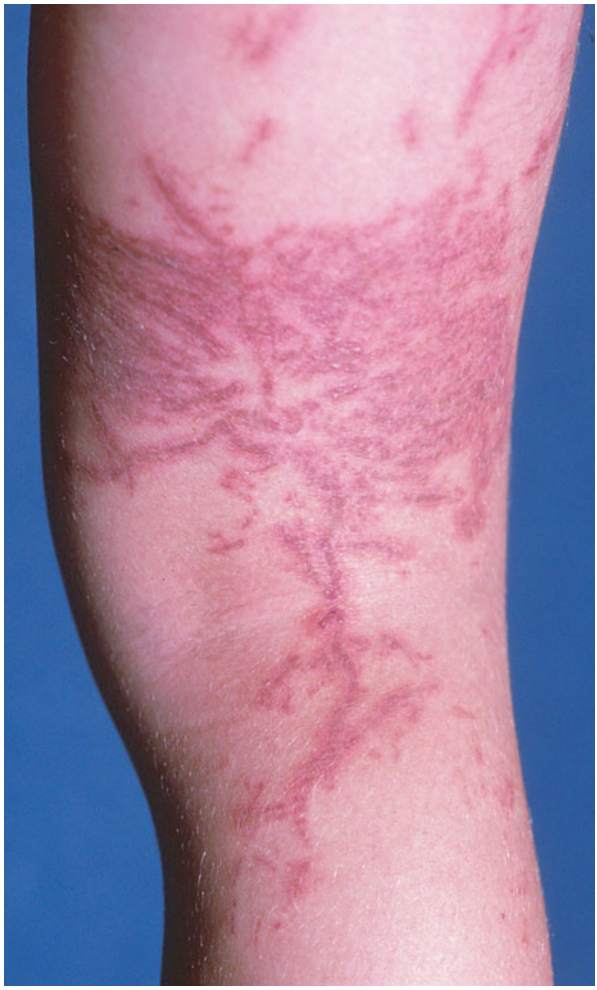

Fig. 3.54 Arabesque-like erythemato-vesicular dermatitis from *Anemonia sulcata* on typical sites

jellyfish and hence an increased quantity of larvae. This makes it likely that seabather's eruption may be caused by different Coelenterates in different waters, but giving rise to the same clinical symptoms. From the pathogenic point of view, the reaction may be of a toxic or allergic nature, as shown by the findings of specific human immunoglobulins.

Differential diagnosis must be made between seabather's eruption (the Caribbean coast of the central Atlantic, in covered skin areas and due to Cnidaria larvae) and dermatitis ("swimmer's itch") caused by Cercariae (that are ubiquitous especially in freshwater and affect exposed skin areas), and by seaweed (in Hawaii, fresh and saltwater seaweed, affecting covered skin areas) (Table 3.6).

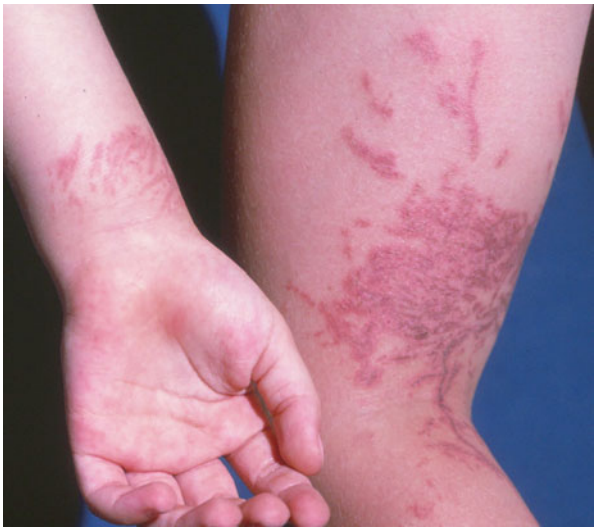

Fig. 3.55 The same case as in Fig. 3.54 with comparable lesions on the volar surface of the wrist (Reproduced with permission from Foti and Coll. [82])

3.7.4 Reactions to Corals

True corals belong to the class of Anthozoa, which contains two orders: Alcyonaria and Zoantharia. Soft corals and sea ferns belong to the Alcyonaria class, and sea anemones and hard corals to the Zoantharia class.

Corals create an underwater landscape of white rock, studded with thousands of holes. At night, a "hand" with 6 or more fingers extends out of each hole towards whatever living creature is passing nearby. To complete the bizarre scenario, these "hands" are covered with hairs, and contact with them can be very harmful. Each "hand" is connected to the others by a narrow strip of tissue that stretches over the surface of the rock, so that the hole is nothing other than a sheath of living tissue. The "hands", known as polyps or animal part of the coral, are covered with cnidocytes and the fingers are retractile (Fig. 3.60).

There are two different types of coral, classified according to whether they have a hard or soft skeleton. The polyps with a hard shell deposit a solid skeleton of calcium carbonate around themselves, secreted by the epidermal cells: in this way, the animal builds itself a cup-like shell (fossil coral) where it lives during the day. The skeleton is the only visible part of the coral, at least by day, and it is the skeleton that remains when the animal dies [3, 16, 215–218].

Soft corals secrete the same kind of calcium carbonate skeleton: the difference lies in the internal cohesion and microcrystalline structure, which determine the consistency of the coral. These corals, named Gorgonia (because they have a flexible axial skeleton) (Fig. 3.61) are abundant in the Caribbean sea, for some unknown reason.

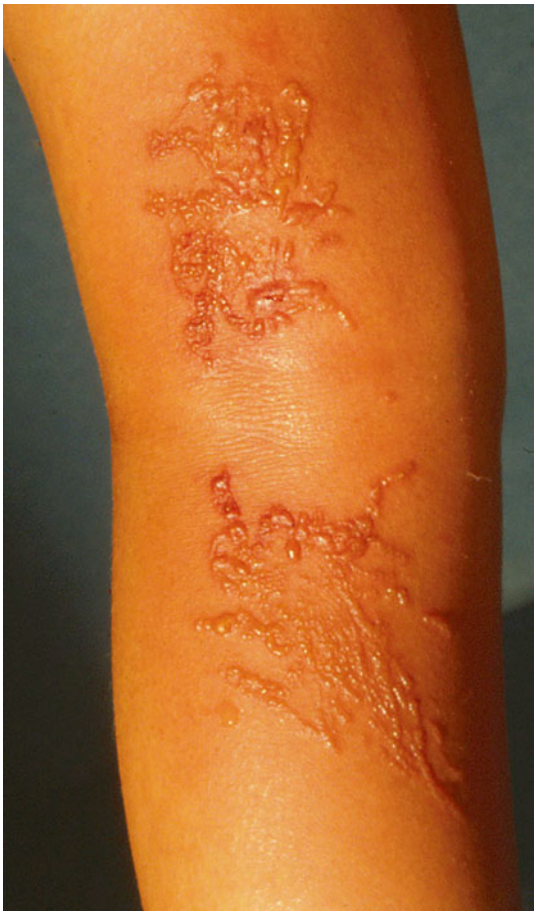

Fig. 3.56 Arabesque-like erythemato-oedemato-vesico-bullous dermatitis from *Anemonia sulcata* on typical sites (Reproduced with permission from Foti and Coll. [82])

Corals can provoke skin lesions of various types. Toxic contact reactions are relatively infrequent and generally fairly mild, rather like those induced by jellyfish and sea anemones. Probably, however, the frequency of irritant contact reactions is underestimated [218].

Instead, wounds from corals are very frequent (Figs. 3.62 and 3.63): despite their fragile appearance, hard corals have very sharp, cutting surfaces. These wounds rapidly evolve into painful ulcers and, unless they are promptly and appropriately treated, into cellulitis. The severity of the latter picture is due to a combination of a number of different factors: mechanical skin laceration, the offensive action of the nematocysts, the introduction of foreign bodies into the wound (calcium carbonate, detritus, micro-organisms, sludge), secondary bacterial infections and climatic conditions (high temperature and humidity) favouring the development of bacteria. These wounds heal very slowly.

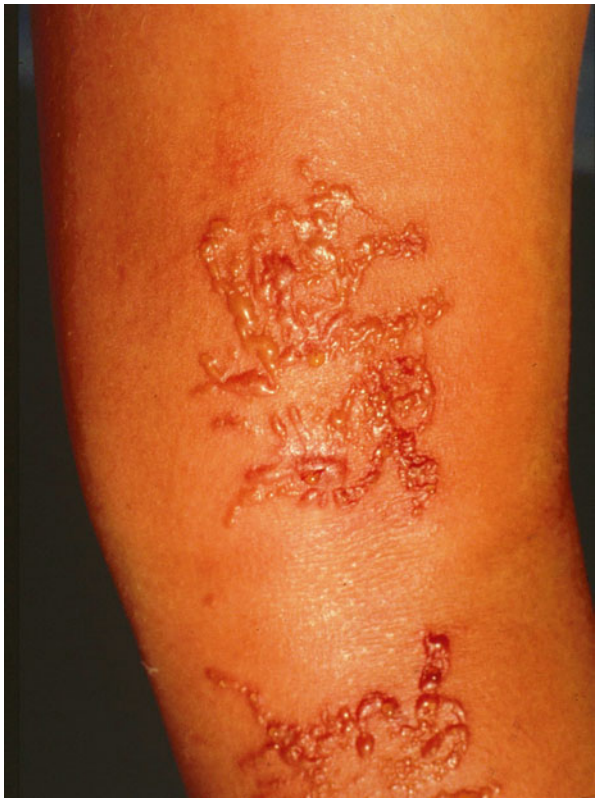

Fig. 3.57 The same case as in Fig. 3.56

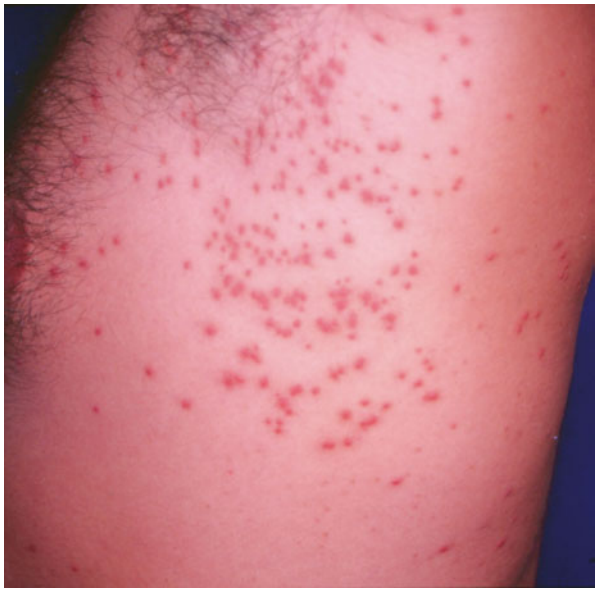

Fig. 3.58 Seabather's eruption: diffuse erythemato-papulo-vesicular dermatitis after swimming in the Caribbean Sea (Reproduced with permission from Bonamonte and Angelini [12])

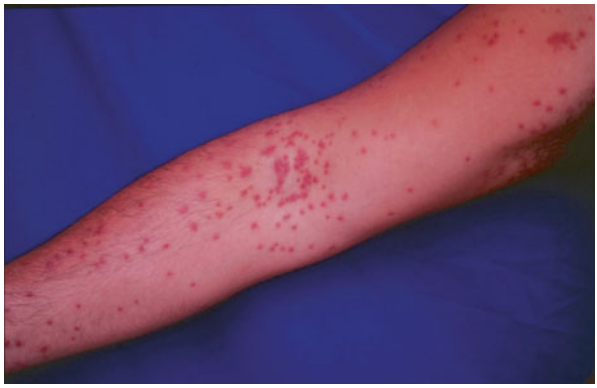

Fig. 3.59 The same case as in Fig. 3.58

Table 3.6 Differential diagnosis among seabather's eruption (SBE), dermatitis from cercariae (DC) and dermatitis from seaweed (DS)

Factors	SBE	DC	DS
Type of water	Salt	Salt and fresh	Salt and fresh
Areas affected	Covered and uncovered	Uncovered	Covered
Cause	Cnidaria larvae	Schistosomes	*Lyngbya majuscola*
Geographical areas	Florida, Cuba	Ubiquitous	Hawaii

3.8 Reactions to Hydrozoa

Physalia species, hydroids and fire corals belong to the class of Hydrozoa.

3.8.1 Reactions to Physaliae

Physaliae (from the Greek *physaleos* = full of air) are floating, bluish-purple animals (they are not jellyfish) that usually live in the tropical regions of the Pacific, Atlantic and Indian Ocean. They are wafted along by the tides and surface winds and sometimes end up on the European Atlantic coasts and in the Mediterranean. In recent years, in fact, large numbers of physaliae have been seen on the Mediterranean coasts, due to warm temperatures that favour their development, strong winds from the south-east that push them towards our shores and the absence of opposing winds.

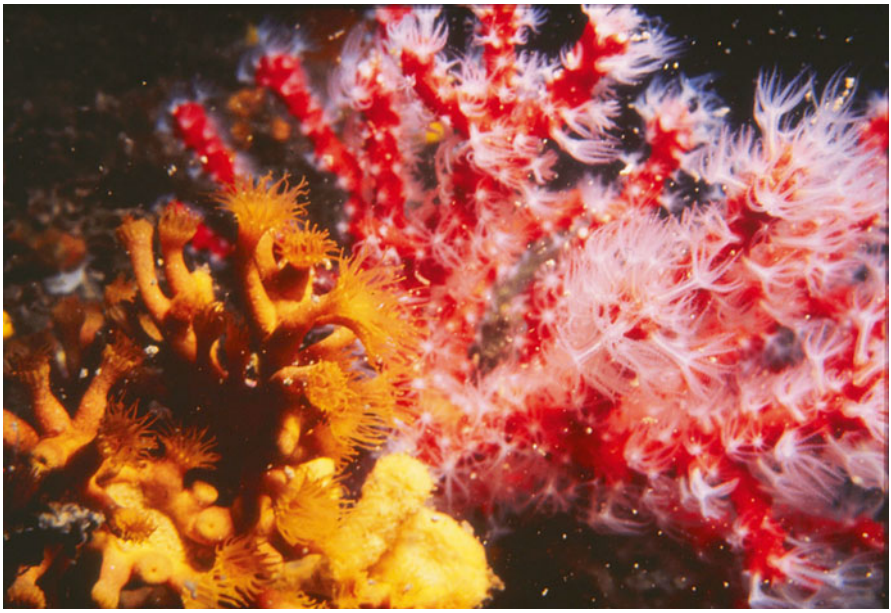

Fig. 3.60 *Corallium rubrum* and *Parazoanthus axillinae* (sea anemone) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

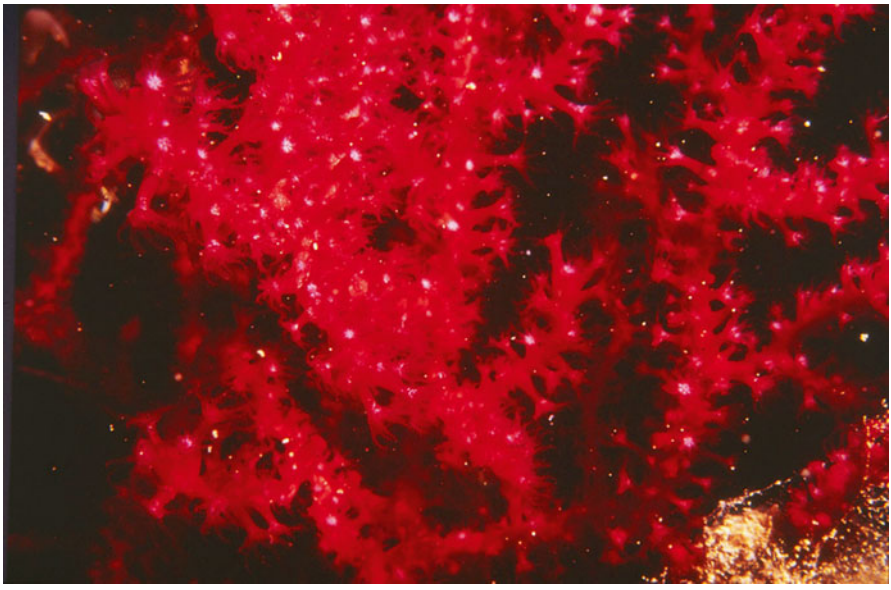

Fig. 3.61 *Paramuricea clavata* (red coral) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

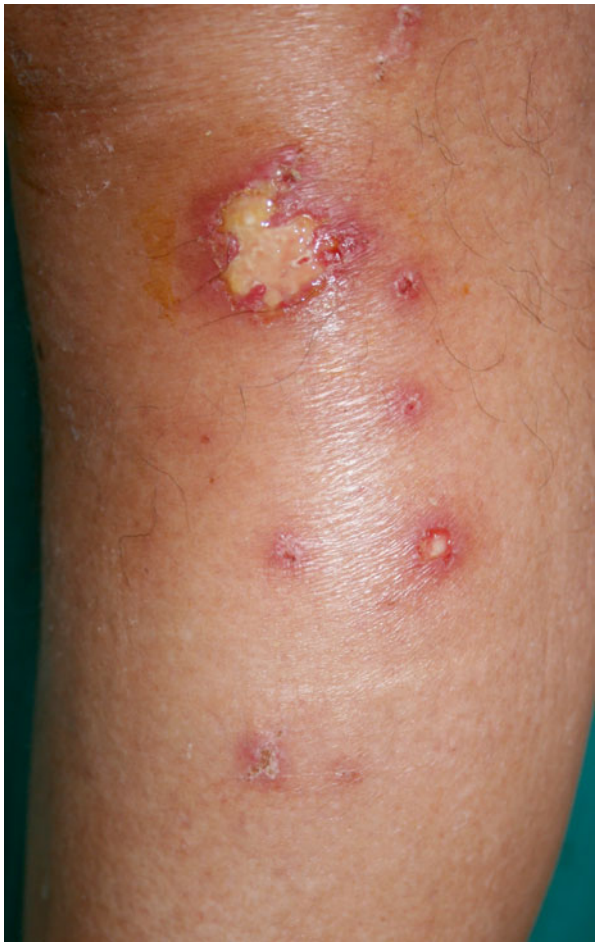

Fig. 3.62 Wounds from corals

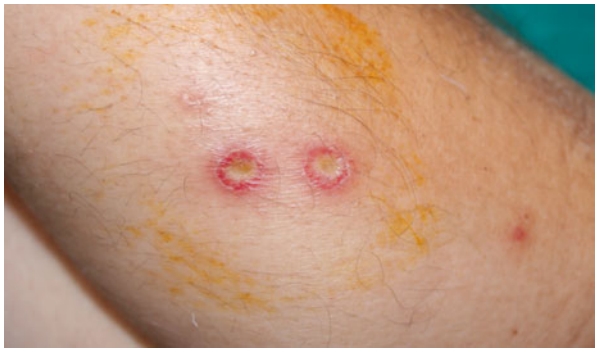

Fig. 3.63 Wounds from corals

Table 3.7 Taxonomy of physaliae

Kingdom	Animal
Subkingdom	Coelenterates
Branch	Cnidaria
Class	Hydrozoa
Order	Siphonophora
Suborder	Siphonanta
Group	Physophora
Family	Physalida
Genus	*Physalia*
Species	*P. physalis*
	P. utriculus

Members of the Cnidaria, physaliae belong to the Hydrozoa class (Table 3.7). The *Physalia* genus includes two species: *Physalia physalis,* the most representative type (present in the tropical Atlantic and the Mediterranean) and *P. utriculus,* present in the Indo-Pacific region and South of Japan. They are more frequently present in hot and temperate waters [15, 30, 219] but occasionally they can be found cast ashore in cold Atlantic waters (Northern France, Belgium and the South West of England).

P. physalis, commonly known as the "sea caravel" or "Portuguese man-o'-war" (in the fifteenth century English seamen gave it this name because of its resemblance to the caravel, the ship used by Portuguese seamen to explore the seas) has a main floating nucleus (the pneumatophore, or float) that looks like a large oblong bladder 10–25 cm long, surmounted by a high oblique crest (it is this that gives it the vernacular name of "Portuguese man-o'-war"). The nucleus is filled with gas (a mixture of oxygen, nitrogen and argon), secreted by differentiated cells, whose release is regulated by an orifice with a sphincter at the tip of the float. The portion above the water level is but the tip of the iceberg, while from the underside of the float hang the reproductive organs (gonozooids), gastrozooids, dactylozooids and slender tentacles covered with nematocysts. The pneumatophore and the elements below it make up a "colony". The tentacles capture the prey and, by retraction and extension movements, carry it to the gastrozooids. When these tentacles are fully stretched they may be as fine as strands of human hair, and measure from 10 to 100 foot long (3–30 m). These characteristics, together with their transparency and the fact that they can float far behind the physalia, make them extremely hazardous. In transparent waters, physaliae may look like small, bloated, blue plastic bags but in fact they are very difficult to see, as they blend in with the blue water. *P. utriculus* (the blue bottle) is smaller than *P. physalis*, the float being up to 10 cm long and 5–6 cm wide, with a predominant fishing tentacle extending for a maximum of 2–5 m [219].

The tentacles are studded with nematocysts deployed spirally, at the level of the mouth and gastric filaments. *Physalia* cnidocysts can penetrate the skin of the palms even through rubber gloves. The venom they contain is a protein complex consisting of 8–9 peptides; this is a very labile toxin that is inactivated at 55 °C. It has weak antigenic properties, a slight necrotizing action, cardiotoxic activity and a fatal

neuromyotoxic activity. The pain after contact with a physalia is due to particular enzymes or substances similar to quinines. The poison is urticant to man and paralysing to its prey (a fish is paralysed within a few seconds): 2 g of fresh filament are enough to induce the death of a 300 g pigeon in 1 h, after injection in the great pectoral muscle. The toxin isolated from the venom is called hypnotoxin because of its hypnotic properties; the paralysing action is thought to be due to quaternary ammoniums [220]. After contact, the poison is injected into the tissues in a fraction of a second and provokes what is commonly called the "physalic syndrome" [1, 5, 102, 220–224].

Physalia stings are normally painful and severe, and *P. physalis* can potentially also cause major systemic symptoms. The pain is extremely violent and can rapidly become unbearable, inducing reflex syncope. It radiates out from the affected area and is accompanied by intense burning sensations. The objective picture is characterized by erythemato-oedematous linear lesions; the erythema is bright red at the centre and surrounded by a darker area. Vesicles and blisters can develop on these lesions. Sometimes after a few hours an urticarial eruption can be observed, with wide wheals which are particularly itchy.

A few minutes after contact, the victim develops a state of anxiety, anguish and the feeling of imminent death, and then lipothymia. Muscle pain may also be present (with violent curvature of the dorsolumbar area), asthma-like breathlessness, nausea with or without vomiting, weakness (following a brief phase of excitement and euphoria), bradycardia and hypothermia. In cases of eye involvement, there may be conjunctivitis, intense oedema, painful corneal ulceration and scarring.

In benign cases the skin lesions resolve after a few hours, leaving hyperpigmented areas that sometimes persist for months, or scars. The general conditions improve rapidly, while breathlessness and a sharp cough, generalized urticaria and violent digestive symptoms (vomiting, painful colic) may persist for some days. In our latitudes, coma is a rare late complication but it is common in the tropical zones [225–227]. Sometimes the linear skin lesions can turn into deep purulent sores.

Burnett and Coll. reported a severe case of poisoning by *P. physalis* in an underwater diver in the Atlantic [228]. A scuba diving instructor was emerging one evening (7.30 p.m.) without a torch from a depth of 9 m near Miami, Florida. The wetsuit left his face and neck free and he was wearing gloves and carrying a lobster in each hand. As he surfaced, the tentacles of a Portuguese man-o'-war struck him in the face. To free himself, he turned over in the water, but this caused the tentacles to wind around his neck and face. The onset of systemic symptoms rapidly occurred, and his extremely severe respiratory, muscular, intestinal and neurological conditions required long, intensive hospital care. After 5 years, anti-*Physalia* IgG antibodies at titres of 1:450 (normal range 1:50 or less) were isolated in his serum.

The authors pointed out some precautions that could prevent such dramatic episodes: scuba divers must wear all-over wetsuits; during evening immersions they must carry a torch to watch out for such animals from below; during emersion they must look up with an arm outstretched towards the surface (even if the tentacles are not seen, they will wind innocuously around the covered arm). When a subject is stung, he/she must resist the natural temptation to break free from the animal, that will only adhere more closely over a wider surface as a result of these manoeuvres.

The tentacles must not be removed in the water (manipulation increases their offensive potential) but only after emerging.

P. utriculus usually causes local pain and, very rarely, minor systemic symptoms. Serious envenomations from *P. physalis* have been reported on both sites of the Atlantic [227]. In 2011, about 10 % of *P. physalis* victims in Aquitania (France) presented life-threatening systemic conditions which required hospitalization [30]. Three fatal envenomations have also been reported, on the Southern Atlantic coast of the United States [229].

3.8.2 Reactions to Hydroids

Many rocks and the tips of corals are encrusted with an irregular layer of sponges, seaweed, Tunicatae and colonies of small polyps (hydroids) of the Hydrozoa class. Only a few hydroids can be distinguished from the other animals and plants attached to hard surfaces. They form colonies about 5 m high, some of which resemble white plumes, and others slender candelabra. The most common species belong to three families (Sertulariidae, Plumulariidae and Aglaopheniidae), of the Leptomedusa order, and live in tropical and subtropical waters. When they are inadvertently touched, many species induce severe symptoms, especially the feather-like *Lytocarpus philippinus* [3]. Their venom, that acts more slowly than jellyfish venom, can induce two types of reactions: an urticarial eruption after a few minutes from contact, and a haemorrhagic, papulous or zoster-like reaction after 4–12 h. The skin symptoms may be associated with lymphadenopathy and systemic symptoms. The reaction can last from hours to several weeks. The subject may become sensitised.

There are various ways in which man can come in contact with the nematocysts. After contact with a rope that was used as the swimming area line of a summer resort, 9 subjects presented multiple erythemato-edematous lesions on various body sites, together with burning and intense pain. One subject, who had sat on the rope, had bullous lesions on the buttocks. *Pennaria disticha*, a benthic hydrozoan (common name: "Christmas tree hydroid") that is common in almost all circum-subtropical coastal habitats, was implicated. It attaches to artificial and natural hard substances where there is some water movement: typical locations include docks, pilings, rocks, reefs, corals and seaweed [230].

3.8.3 Reactions to Fire Corals

Unlike the toxins in coral nematocysts, that are not very harmful to man, those of "stinging or fire corals" of the *Millepora* genus (Milleporina order of the Hydrozoa class) are much more serious. These hydroid corals form a hard skeleton that appears very similar to that of true corals; they are very widespread in tropical seas in shallow waters. They give rise to cleaved and branching calcareous formations that can encrust other corals and objects, and range in colour from white to yellowish-green. The best known species are *Millepora alcicornis* (Fig. 3.64), *M. complanata* and *M. squarrosa.*

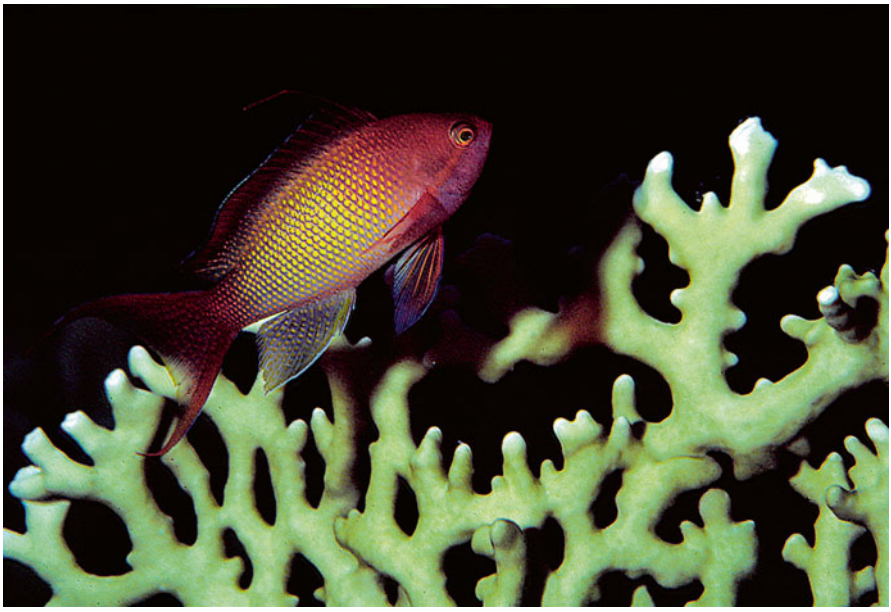

Fig. 3.64 *Millepora alcicornis* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

The main clinical manifestations attributed to their nematocysts are: erythema with associated itching, contact urticaria, eczema, vesico-bullous eruptions and lichenoid and granulomatous lesions. Sometimes, several different clinical pictures can be observed in succession in the same patient. For instance, some cases have been described where the dermatitis was of urticarial type at the time of contact, but then rapidly evolved into erythemato-oedemato-bullous lesions, followed by persistent lichenoid manifestations [231]. In other cases, delayed reactions have featured generalized lichenoid or granulomatous lesions whose onset occurred a few weeks after the primitive contact [232]. Observations of persistent and recurrent contact dermatitis have led some researchers to assume that there is not only a type I hypersensitivity response but also a cell-mediated immune response, which has been confirmed by histological and immunohistochemical findings [90, 232, 233]. In exceptional cases, generalized symptoms such as fever, nausea, vomiting and abdominal pain can be observed.

3.9 Diagnosis

The correct treatment of Coelenterate poisoning syndromes obviously requires a correct clinical diagnosis and the identification of the species responsible [234]. In general, the clinical diagnosis is not particularly difficult: the type of onset of the reactions and the clinical pictures are in most cases very clear. However, it is

important to bear in mind the possibility that a subject may develop skin and systemic reactions even without referring direct contact with a cnidarian, perhaps because it went unnoticed or because there was contact only with isolated nematocysts suspended in the water. Moreover, in cases with no clear history of contact or with a delayed onset of the symptoms, perhaps after returning from a holiday, it may be difficult to make the correct diagnosis.

In each case of an envenomation sting it is important to take a careful history and carry out the proper diagnostic procedures. Burnett produced a very useful handbook that helps by listing the information to be collected (Table 3.8) [80]. If possible, the offending animal should be photographed, as well as the skin rash. The affected skin can be scraped with a blade or stripped with cellulose tape to collect cells for microscopic examination to identify the nematocysts. The description of the rash must include three elements: (1) the distribution of the lesions, localized or systemic; (2) the configuration of the lesions: linear or circular, symmetrical, confluent; (3) a description of the lesions: macules, wheals, papules, nodules, vesicles/bullae, pustules and so on. Indeed, it is important to make a clinical description of

Table 3.8 Essential clinical history and circumstantial elements in cases of cnidarian stings

History of the sting
Date, season, geographical location
Weather, tide, water conditions
Patient activity at the time (swimming, sunbathing)
Jellyfish species (photograph)
Length of tentacle contact with the skin
Time of persistence of tentacles on the skin
Description of clinical cutaneous manifestations
Sites of the body stung
Symptoms
Dizziness
Nausea, vomiting
Faintness
Sweating, local or systemic
Piloerection
Muscle cramps
Fever
Increased heart rate
Shortness of breath
Coma
Past medical history
Significant diseases
History of atopy (hay fever, asthma, eczema)
Drugs at the moment of sting
First aid
Condition of the patient at the time of hospitalization
Hospital treatment
Skin scrapes for nematocysts identification
Skin biopsy, if necessary

Modified from Burnett [80]

the rash both at onset and during any evolution. Full information can help to arrive at an aetiological diagnosis, with the help of marine biology experts, taking into account the geographical location [80]. Clearly, recognition of the animal responsible does not only have a clinical-diagnostic but also a therapeutic relevance. The collaboration between the dermatologist and the marine biologist is, therefore, extremely important in order to identify the species, for ecological and epidemiological reasons, thereby establishing which animals are present in a given locality, season and period.

It is important to search for specific immunoglobulins in serological tests, even if this is not an easy routine approach. Some studies have shown that repeated exposure to these animals can result in the formation of specific IgE; that significant levels of these circulating antibodies can persist for several years; and that antibodies to one specifies can cross-react with antigens from other species [235, 236]. In affected patients, specific IgG-blocking antibodies have also been demonstrated with RAST using protein A of *Staphylococcus aureus* to bind the IgG [236]. The presence of the latter type of antibodies may have a protective effect, while increased specific IgE levels in the absence of blocking antibodies suggest a particular susceptibility. For this reason, before "labeling" a patient with specific IgE levels as a subject at risk, it is best to ascertain the IgG-blocking levels, too.

3.10 Prevention

Marine envenomations occur worldwide, 500,000 jellyfish stings being estimated to occur in Chesapeake Bay and up to 200,000 stings in Florida waters annually [93], and at least 67 deaths have been attributed to the box jellyfish alone, in the Indo-Pacific region [177]. These and many other data in literature underline the urgent need for methods of prevention to reduce the frequency of jellyfish envenomations. However, considering the great variety of species and unexpected nature of attacks, it seems likely that there are no safe preventive measures against Coelenterate venom.

Methods to reduce jellyfish encounters have traditionally relied on mechanical barriers. In Australia and the USA, where this is a real problem as there is a risk of a fatal outcome, one common barrier device adopted by surfers and divers is a personal wetsuit/stinger suit. These suits, however, often leave the face, hands and feet exposed, and are not used by snorkelers and swimmers. Another method is to surround swimming areas by netting to exclude jellyfish. This is a common practice at many Australian and Pacific island beaches. However, while these nets exclude the large box jellyfish (*Chironex fleckeri*), that has a bell diameter of 20–30 cm, the 2.5 cm holes in the nets allow the smaller stinging Irukandji jellyfish to pass through. In Queensland, Australia, 60 % of the victims with Irukandji syndrome are stung within the confines of stinger nets [237].

The use of barrier creams (that obviously do not protect the eyes) has not been found effective [93]. Recently, a double-blind, randomized, placebo-controlled trial was conducted in Florida, with 82 healthy volunteer participants planning to snorkel for 30–45 min [238]. Ten minutes prior to swimming, each participant was directly

examined, and a blinded sample of Safe Sea (Nidaria Technology Ldt, Jordan Valley, Israel) was applied to one side of their body, and of Coppertone® (Schering-Plough, Kenilworth, NJ, USA) on the contralateral side as placebo control. Sides were randomly chosen by participants. The incidence of jellyfish stings was the main outcome measure. Thirteen jellyfish stings occurred during the study period, accounting for a 16 % incidence. Eleven stings occurred with the placebo, 2 with the sting inhibitor, resulting in a relative risk reduction of 82 %. No side effects were reported. The conclusion was that the sting inhibitor Safe Sea is a topical barrier cream that is effective in preventing >80 % jellyfish stings in real-world conditions [236]. Safe Sea prevents nematocysts from firing (once the stingers have fired, however, Safe Sea is unable to block or neutralize the sting itself) through four different actions: (1) the inhibitor is highly hydrophobic, so it decreases tentacle contact with the skin; (2) the inhibitor contains glycosaminoglycans that mimic the glycosaminoglycans making up the jellyfish bell. Because the bell is part of the jellyfish self-recognition system, the inhibitor mimics this self-recognition system, thereby interfering with nematocysts firing; (3) the inhibitor contains a competitive antagonist to non selective chemoreceptors on jellyfish; (4) finally, calcium and magnesium block transmembrane signaling and reduce the osmotic force within the nematocyst capsule necessary to create the firing force. The study did not, however, determine the effective duration of protection after a single application. The sting inhibitor is based on the chemical properties of the mucous coating of clownfish. Clownfish inhabit sea anemones but clownfish mucus prevents them from being stung [239].

Preventive actions must include a whole series of educational campaigns. Apart from some norms that are already widely known (Table 3.9) [240], pre-travel health education is considered very important: travelers to the various marine sites and in particular to specific regions at risk must be aware of the aquatic risks in order to be able to avoid them. For these purposes, it is imperative that government authorities, aquatic resorts, and aquatic operators provide adequate warning to travelers of the potential threats ("pre-trip information"). It is also essential to put up appropriate warning signs in all affected areas, and that multilingual brochures be provided to tourists by resorts and operators. Vinegar should be quickly and easily accessible (bottles of up to 5 l attached to the warning signs, or nearby) to locals and tourists for prompt access in the event of a sting. Finally, specialized life guards should be appointed by coastal tourist resorts.

Table 3.9 Prevention of jellyfish stings

1. Swim only at beaches attended by properly trained lifeguards and with adequate treatment facilities
2. Avoid swimming in infested waters, especially after a storm, because stings can results from floating residues of damaged tentacles
3. When snorkeling or scuba diving, wear protective clothing (wetsuits and gloves). In areas where Irukandji syndrome can occur, wear a lycra suit
4. Do not touch apparently dead or beached jellyfish
5. Use sunblock and other creams containing jellyfish repellent
6. Bathing beaches must be closed during major jellyfish infestation periods

Table 3.10 First-aid treatment of jellyfish envenomation

1. Remove the victim from the water
2. Ensure vital functions: airways, breathing, circulation
3. Do not remove wetsuit if patient is wearing one
4. Immobilize the affected part to prevent further envenomation by adherent tentacles
5. Do not scratch the affected part for the same reason as point 4, and because this will stimulate muscle activity, speeding up the circulation of the toxins
6. Wash the affected part with seawater
7. Do not use fresh water: because it is hypotonic it would cause the nematocysts to burst
8. Do not use alcohol, liqueurs or perfumes: they too will cause the nematocysts to burst
9. Do not rub the skin to remove sand and tentacles
10. To prevent further envenomation (and to reduce the risk of the rescuer being stung), disarm the nematocysts using household vinegar (acetic acid 5 %) (valid in the case of box jellyfish, *Physalia* species and *Pelagia noctiluca*), sodium bicarbonate (baking soda), magnesium sulfate or formalin solution (that can fix nematocysts)
11. If these solutions are unavailable, papain, available as a powdered meat tenderizer, may be applied directly to the stung area as a powder or mixed in water as a slurry
12. Remove the tentacles with bare hands (but remember to wash them carefully afterward to avoid contaminating other zones) or gloves, or using a paste made of seawater and bicarbonate (or talcum powder, flour, dry sand) to cause the tentacles to agglomerate. They can also be removed with a pointed tool, a blunt-edge knife, or a plastic object with an edge (credit card)
13. To control the pain, use parenteral analgesics or narcotics. If it is not severe, oral analgesics can be used (ibuprofen, acetaminophen, acetylsalicylic acid). Local anaesthetics (lidocaine) will take 40 min to act
14. An analgesic effect is also obtained by applying cold (cold packs or ice wrapped in a cloth for up to 15 min, then repeated as often as necessary) and heat (thermal packs and hot showers: water temperature 42–45 °C for 20–30 min or until relief of the pain. If these temperatures are not tolerated, apply the highest tolerated temperature)
15. In cases with systemic symptoms, the patient must be rapidly transported to the intensive care inpatient Unit
16. Identify the type of jellyfish (indigenous species) and preserve a portion of tentacle for future identification

3.11 Treatment

Until the toxins of the various Coelenterate species have been identified, the treatment of cnidarian stings will necessarily be aspecific and symptomatic. At present, only one specific antiserum is available, for poisoning by *Chironex fleckeri*, that has also been found useful against *Chiropsalmus quadrigatus*. This antiserum, produced by The Commonwealth Serum Laboratories of Melbourne, must be inoculated as soon as possible after contact with the jellyfish. The antivenom is prepared from sheep serum and may therefore pose a risk of allergic reaction in sensitized individuals, even if such reactions seem to be rare [241]. The preferred route of administration is intravenous (each ampoule contains sufficient activity to neutralize 20,000 intravenous LD_{50} mouse doses), although the intramuscular route may also be chosen (but at triple the dosage) [22].

To alleviate the symptoms of Coelenterate stings, fishermen and the inhabitants of seaside towns use old-wives' remedies that still have some uses, such as vinegar

(5 % acetic acid in water), ammonia, urine, formaldehyde, potassium permanganate crystals, warm water, Coca Cola [242], ice, fig juice, boiled cactus, heated stones [243]. Nevertheless, many of these remedies have no scientific basis.

The following measures should be borne in mind as specific treatment programs for these conditions [1, 9, 14, 22, 93, 104, 136, 167, 173, 221, 243–251].

3.11.1 First-Aid

Uniform first-aid for jellyfish envenomation is controversial, also in view of the many different species implicated. First-aid care (Table 3.10) must be focused on maintaining cardiovascular function. After moving the patient away from the water, s/he should lie down, be kept warm and the airways be kept open. If necessary, pulse rate and blood pressure should be stabilized with closed chest massage. It is important to reassure the patient, in order to reduce muscle pump activity accelerated by panic. One of the main therapeutic goals is to control the pain, that should be done, if possible, only with parenteral analgesics or narcotics. In cases of milder pain, oral pain-killers, like ibuprofen, acetaminophen or acetylsalicylic acid, are the drugs of choice, to be administered as soon as possible. Local anaesthetics like lidocaine are ineffective unless by occlusive application, and even so, they take 40 min to act. Topical corticosteroids are also ineffective. The use of papain containing meat tenderizers is useless because it is not absorbed.

The analgesic effect of the application of heat is controversial: on one hand it should inactivate any heat-sensitive proteins still present, but on the other, by inducing vasodilation, it would foster a greater absorption of the toxins. Hot temperatures are not generally tolerated by young children and could also cause burning if vast areas of skin are exposed for long periods. Still, there is some evidence that hot temperatures, if applied sensibly, can relieve the pain not only of fish stings but also jellyfish and *Physalia* stings. Heat is generally applied via thermal packs, basins of hot water, and hot showers. Showering can be useful because it should wash away the remaining stinging cells, and different temperatures can be set, continuing the heat application until pain relief is achieved. Standard advice is to keep the water temperature at 42–45 °C for 30–90 min or until the pain subsides, but some patients are unable to tolerate such high temperatures. In any case, the best practice is to use the highest temperature that can be safely applied and is tolerated by the individual patient [243].

The application of cold can also be helpful in jellyfish stings, because of its analgesic effect. This is usually done using specific cold packs (those used for sports injuries) or ice wrapped in a cloth and applied to the stung area for up to 15 min, then repeated as often as necessary. This controls pain in over 90 % of cases [250].

The affected skin areas can be gently washed with seawater without any risk. For this purpose, it is absolutely essential to avoid using freshwater as this is hypotonic and can cause the nematocysts to burst. For the same reason, the subject must not shower until the toxins have been neutralized. The skin must not be rubbed to remove sand, again to prevent the nematocysts from bursting. Tentacles can be removed manually (remembering to wash the hands immediately after, to prevent

secondary stings). A paste made with saltwater and sodium bicarbonate can also be used, left on for 5 min. The use of talcum powder or flour can have the same effect, causing agglomeration of the tentacles, that can then be removed with a knife or sharp tool, or with the edge of a plastic instrument, after which the zone must again be carefully washed with seawater.

Topical preparations applied to prevent adherent nematocysts rupture, or to remove tentacles, are important. Three solutions are usually advocated. Household vinegar or acetic acid in solution (3–10 %) may be used topically to prevent the discharge of nematocysts from *Chironex fleckeri*, *Physalia physalis* and *Alatina alata*, but should not used in stings from *Chrysaora quinquecirrha* and *Cyanea capillata* because it may stimulate discharge [229]. Recent studies of nematocysts discharge from *Pelagia noctiluca* oral arms showed that acetic acid treatment has an inhibitory effect on discharge activation also for this jellyfish that is very common in the Mediterranean [251]. Topical application of baking soda slurry (50 % baking soda: 50 % saltwater) can be used in cases where vinegar is not efficious. Other useful topical preparations are magnesium sulfate (also for stings by *Pelagia noctiluca*) and formalin solution (that can fix the nematocysts and stop them from bursting).

As to the use of alcohol, *in vitro* it has been observed to stimulate nematocyst bursting, although many experiences have described this means as useful. Hydroalcoholic solutions, such as perfumes, after-shave lotions and spirits (ethanol) must not be used, as in some cases they may prolong the agony. Finally, topical use of urine, papain and aluminum sulfate solutions is ineffective, and is not recommended.

The use of first-aid pressure-immobilization bandage is a controversial issue. According to current data the use of this practice in cubozoan envenomation is not recommended [246]. Although arterial tourniquets have been used in the past they, too, are no longer recommended [22].

3.11.2 Fatal Reactions

Severely stung patients should be transferred to an intensive care inpatient Unit. Specific antivenoms are not available for Atlantic and Mediterranean cnidarians. The only specific drug for use in patients developing cardiac dysfunction is verapamil [252]. However, there are "pros" and "cons" for the use of this drug: in any case, in the Atlantic and Mediterranean waters, box jellyfish stings are rare and *Physalia* stings are not usually severe enough to alter the heart rhythm, thus limiting the need to use this agent [252]. The employment of magnesium sulfate in severe cases of Irukandji syndrome is equally a matter of debate [247]. Systemic treatment is therefore mainly symptomatic.

3.11.3 Medium- and Long-Term Reactions

Topical treatment with corticosteroids and anesthetics is useful to relieve the inflammatory process and burning sensations. It is wise to avoid products with a benzocaine base, as this has a potential sensitizing action, and so it is better to select 5 %

lidocaine derivatives. Instead, when the eyes are affected these remedies are not indicated, as they could cause further harm, and only topical steroids should be used.

Topical wound care requires daily cleansing. Hemorrhagic bullae may be punctured but the roof must be left intact. Topical antibiotics are not usually necessary; in cases of secondary infections or involvement of vast skin areas systemic antibiotics can be used. Gangrene and necrotic and ulcerative lesions need debridement and, if necessary, subsequent grafting.

Telangiectasias can be removed with laser therapy. Keloids require intradermal corticosteroids. Fat atrophy usually resolves spontaneously or can be cosmetically treated by injecting dermal filters.

Joint contractions require plastic surgical and physical therapy. Hyperpigmentation can be treated with topical bleaches.

Recurrent or delayed episodes can be treated in the same way as the first episode; these eruptions usually cause pruritus but not pain. A granulomatous reaction requires intradermal corticosteroids, and for a granuloma annulare, potent occlusive topical corticosteroid treatment should be applied.

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Dermatitis Caused by Echinoderms

4

Domenico Bonamonte, Pietro Verni, Angela Filoni, and Gianni Angelini

Echinoderms (from the Greek *echinos* = bristle or spiny appearance) (Echinodermata phylum) are slow-moving animals with a rotate pentamerous symmetry. About 6,000 species are known, 80 of which are toxic or venomous. Their various different shapes have led to a subdivision into five classes. Some are spherical and covered in spines or strong spicules (Echinoidea or sea urchins); some are star-shaped with five points or ray-like arms of variable length (Asteroidea or starfish) (Fig. 4.1); some have a cylindrical body (Holothuroidea or sea cucumbers) (Fig. 4.2); some are flower-like (Crinoidea, sea lilies or feather stars); others have long, branching arms that can twine around solid bodies (Ophiuroidea) (serpent stars: from the Greek *ophis* + *idis* = snake-like) (Table 4.1, Fig. 4.3) [1].

Apart from the Holothuroidea, that have a soft body, all the other Echinoderms have a brittle endoskeleton of regularly arranged calcareous plates. The sea urchin skeleton is rigid and inflexible, whereas that of starfish consists of calcareous plates with some space between them, so that it can move its arms to capture prey or turn over when it falls on its back. Instead, the Crinoidea and Ophiuroidea are much more mobile, and have sinuous swimming movements.

Echinoderms have a water vascular system with tubular cavities for the water to circulate through, and tubular feet extending out from the body. In starfish and sea urchins, these tube feet cover the whole body; they are like narrow tubes fitted with a suction cap at the end. As they can retract and extend, they allow the animal to

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Fig. 4.1 *Sphaerechinus granularis* and *Echinaster sepositus* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania,Italy)

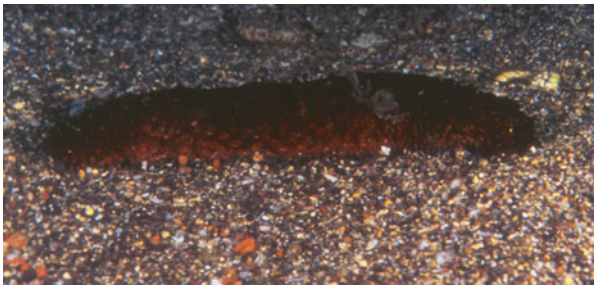

Fig. 4.2 Holothuria (sea cucumber) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Table 4.1 Echinodermata classes and most common toxic species

1.	Echinoidea (sea urchins)
	Species:
	Paracentrotus lividus
	Arbacia lixula
	Sphaerechinus granularis
2.	Asteroidea (starfish)
	Species:
	Echinaster sepositus
	Acanthaster planci
3.	Holothuroidea (sea cucumbers)
	Species:
	Cucumaria
	Stichopus
4.	Crinoidea (sea lilies)
5.	Ophiuroidea

Fig. 4.3 Crinoidea (sea lily) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

move slowly along the seabed (this is why they are called pedicellariae) and capture prey.

Starfish and sea urchins are macrophages and capture their prey, while the other Echinoderms are microphages and feed on plankton and detritus. These species can be found in all the seas, from the tropics to the Arctic.

Of the five groups, two kinds of starfish and various kinds of sea urchins are poisonous. Some Holothuroidea are poisonous to eat, and because they discharge very slimy filaments containing toxins into the water from the visceral extremity they are also poisonous to other fish. The toxin contained (holothurin) is a glucoside; through hydrolysis it gives rise to an aglycon of steroid type and various glucide residues that are highly toxic to all organisms, from protozoa to mammals. The effect is often fatal, being of neurotoxic type and provoking an irreversible blockage of transmission of the nerve impulses at the level of the neuromuscular synapses. There is no known specific treatment [1–8].

4.1 Dermatitis from Sea Urchins

About 750 species of Echinoidea have been identified, some of which are present in the Mediterranean: in particular, *Paracentrotus lividus* (Fig. 4.4), *Arbacia lixula*, *Sphaerechinus granularis* (Fig. 4.5).

Sea urchins live on rocks and in crevices underwater and are rarely seen on the sand. Their sharp calcareous spines are mobile and attached to the body by articulations on the test (hard shell). They form by means of calcification of cylindrical projections of the sub-epidermal connective tissue. The calcareous crystals are arranged radially around a central canal containing connective tissue in the post-larval stage, that then calcifies.

The spines contain calcium sulphate, magnesium carbonate, calcium carbonate and silicium. Their surface is coated with a thin organic sheath consisting of pigment, epidermal residues and perhaps glands with a toxic content. Toxic species of

Fig. 4.4 *Paracentrotus lividus* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Fig. 4.5 *Sphaerechinus granularis* and *Caulerpa taxifolia* (green alga) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

sea urchins are to be found along the coasts of Europe, the Atlantic and the Pacific. The toxins are contained not only in the spines but also in the pedicellariae. In some species, toxins are also present in the gonads during the reproductive period. The toxins serve defence and offence purposes, to capture prey (Echinoidea, like Asteroidea, are macrophages), although the functional significance of the toxins in the gonads is quite unknown. The sea urchin toxins have not yet been identified but, surprisingly, they do not seem to be saponins like those of the Asteroidea and Holothuroidea, even if they have the same neurotoxic action. The toxins in the gonads can be harmful to man when these species are eaten as seafood [9]. However, only rarely have fatal cases been reported; the symptoms generally include nausea, vomiting, diarrhoea, headache and allergic reactions that subside after a short time without any further complications.

The sea urchins present in the Mediterranean belong to the less toxic varieties. Two different kinds of reactions to sea urchins can be observed [10–22].

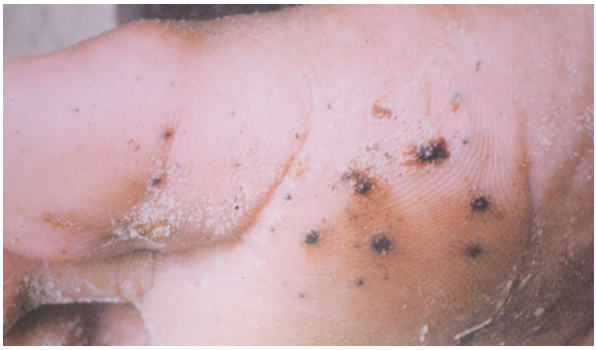

Fig. 4.6 Fragments of sea urchin spines inside the sole (Courtesy of Prof. Vidal Haddad Jr, Departement of Dermatology, Botucatu, University of São Paulo, Brazil)

Fig. 4.7 Fragments of sea urchin spines inside the sole (Courtesy of Prof. Vidal Haddad Jr, Departement of Dermatology, Botucatu, University of São Paulo, Brazil)

Fig. 4.8 A sea urchin hawker

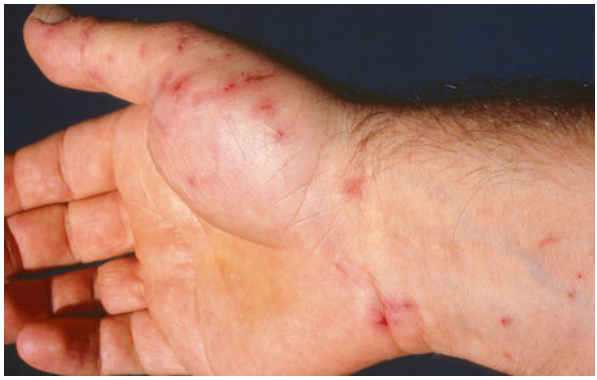

Fig. 4.9 Abrasions from sea urchin spine pricks

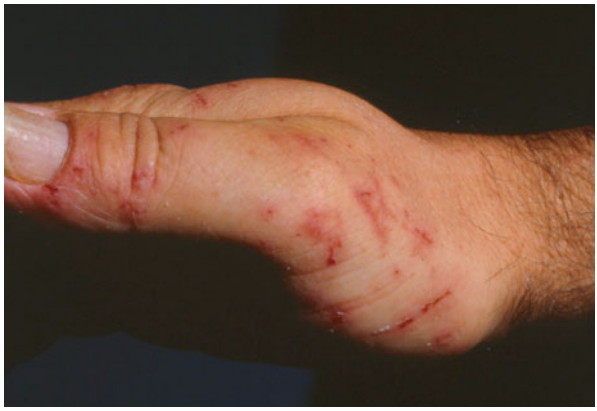

Fig. 4.10 The same case as in Fig. 4.9. Abrasions from sea urchin spine pricks

4.1.1 Immediate Reactions

Swimmers for professional (fishermen) and sports purposes must beware of sea urchin spines. These develop in various ways in the different species, and are sharp and very fragile. On contact, usually by stepping on the animal or careless handling, the spines penetrate the skin very easily and break off, making the fragments inside the wound very difficult to extract. Penetration of the spines (Figs. 4.6, 4.7 and 4.8) causes immediate, sharp, burning pain which may last a few hours, followed by skin redness and oedema of the affected part (Figs. 4.9 and 4.10); in some cases the lesions bleed copiously. Torpor, paraesthesias, breathlessness and localized muscular pain have also been observed. Secondary infections are not rare, and eventually cause ejection of the spines. At the site of penetration of the spines a black or purple discoloration can develop, due either to retained fragments in the wound or to a tattoo-like effect caused by dye released from spines that have come out intact, but this discoloration disappears within 48–72 h [22]. Systemic symptoms are uncommon but can occur if the sea urchin species is particularly poisonous; these include nausea, ataxia, syncope, muscle cramps, paralysis, and respiratory distress. Tenosynovitis, fasciitis, arthritis, and bursitis have also been reported after sea urchin injuries [23].

The treatment of immediate reactions is by applying water as hot as is bearable (43–46 °C for 30–90 min until maximal relief is obtained) on the oedematous, painful lesions (to inactivate heat-sensitive toxins). Infected lesions must be treated with topical or systemic antibiotics. The dermatitis usually resolves within 1–2 weeks, provided that no spines are left in the skin. Immediate and complete removal of the spines is obviously a priority, although this is often difficult owing to their fragility and the presence of dyes that make them difficult to distinguish from the surrounding tissue. It should be borne in mind that whilst the spines of some species can be phagocytized by the tissues in 24–48 h, those of other species do not dissolve. In the latter case surgical removal may be necessary, after an X-ray or ultrasonography. Infiltration of the wound site with 1–2 % lidocaine without epinephrine can be useful in some cases to relieve the pain. Particular complications can arise when the spines enter the area of a joint or in contact with a nerve. Tetanus prophylaxis should be given if necessary. The spines of some sea urchins (*Diadema antillarum*) can pierce the soles of shoes, gloves and the wetsuit. Salicylic acid plasters may be sufficient in superficial injuries, but are quite inadequate if the spines have penetrated deeply into the skin.

In the West Indies, the spines are extracted using a method that combines scientific and mystical elements. The affected skin part is rubbed with lime juice (citric acid) and then very hot vinegar (acetic acid) is applied. After about 10 min, more vinegar is applied and the zone is heated with a candle held at 1 cm from the skin. This causes the spines to dissolve. After a further 10 min, candle wax is spread on the part and once this has hardened, it is peeled off bringing the remaining spines with it [4].

In patients with multiple black spines (> 50) in the soles of the feet, the erbium: YAG laser has been successfully used. The spines were easily destroyed and the lesions healed within 2 weeks without complications or scarring. One or two treatment sessions were enough to remove the spines, and no formation of delayed granulomatous reactions was observed over many months of follow-up [24].

4.1.2 Delayed Reactions

The onset of delayed reactions can be seen 2–3 months after the primitive contact; they may be nodular or scleroedematous [25]. Both types of reaction can persist for a very long time, although they may resolve spontaneously. Granulomatous nodular lesions have a hard, parenchymatous consistency and range in size from 4–5 mm to 1–2 cm in diameter; they are a darkish or brownish-red colour (Figs. 4.11, 4.12, 4.13, 4.14, 4.15, 4.16 and 4.17). Nodules may be stained by the dye in the spines and may have a central umbilication or keratotic surface. The sites most often affected are the hands (back, palms), elbows and knees. Granulomas at the level of the nail quick can bring on severe forms of onychodystrophy [26]. In 1972, using hydroalcoholic extracts of sea urchin spines Meneghini elicited a positive delayed intradermal allergic reaction in two fishermen with granulomas [27]. We have since observed the same reaction in various other subjects (Figs. 4.18 and 4.19).

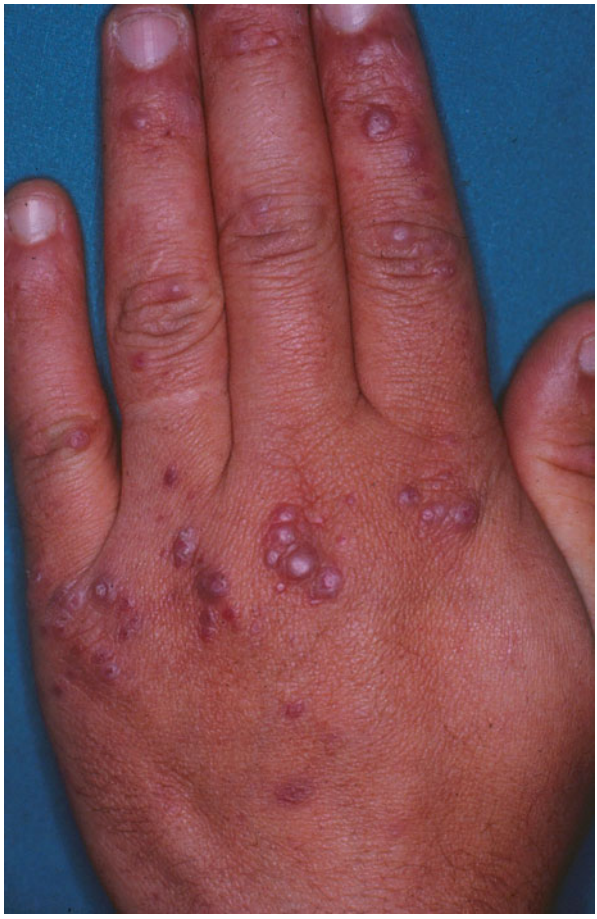

Fig. 4.11 Granulomas from sea urchins (Reproduced with permission from Cassano and Coll. [21])

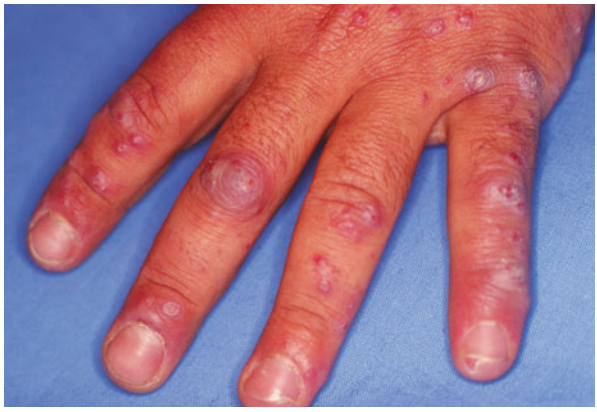

Fig. 4.12 Granulomas from sea urchins

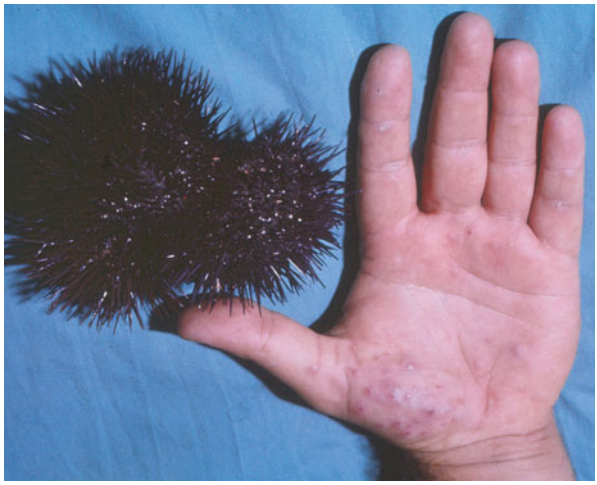

Fig. 4.13 Granulomas from sea urchins (Reproduced with permission from Cassano and Coll. [21])

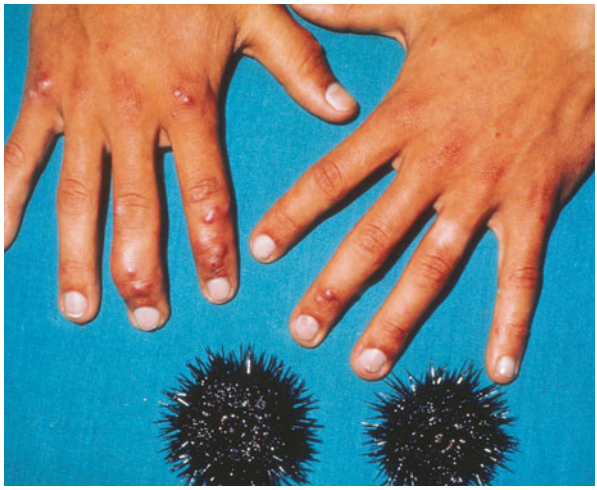

Fig. 4.14 Granulomas from sea urchins (Reproduced with permission from Bonamonte and Angelini [25])

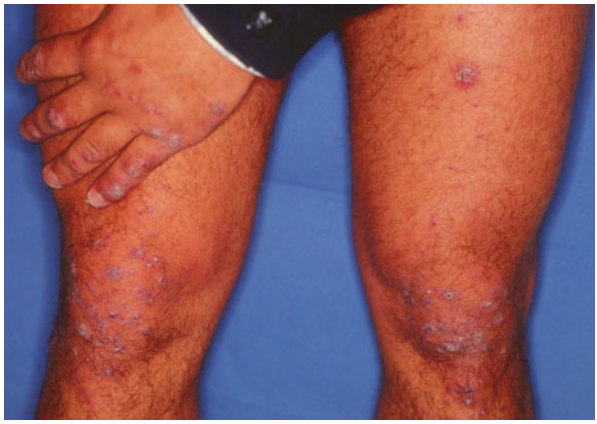

Fig. 4.15 Granulomas from sea urchins on typical sites

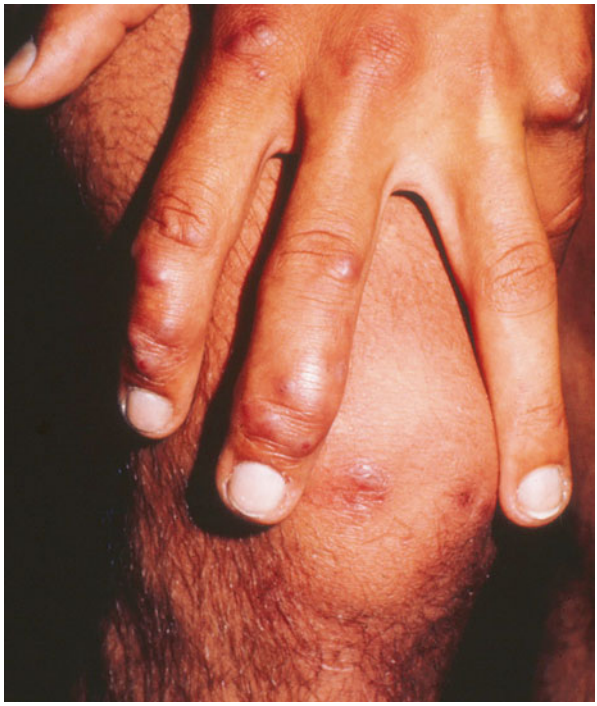

Fig. 4.16 Granulomas from sea urchins on typical sites (Reproduced with permission from Cassano and Coll. [21])

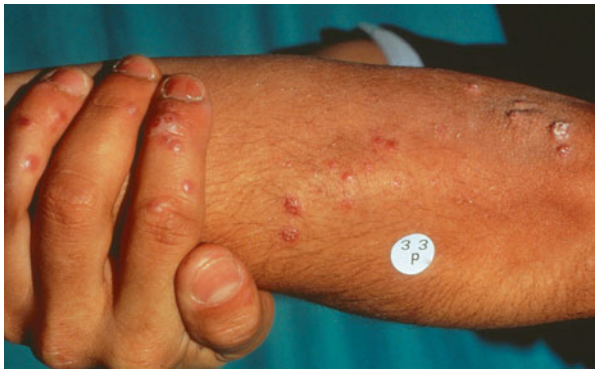

Fig. 4.17 Granulomas from sea urchins on typical sites

The pathogenesis of sea-urchin granuloma remains uncertain; the affection is usually considered to be a foreign body reaction or an unusual immunological response to an as-yet unidentified antigen [17, 28–30]. Sea urchin spines are composed of calcium carbonate, a substance that is considered to be immunologically inert. The induced lesions are therefore an immune reaction to unknown antigens. Among possible sensitization agents, a protein derived from the spine epithelium or a substance entering the wound with the puncture (venom from pedicellariae, bacteriae, slime, etc.) have been proposed [11, 27–29, 31].

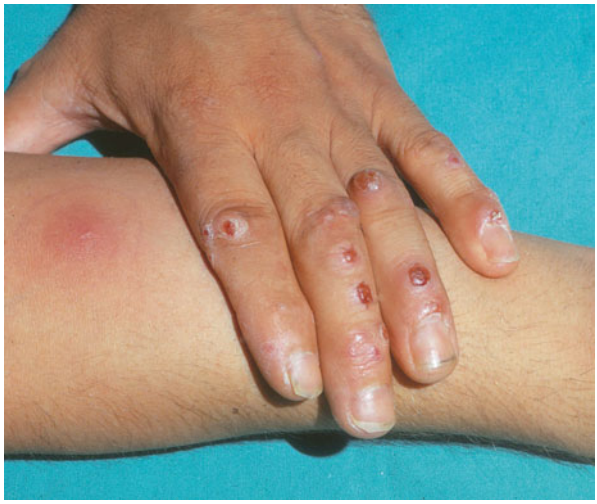

Fig. 4.18 Positive delayed reaction after 48 h to intradermal test with hydroalcoholic extract of sea urchin spines

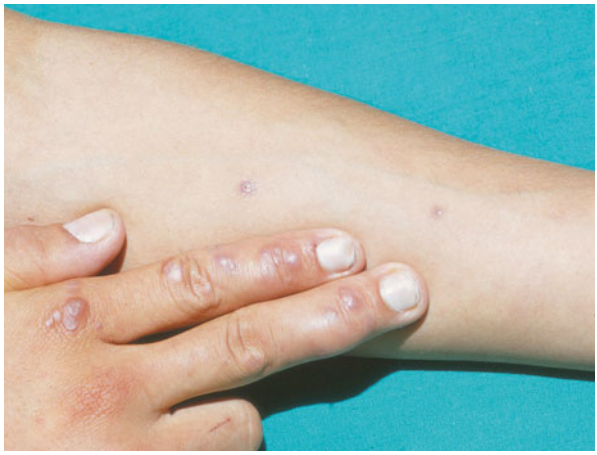

Fig. 4.19 Positive delayed reaction after 48 h to intradermal test with hydroa1coholic extract of sea urchin spines

An ample histopathological study of 50 biopsy specimens from 35 patients with granulomas provoked by *P. lividus* showed that sea-urchin granulomas span a wide morphological spectrum, from which no definite aetiopathogenic conclusions can be drawn [32]. In most cases (70 %) a predominantly granulomatous inflammation reaction was present, while in the other 30 % of cases a non-granulomatous inflammation was evident, showing acute suppurative dermatitis or chronic non-specific dermatitis. All the granulomatous patterns, namely sarcoid (20 %), foreign body (26 %), necrobiotic (12 %), suppurative (8 %), and tubercoloid (4 %) types, were identified [32]. There were very evident epidermal alterations (hyperplasia, spongiosis/exocytosis, umbilication, perforation). Umbilication was present in 30 % of the biopsies, and perforation was identified in 20 % [32]. The spontaneous elimination of spine fragments has frequently been described, and various authors have

mentioned the possibility of a transepidermal elimination of calcium carbonate rather than its reabsorption [11, 12, 14, 17, 33–35]. These factors, as well as the results reported by De La Torre and Toribio [32], have led to the inclusion of sea-urchin granulomas among perforating disorders [36–38]. In 66 % of the biopsies performed in the above study, the infiltrate penetrated down to the level of the reticular dermis or deeper [32]. Another frequent finding was fibrosis, either diffuse or concentric around granulomas [32]. Only in few cases was the foreign matter identified, as has already been pointed out by other authors [10, 20, 39]. In eight biopsies, De La Torre and Toribio saw microparticles with a crystalline appearance either in giant cells or in the dermis, sometimes inside a vacuolar space, while in four biopsies they found epidermoid cysts, probably due to alterations of the infundibular structures induced by the inflammatory infiltrate [32].

In another study, De La Torre and Coll. investigated mycobacterial DNA in formalin-fixed and paraffin-embedded skin biopsy specimens from sea-urchin granulomas. For this purpose, on 41 biopsy samples they conducted tests combining polymerase chain reaction amplification using *Mycobacterium* genus-species primers with subsequent restriction enzyme analysis, enabling identification of the species. Amplification of a 924-bp DNA fragment encoding mycobacterial 16S rRNA gene was positive in eight biopsy specimens from seven patients. *M. marinum*-specific restriction patterns were identified in three samples [40]. Previously, only in 1 case had acid-fast bacilli been identified, and the authors suggested that echinoderm granuloma could be a new mycobacterial infection [41]. The identification of *M. marinum* raises the hypothesis that it may play a pathogenic role in some cases of sea-urchin granuloma. It is quite likely, in fact, that echinoderm spines could occasionally harbour *M. marinum*, even apart from the fact that several *Mycobacterium* species that are pathogenic to humans can infect aquatic species [42, 43]. When they penetrate the skin, the spines can transfer other substances such as seaweed, that can also induce granulomatous reactions [42].

Nodular lesions can be treated with intralesional injections of corticosteroids (e.g. triamcinolone acetonide 10 mg/ml) or liquid nitrogen.

Repeated penetration of sea urchin spines can induce the onset of chronic occupational traumatic scleroedema in seamen (see Chap. 13).

4.2 Dermatitis from Starfish

Starfish (of which there are about 2,000 different species) have spines made of calcium carbonate crystals mixed with organic substances (Figs. 4.20 and 4.21). The spines are held erect by special muscular structures. The calcite envelops a glandular tissue that can secrete a toxin: a saponin like that of Holothuroidea with a haemolytic, antibiotic action consisting of steroid glucosides, among which aglycon (in Holothuroidea this is a derivative of lanosterol), of a steroid nature, is a derivative of cyclopentanoperhydrophenanthrene [1]. These saponins are highly tensioactive agents that can induce an irreversible blockage of neuromuscular transmission. Starfish toxin spreads inside the water so that when many such animals are present, contact with the surrounding water can induce a papulo-urticarial, itchy eruption.

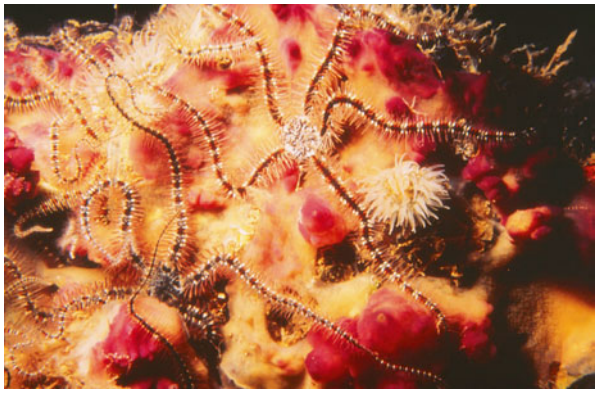

Fig. 4.20 *Ofiotrix fragilis* on a sponge (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

Fig. 4.21 Mediterranean starfish (Courtesy of Mr. Enzo De Santis, Palese (Bari), Italy)

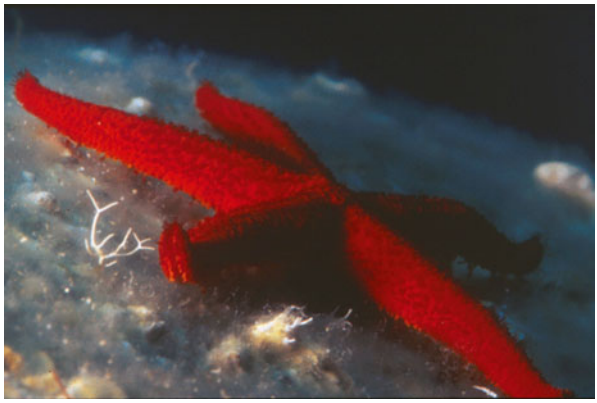

Fig. 4.22 *Echinaster sepositus* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

One of the most common starfish in the Mediterranean is *Echinaster sepositus* (Fig. 4.22), which is bright red and particularly common in the Gulf of Naples. The dermatitis can be treated with a lotion with a 0.5 % calamine and menthol base.

Some starfish, like *Acanthaster planci* (or "crown of thorns"), can inflict a painful sting which may result in granulomatous lesions. This starfish, that lives

in the Indo-Pacific region, spanning from Polynesia to the Red Sea, can be as long as 60 cm. *Acanthaster* has from 13 to 16 arms or rays. The outer surface of the body is entirely covered with a series of large, sharp calcareous spines (they may reach 4–6 cm in length) that are very difficult to remove after penetration in the skin. The cutaneous glands also secrete a venom that can induce a severe inflammatory reaction, as well as erythema, oedema, nausea, vomiting, torpor and sometimes even paralysis. Another, similar starfish, *A. elissi*, is present in the eastern Pacific region [43].

The spines of *Acanthaster* easily penetrate gloves and thin shoe soles. They must be surgically removed to avoid the formation of granulomas. The affected area must be immersed in water as hot as is bearable (45 °C) for 30–90 min or until the pain goes off. Infiltration of the wound with 1–2 % lidocaine may relieve the pain. The inflammation can be treated with topical steroids. To prevent damage, the animal should be handled wearing thick gloves, since only the soft underside of the starfish can be touched with bare hands [43].

4.3 Dermatitis from Sea Cucumbers

Sea cucumbers are sausage-shaped, sea bottom-feeding Echinoderms that can induce an irritant papulous contact dermatitis and lesions of the eye, by means of a toxic liquid substance known as holothurin, that is secreted from their body walls [2]. Conjunctivitis, and even blindness, can result from corneal involvement due to contact with this toxin. Prevention against sea cucumber dermatitis is achieved by covering and so protecting the skin and eyes from contact with the creatures, and by fully informing children and divers about the risks of handling them.

Some sea cucumbers eat the nematocysts of Coelenterates and these can remain intact for use in personal defence. The treatment of skin reactions due to contact with sea cucumbers consists of washing the affected area with soap and water to remove the toxin, and then treating as for contact dermatitis, while bearing in mind the risk of a possible contact with the nematocysts of Coelenterates.

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Dermatitis Caused by Molluscs

5

Domenico Bonamonte, Pietro Verni, Angela Filoni, and Gianni Angelini

The phylum of Molluscs (from the Latin *mollusca* = a variety of nut with a soft shell) includes about 45,000 species with a wealth of disparate shapes and functions, living in different habitats. Molluscs are present in waters all over the globe; they can be static or mobile, nude (Fig. 5.1) or covered with a protective shell, herbivores or carnivores, microphages or macrophages. The biotoxins isolated from Molluscs have various chemical and pharmacological structures; some are only urticant or have a repellent smell or taste, others are highly toxic and paralyse the prey. In some Molluscs, the filtrating bivalves, the toxins are exogenous and come from phytoplankton. Of the five classes belonging to this phylum, the three with the greatest toxicity are Lamellibranchia, Gasteropodia and Cephalopodia (Table 5.1) [1, 2].

There are 11,000 species of Lamellibranchia, which have a bivalve shell closed by two abductor muscles (the bivalves include mussels and clams, oysters, scallops), and live on the rocks or burrowed in the sand and mud. They are macrophages and feed on organic material suspended in the water; this material is captured and filtered by the ciliary brachial movement. When attacked by a marine predator, or exposed by low tide to land predators, Molluscs contract the strong abductor muscles and tighten the two valves of the shell, entering an anaerobic state. For this reason they do not produce biotoxins for offence and defence but as they are filtrating macrophagic animals (a large mollusc can filter up to 38 l of seawater per day), they can ingest micro-organisms that produce biotoxins, and so become poisonous.

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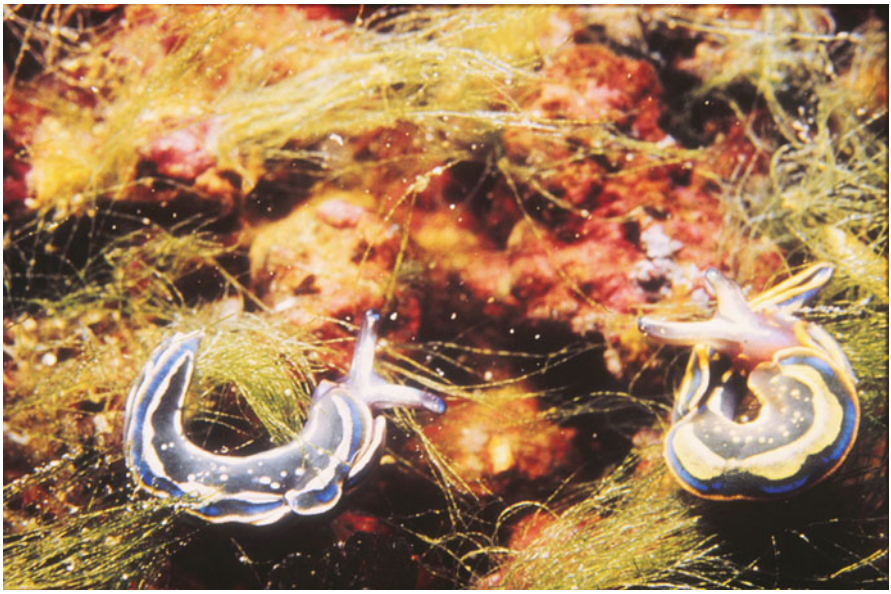

Fig. 5.1 *Thuridilla hopei* (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

Table 5.1 The phylum of Molluscs. The toxic species are indicated

1. Class: Lamellibranchs (bivalves)
Species:
Mytilus galloprovincialis
Ostrea sp.
Anomia sp.
2. Class: Gasteropods (shells)
A: Subclass: Opistobranchs
B: Subclass: Prosobranchs
Species: Muricidae (jagged shells)
Species: Conidae (conical shells)
Conus aulicus
Conus geographus
Conus gloria maris
Conus marmoreus
Conus striatus
Conus textile
Conus tulipa
3. Class: Cephalopods (octopus, squid, cuttlefish)
Species:
Octopus vulgaris
Octopus macropus
Eledone moschata
Eledone aldrovandi
Sepia officinalis
Hapalochlaena maculosa (O. maculosus, "blue-ringed octopus")
Hapalochlaena lunulata
Hapalochlaena fasciata

Obviously, the toxins are innocuous to the Molluscs themselves, for unknown reasons. Toxic micro-organisms can be ingested during the so-called "red tides" caused by toxic seaweed species, and the cases of food poisoning after eating contaminated shellfish (clams, oysters) can be attributed to these causes. In some bivalves, saxitoxin has been isolated, a toxin produced by Dinoflagellates whose explosive proliferation is responsible for the red tides.

Gasteropoda may be nude or covered by a shell, generally spiral-shaped. As they are both herbivores and carnivores, they produce a large variety of biotoxins for offence and defence. The best known Gasteropoda belong to the Opisthobranch (from the Greek *opistho* = posterior) and Prosobranch subclasses: the former have entirely or partially lost their shell while the latter have a highly variable range of hard shells that are generally very beautiful. The best studied species of Prosobranchs are the Muricides (from the Latin *murex* = hard shell), that have lovely jagged shells with many sharp edges, and the Conides, hundreds of species with pretty, smooth conical shells of various colours.

An interesting historical note is that Muricides contain a chromogen that is oxidized in contact with the air, producing a reddish-purple pigment (purple is 6,6′-dibromoindigo), from which the pigment "Tyrian or Byzantine purple" was extracted as a valuable dye in ancient times. In fact, in various Mediterranean centres where they produced purple, large deposits of *Murex* shells have been found. The toxins produced by the Conides (cone shells) are highly virulent, even if they are little known, and have different pharmacological actions depending on the species.

Cephalopod Molluscs (octopus, squid, cuttlefish) immobilize their prey with toxic secretions from their salivary glands. One of the best known members of this class is the octopus, both thanks to fantastic tales (attacks on scuba divers or ships) and to the fact that in 1950, enteramine (5-hydroxytryptamine or serotonin) was extracted from *Octopus vulgaris* (the most common cephalopod in the Mediterranean). This substance was discovered simultaneously by Vittorio Erspamer in the salivary glands of *O. vulgaris* [3] and by Rapoport in beef blood serum (hence serotonin). In addition to serotonin, Cephalopods contain other amines in their salivary glands (tyramine, metatyramine, dopamine, octopamine, histamine) and cephalotoxin, a glycoprotein with a paralysing action on crustaceans [1]. Cephalotoxin has also been isolated in the salivary glands of two Mediterranean octopus species, *O. vulgaris* and *O. macropus*.

5.1 Reactions to Cephalopods

Cephalopods are widespread in all tropical and temperate seas, being restricted to a few species only in the Arctic and Antarctic. They live in higher density water than normal sea water, generally at depths of less than 100 fathoms (a fathom is equal to 6 foot or about 1.83 m). The adults of the species prefer rocky bottoms, although they can sometimes be seen in sandy areas. Cephalopods tend to be solitary, pugnacious creatures and when they become aware of the presence of an enemy, they shoot rapidly backwards, spewing out powerful jets of water from the siphon at their anterior opening, with their tentacles stretched out horizontally and their head thrust forward. When they are disturbed, they discharge a dark cloud of "ink" that masks

Fig. 5.2 *Octopus vulgaris* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

their retreat. Sometimes, octopuses may eat their own tentacles. They can reach a maximum length of 9 m, while giant squid can be as much as 19 m long.

In the Mediterranean, *O. vulgaris* (Fig. 5.2), *O. macropus* (Fig. 5.3), *Eledone moschata*, *E. aldrovandi* and *Sepia officinalis* (Fig. 5.4) are the most common. They are generally inoffensive and timid creatures but thanks to their hard, bony, parrot-like beaks, these Molluscs can take small bites, leaving small, lacerated star-shaped wounds with oedematous margins, which provoke local burning pain which can affect the whole limb. Such wounds can bleed abundantly. Lesions induced by our octopuses, especially *O. vulgaris* and *O. macropus*, are not generally followed by systemic disturbances. A toxin with a proteolytic action, eledoisin or muscatin, was isolated by Erspamer from *E. moschata*. This causes vasodilation and hypotension in laboratory animals and in man.

Particularly during the summer months, the coasts of Australia are populated by a small, venomous octopus, 10 cm long (including its tentacles), the *Hapalochlaena maculosa* (or *O. maculosus*), whose bite may be fatal also to man. It has characteristic markings featuring two blue rings on a brownish-yellow background, hence its name "blue-ringed octopus". When it is aroused, its background colour goes very dark, while the blue rings get brighter and shine like the brilliant eyes on a peacock's tail.

The *Hapalochlaena* genus is found all along the Australian coast: *H. maculosa* in southern regions, and the greater blue-ringed octopus (*H. lunulata*) in more tropical areas. A third species, the blue-lined octopus (*H. fasciata*) has been described along the east coast of Australia. This genus has been associated with a grave

Fig. 5.3 *Octopus macropus* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Fig. 5.4 *Sepia officinalis* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

neurotoxic envenomation resulting in respiratory failure and death [4–11]. The blue-ringed octopus is found in tidal rock pools and is very attractive, inviting inspection particularly by children and tourists, who are at risk when they pick it up or step on it. The poison contains tetrodotoxin (also found in pufferfish), secreted in the octopus saliva. This causes the blockade of neuronal sodium channels, leading to weakness, numbness or paraesthesia, breathing difficulties and ultimately, respiratory paralysis. The bite may initially be painless and the onset of symptoms will only occur after 5–10 min. A burning pain radiates outward to the whole limb. Typically, there will be copious and prolonged bleeding at the site of the lesion. Local itching may be associated with an allergic urticarial eruption. This is followed by muscular weakness and numbness about the face or neck, difficulty in breathing, nausea, vomiting, and speech disorders. In serious cases, there is rapid progression to flaccid paralysis and apnea. The patient may become completely paralyzed and unable to respond, sometimes with fixed, dilated pupils, even if the sensory system is unharmed; in fact, care should be taken to avoid making negative remarks that the alert patient may overhear [10].

There is no effective antidote. Treatment is symptomatic and in less serious cases there will be some improvement after 4–10 h. Complete recovery may take 2–4 days. It is necessary to get the patient out of the water immediately. In cases with apnea, breathing should be supported with mouth-to-mouth respiration and the patient should be hospitalized as an emergency case. A pressure immobilization bandage should be applied to the affected limb. Endotracheal intubation and artificial ventilation may be required until the effects of the venom wear off [10].

In conclusion, apart from the limited number of species (blue-ringed octopi) that can induce systemic symptoms and a lethal outcome, most octopus species will cause an immediate, modest reaction with skin swelling and redness around the bite, due to the injection of toxic secretions containing cephalotoxin, other amines or toxic saliva produced by the posterior salivary glands [11–14].

From the histological standpoint, like those of Coelenterates, an octopus bite may cause a delayed reaction due to the persistence of toxic antigens in the skin, causing a continual activation of T cells and macrophages [15]. Although no specific cases of a delayed reaction to an octopus bite have been documented, one case of granuloma annulare was reported, that developed 2 weeks after an octopus bite that had elicited an immediate toxic reaction: this case can be considered as a delayed reaction to an octopus bite [13]. Misago and Coll. reported a case of a delayed reaction to a bite by a common octopus (*O. vulgaris*), a species that is ubiquitous worldwide [16]. The immediate toxic reaction on the forearm, with erythema and swelling following a bite on the right wrist, was followed by complete resolution after systemic cortisone treatment. One month later, a gradual eruption of asymptomatic subcutaneous nodules was observed, measuring 7–10 mm in diameter, that were distributed largely on the flexor surface of the forearm, together with a subcutaneous induration (20 mm in diameter) on the wrist at the site of the bite. The skin above the nodules was normal in color or

slightly erythematous. Biopsy of a subcutaneous nodular lesion revealed a diffuse, dense infiltrate in the subcutaneous fat lobules, partially involving the fibrous septa, the dermal-subcutaneous junction and the deep dermis. The infiltrate consisted of numerous multinucleated giant cells, sometimes huge and bizarre, together with epithelioid cells intermingled with lymphocytes and eosinophils [16]. No giant Touton-type cells were present, nor xanthomatized histiocytes, signs of necrobiosis, vasculitis or abscess formations. Nor were any foreign bodies found. Treatment with 10 mg of oral prednisone daily resulted in complete resolution of the skin eruption after 2 weeks. However, 2 weeks after the suspension of treatment a further skin eruption appeared, featuring many small reddish-brown papules (2–3 mm in diameter), again on the forearm. Histology of a papule identified an infiltrate in the upper part of the reticular dermis, with numerous multinucleated giant cells and epithelioid cells together with lymphocytes and eosinophils, abundant deposits of basophilic mucin among the collagen bundles, partial degeneration of collagen, and a somewhat palisading granuloma. This second episode was also interpreted as a delayed reaction to an octopus bite. Subsequent treatment with oral prednisone caused healing within 3 weeks; follow-up at 2 years was negative [16]. An octopus bite, therefore, must be included among marine injuries that can cause a delayed-type reaction associated with granulomatous dermatitis/panniculitis.

5.2 Reactions to Conidae and Other Molluscs

Some bivalves (*Mytilus galloprovincialis*, *Ostrea* species, *Anomia* species) living in shallower waters can induce cutting wounds of a superficial or deeper nature, depending on their structure and arrangement on the rocks.

The Conidae family includes about 400 species, all of the *Conus* genus, and virtually all confined to tropical and subtropical waters. The species *Conus aulicus*, *C. geographus*, *C. gloria maris*, *C. marmoreus*, *C. striatus*, *C. textile*, and *C. tulipa* have a well-developed venom apparatus and can kill a man. Depending on their size and the nature of their venom apparatus, many other species are potentially harmful to man. The venom in cone shells contains up to 200 different active components, the conotoxins, that have a neurotoxic and myotoxic potential [15]. Cone shells live in tidal areas at different depths, from shallow waters down to several hundred metres, in different microhabitats: seaweed, coral reefs, sandy bottoms. The most dangerous species to man are the sand dwellers. The cone shell found in the Mediterranean sea (*C. mediterraneus*) is relatively harmless.

A cone shell sting immediately elicits intense, burning sensations, torpor and tingling or numbness, which rapidly spread from the affected area to the whole body and are especially pronounced at the lips and mouth. There may also be disorders of speech, swallowing and vision (double images, blurred vision). These symptoms are followed by localized ischaemia and cyanosis in the affected area. In severe cases there may be the onset of muscular paralysis and coma, although respiratory

distress is not usually a feature, and death will ensue due to heart failure within 6 h of the bite. If the patient survives, the systemic symptoms should subside after about 24 h but the skin reaction will persist for several weeks [17–20].

There is no specific treatment for cone shell stings: making an incision to suck the poison out of the wound does not seem to help and should be avoided. A good first aid approach is to contain the spread of the venom by a pressure-immobilization technique [2]. When the sting is on a site where such a manoeuvre is possible, a gauze or fabric pad about 6–8 cm in diameter and 2–3 cm thick should be pressed against the wound, and bound tightly enough to prevent venous return but without hindering arterial flow. The pad must be removed after the victim arrives in hospital, and symptomatic systemic treatment is begun.

Because of the great beauty of their shells, Conidae are highly prized by collectors, who sometimes fail to take adequate precautions when handling them. As a preventive measure, gloves must be worn and the shells should be picked up only by their wide, posterior extremity and dropped immediately if the animal extends its radular shaft. They should be handled as little as possible and should not therefore be cleaned of detritus while still alive. Cone shells should never be kept in a pocket as they can inflict stings even through clothing.

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Lesions Caused by Arthropods

6

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This work is focused upon marine animals that can induce dermatitis through various pathogenic mechanisms. On this basis, there would be no point in considering those species that lack toxins and can only produce traumatic lesions. However, the need to follow a zoological classification of marine species dictates at least a brief mention of various species that lack biotoxins, such as the Arthropods.

Unlike the huge number of venomous land species (scorpions, spiders, chilopods, insects), marine Arthropods do not secrete venom. Of the vast phylum of Arthropods, only most Crustaceans and 5 surviving species of *Xiphosuri* are marine animals.

Crustaceans (crabs, shrimps, lobsters, barnacles) (Figs. 6.1 and 6.2), belonging to the Arthropod class, include freshwater forms, and have branchial or integumentary respiration systems. In the larval stages, and sometimes even as adults, they account for an important part of plankton and serve as food for many pelagic animals. They have two pairs of antennae and a variable number of articulated, typically cleft appendages. They have a chitinous, often calcified exoskeleton, subdivided into mobile, jointed segments. These are generally fused to form the head, thorax (or cephalothorax) and abdomen and all except the last are supplied with two articulated appendages [1, 2].

Apart from a few cases of hermaphroditism, there are separate sexes; parthenogenesis is frequent. Development generally occurs by means of metamorphosis,

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Fig. 6.1 *Palinurus elephas* (lobster) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Fig. 6.2 *Gnathophillum elegans* (shrimp) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

often through long and complex processes: the nauplius is the typical larval form but a more advanced developmental stage, the zoea, can also hatch from an egg.

These animals, such as crabs and lobsters for instance, appear to be well protected, whatever their size. They have a solid carapace and are armed with two strong claws that end in pincers. Thanks to these mechanical devices, Crustaceans do not need chemical weapons to capture their prey or to defend themselves from predators. However, these defences are not always sufficient. It is well known that an octopus, although it is a mollusc with a soft, bare body, has no difficulty in devouring even large crabs despite the fact that they could amputate undefended tentacles with a single strike of their claws.

Crustaceans, or shellfish, have always been very popular as food. Nevertheless, in some parts of the world (Japan, New Zealand, the Pacific archipelago) various cases of shellfish poisoning have been reported. Studies of the suspected species have shown that in some periods of the year and only in some regions, some of them contain saxitoxin, tetrodotoxin and other neurotoxins [3].

In some species the toxicity has been demonstrated to be due to the presence of *Gonyalux*, the same Dinoflagellate that is implicated in the "red tides" that make bivalves poisonous [4]. It is a strange and so far inexplicable fact that the biotoxin should be present only in a few species of Crustaceans.

6.1 Reactions to Crustaceans

The class of Crustaceans includes some species that are well known and widespread in the Mediterranean. Any harmful effects are purely mechanical (lacerating wounds) provoked by the claws of large crabs, for instance, such as *Eriphia verrucosa* and *Homarus gammarus*.

Dermatitis of the hands has also been reported in lobster catchers. This is characterized by a pruriginous eruption, complicated by hypercheratosis and ragade-like cracks. There are various underlying pathogenic mechanisms: trauma during manoeuvres for catching and de-weeding the crustacean, the contact with sea water and the sensitizing action of some seasonal seaweeds.

Mechanical lesions can also be caused by Balani (from the Greek *bálanos* = an acorn), belonging to the Cirripedus crustacean genus (from the Latin *cirrus* = a bifidus appendix) of the barnacle family. These species are non parasitic and have six appendages for conveying small plankton-like animals to the mouth for food. They are sessile animals covered with a calcareous shell with sharp edges, that can cause cutting wounds of variable severity. Barnacles colonize hard substrates (quays, buoys, the hulls of ships, harbour bottoms) in particularly polluted waters (Fig. 6.3).

Bites and cutting wounds caused by Crustaceans must be treated with care. Secondary infection is a concern: prophylactic antibiotics may be necessary, depending on the severity of the traumatic wound.

It should also be borne in mind that Crustaceans are one of the most prevalent causes of food allergy worldwide. The muscle protein, tropomyosin, is the major allergen in shrimp and is also present in Mollusks and Arthropods [5–9]. Owing to

Fig. 6.3 *Lepas anatifera* (barnacle) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

its ubiquitousness and IgE recognition, tropomyosin is notorious as a cross-reactive panallergen [10, 11]. As a consequence, patients who are allergic to Crustaceans can also show a clinical reaction to Molluscs and mites [10, 11]. Other allergens have recently been identified in Crustaceans, such as arginine kinase [12], myosin light chain [13], sarcoplasmic calcium-binding protein [14], troponin-C, and triosephosphate isomerase [15].

The diagnosis of the allergy to Crustaceans is based on the clinical history, skin prick tests, serum-specific IgE, and oral food challenges if possible. Once the allergy to Crustaceans has been ascertained, patients need to be carefully instructed to take care to avoid any exposure to Molluscs [9].

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Dermatitis Caused by Sponges

7

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Sponges, members of the Porifera phylum, class Demospongiae, normally lie stationary, attached to the sea bottom or sometimes the lake bottom. There are more than 10,000 species of sponges, that are highly variable as to shape, size and colour, ranging from practically invisible to 2 m in length and from pastel tones to bright hues: red, yellow, orange and blue (Fig. 7.1) [1–4].

Sponges are the most primitive pluricellular organisms, composed largely of epithelioid cells; the individual cells, known as choanocytes, are flagellated, have a considerable functional autonomy and do not form organs: they have no structure that could be compared to Metazoan structures. They generally possess a sac enclosing a cavity, named the spongocele. The external wall is studded with pores for the penetration of water and the nutrients: bacteria, unicellular seaweeds and organic particles. Sponges are thus filtering, microphagic animals with an endocellular digestive system.

The walls of sponges also consist of calcareous and siliceous spikes of various shapes and of a lattice-like skeleton made of spongin, a scleroprotein. The bath sponges we use are nothing other than the skeletons of Porifera.

Human use of sponges dates back to ancient Greek and Roman times, when those with a high content of spongin were adopted for washing and to pad helmets and armour, while harder ones were employed for abrasive purposes to clean parchment and various objects. Some sponges were used for therapeutic purposes: the ash

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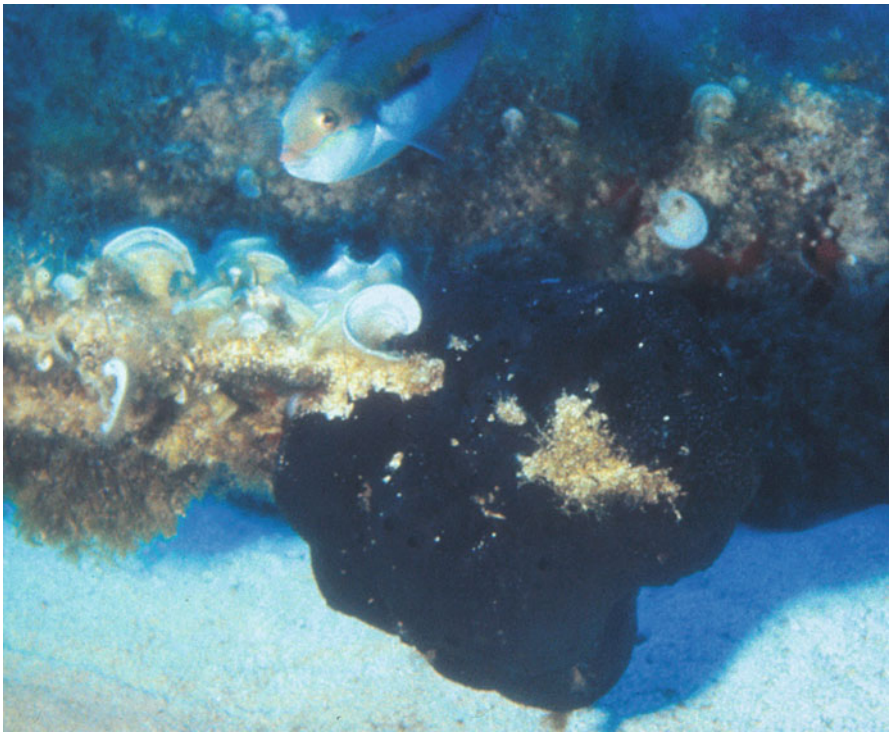

Fig. 7.1 *Euspongia officinalis* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

of *Euspongia officinalis* (Fig. 7.2) was employed to treat goitre, owing to its high iodine content ranging from 2 to 16 % of its weight. Natural sponges have now been virtually eliminated in favour of artificial ones.

Sponges have long been known not to be entirely innocuous. The siliceous sponges of the Mediterranean, for instance, (*Suberites domuncula* is one of the most common) contain suberitin, a protein biotoxin with a neurotoxic and haemolytic action [5, 6]. Another highly toxic sponge for fish (which do not feed on sponges except in exceptional cases, and indeed go out of their way to avoid them) is *Latruncula magnifica*, a beautiful red sponge that lives at depths of 6–30 m in the Red Sea. Two toxins, latrunculin A and B have been isolated from this species [7]; they are macrolide complexes with 16 and 14 atoms of carbon, respectively, in a closed-ring structure and containing a thiazolidinone residue.

Owing to their canal system and alveolar structure, sponges offer an ideal habitat for micro-organisms. However, although they live on the sea bed, they are never covered in encrustations and so present a clean, smooth surface (unlike an amphora lying at the bottom of the sea, for instance). It has therefore been suggested that sponges may exert some kind of antimicrobial activity and in fact, antibacterial substances such as phenol, pyrrole and indole bromurate, and derivatives of furan, terpene, sesquiterpene and diterpene have been isolated from *Microciona prolifera* (a red sponge found on the Atlantic coast) [1].

Fig. 7.2 *Phorbas tenacior* (blue sponge) and *Serpula vermicularis* (Polychaeta) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

Sponges populate not only a vast geographical habitat but also a very diversified vertical habitat, ranging from tidal zones to depths of over 2800 m.

7.1 Reactions to Sponges

In most cases contact with sponges is free from harmful effects, apart from a possible abrasion. Nevertheless, some species of sponges can cause more serious skin manifestations. These may be induced either by the spicules on the horny but elastic skeleton, or by the toxins (crinitoxins) present on the surface of the organisms, or secreted into the water. Victims of accidents associated with sponges are largely limited to sponge fishers, divers, people in search of sponges for their collection, or biology students [8–16].

The majority of sponge stings are reported in Australia, the United States, Hawaii, the Caribbean Islands and Brazil. *Neofibularia mordens* in South Australia caused the most severe stings [8, 13–15]. Other *Neofibularia* species have been reported in Northern Australia, and *Biemna* species [15, 17], and *Haliclona* species in Eastern Australia [18]. Harmful effects have also been reported due to contact with some species of freshwater sponges, *Ephydatia* in Central Australia [8] and *Lissodendoryx* [13]. *Tedania ignis* (the "fire sponge"), *T. nigrescens*, *T. anhelans*, *Neofibularia nolitangere* and *M. prolifera* (red sponge) have induced effects in the United States, Hawaii and the Caribbean Islands [12, 15, 16, 19]. Skin irritation from handling *Tedania* species has also been reported in New Zealand [13] (Table 7.1).

Table 7.1 Clinical reactions to sponge stings

Species	Reaction	Location
Tedania ignis ("fire sponge"), *T. nigrescens*, *T. anhelans*	Immediate subjective reactions and a modest skin irritation lasting from a few minutes to 24 h. Delayed reactions are possible, ranging from moderate to severe, with pain, pruritus and an erythemato-bullous eruption	United States, Australasia, West Indies
Neofibularia nolitangere ("poison bun", "touch-me-not"sponge)	Pain and local swelling 1 h after contact	North and Central America
Microciona prolifera (red sponge)	Local erythema and oedema associated with joint stiffness. Bullous lesions after some hours. In some cases symptoms persist for months	United States
Neofibularia mordens	Subjective symptoms associated with erythema and swelling. These symptoms may persist for days or weeks	South Australia

Clinical manifestations may be immediate and/or delayed. The onset of symptoms of itching, prickling, stinging, or burning occurs a few minutes after the contact and is followed within a few hours by pain, swelling, and stiffness. When the fingers are involved, they often become stiff in about 24 h. The first skin sign is erythema, that progresses to a papulo-vesicular or bullous eruption with a serous or purulent exudate. Within a few days the dermatitis becomes squamous. The onset of clinical manifestations may occur even many days after the contact [16, 20, 21].

T. ignis and other *Tedania* species are abundant in the Miami area and along the Keys in Florida, in West Indies and Australia. Although *T. ignis* has no commercial value, it is a beautiful sponge, both in the way it grows and because of its reddish-orange or brilliant vermilion shade, that sometimes verges on orange or orangey-yellow. Contact with these sponges induces itching or stinging and after a few hours, pain, erythemato-bullous lesions, oedema and immobility of the fingers. The symptoms resolve in about 2 days. *T. ignis* may also give rise to an erythema multiforme-like eruption [9].

N. nolitangere (the "poison-bun" or "touch-me-not" sponge) owes its name to the fact that its sting provokes a much more violent reaction than the one described above. It lives in slightly deeper waters and is relatively difficult to recognize, as it resembles many other more common sponges as to size, shape and colour. This sponge generally grows in small clusters and its osculi (pores) are as wide as a man's finger; it is brown on the surface and has a consistency like that of soft bread. *N. nolitangere* colonizes the waters of Central and North America.

Contact with *M. prolifera*, the red sponge present along the east coasts of the United States, causes erythema and oedema. Later, blisters develop on the affected area and have a purulent evolution. Unless it is adequately treated, the dermatitis can persist for several months. Patch testing with a fragment of the sponge will confirm the diagnosis.

Apart from the above contact dermatitis forms due to chemical agents, some sponges can induce traumatic dermatitis as a result of contact with the spicules, which are composed of silicone dioxide or calcium carbonate. These spicules penetrate the skin and are difficult to remove but they can cause foreign-body reactions unless they are successfully eradicated. Freshwater sponges differ from marine sponges in that their spicules are in suspension in the water, and provoke a generalized erythematous papular eruption [3]. Recently, the onset of blindness has been described in individuals exposed to these spicules in Brazilian rivers [3]. It can be helpful to apply first of all an adhesive plaster to the affected part, to which the spines will attach, and then after peeling off the plaster, to apply isopropyl alcohol.

Preventive measures include wearing gloves when fishing for sponges, while scuba divers in tropical waters should wear all-over covering. The diagnosis, especially of possible delayed reactions, may be difficult unless the patient recalls the history of contact with a sponge.

Treatment of the dermatitis is by applying acetic acid (vinegar) compresses for 15–30 min, 3–4 times a day. Isopropyl alcohol (40–70 %) may also be useful. Topical corticosteroids may be applied later. In the presence of marked exudation of the lesions, it will be necessary to administer systemic corticosteroids. The itching sensation can be controlled with systemic antihistamine treatment. Patients who present with early signs of a reaction immediately after the contact should be warned of the risk of delayed effects.

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Dermatitis Caused by Algae and Bryozoans

8

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8.1 Dermatitis from Algae

About 30,000 different species of marine and freshwater algae and micro-organisms (Prokaryotes and Eukaryotes) have been identified, that are classified among vegetable species because they are autotrophic (Table 8.1, Fig. 8.1) [1]. Most algae contain chlorophyll, and many have flagella that enable them to move through the water. They are highly variable in size, shape and colour, ranging from microscopic (just 1 μ in diameter) to gigantic forms up to 300 foot long (90 m).

As members of the most ubiquitous of the vegetable kingdoms, algae can be found in all environments: geysers, saltwater, freshwater, snow, ice, the Arctic Circle. Some are saprophytic or symbiotic, and develop on other plants or animals. Curiously, algae have been found on sea beds down to 12,000 feet (3660 m), although the sunrays can only penetrate ocean waters down to 900 feet (275 m).

Marine and freshwater algae that produce biotoxins and are therefore of medical interest belong to the Cyanophyceae (cyanobacteria, commonly but erroneously known as blue-green algae) (Prokaryotes) and Dinophyceae (Eukaryotes) classes. However, even among these two classes there are only a few toxic species. Cyanobacteria, that are rounded or filament-like in shape, live in fresh- or saltwaters. In some periods of the year they reproduce in great masses, giving rise to the so-called "blooms" in lakes and the seas. There are few freshwater species of

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Table 8.1 Classification of algae

Prokaryotes	
Bacteriophyta	
Cyanophyta (cyanobacteria or blue-green algae)	Cyanophyceae
Eukaryotes	
Rhodophyta (red algae)	Rhodophyceae
Chlorophyta (green algae)	Chlorophyceae
	Prasinophyceae
	Charophyceae
Euglenophyta	Euglenophyceae
Xanthophyta (yellow algae)	Xanthophyceae
Bacillariophyta (diatomea)	Bacillariophyceae
Chrysophyta (yellow-brown algae)	Chrysophyceae
Phaeophyta (brown algae)	Phaeophyceae
Pyrrhophyta (Dinoflagellates)	Dinophyceae
Cryptophyta (Cryptomonads)	Cryptophyceae

Modified from Ghiretti and Cariello [1]

Fig. 8.1 *Caulerpa taxifolia* (green alga) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

Cyanophyceae, notably *Microcystis aeruginosa*, *Anabaena flos-aquae* and *Aphanizomenon flos-aquae*. The best known toxic marine Cyanophyceae species include *Lyngbya majuscola, Oscillatoria nigroviridis, Spirulina platensis* and *Schirotrix calcicola*. Some of these live on coral reefs and are responsible for the sudden outbreaks of poisonous fish in the area. A large proportion of cyanobacteria produces one or more toxins. Cyanotoxins belong to various groups of substances, each of which exerts specific toxic mechanisms in animals. Some cyanotoxins are strong neurotoxins (anatoxin-a, saxitoxins), others are hepatotoxic (microcystins,

nodularin, and cylindrospermopsin), and yet others (lipopolysaccharides) can provoke gastroenteritis and skin disorders [2]. Various episodes of skin irritation have been reported in South Australia in people enjoying normal water recreation activities in waters contaminated by cyanobacteria [3, 4]. The skin toxicity has been attributed to lipopolysaccarides (LPSs) (components of the cell wall of all Gram-negative bacteria, including cyanobacteria), that are produced by all cyanobacteria [5]. Marine and freshwaters cyanobacteria can elicit allergic and irritant responses in human and animal tissues that come in contact with these compounds, as has been demonstrated in studies with patch testing [6–8].

The so-called "red tides" (an inappropriate term as they have no connection with the tide) feature the sudden appearance of turbid, reddish zones on the sea surface. This is due to the immense number of micro-organisms present and to the colour of the pigment in their cells. Blue-green algae, diatomea and protozoa are those present in the red tides: the vast number of toxic Dinoflagellates causes mass death of the fish and other species present in the zone. The red tides are not the same as the blooms, as the former are unforeseeable whereas the latter appear regularly once or twice a year. They are the result of a higher content of nutrient substances in the water, which in turn causes proliferation of the plankton populations. In the red tides, the water becomes a concentrated suspension of micro-organisms, that nearly always belong to a single species, unlike the variety present in the blooms. Red tides disappear as fast as they appear: they subside in a couple of days, although their effects last a long time. The most common Dinoflagellate species are *Gonyaulax catenella* (containing gonyautoxin), *G. tamarensis, Gymnodinium breve* (containing brevetoxin). The species that cause fish to become poisonous in tropical seas are *Gambierdiscus toxicus* and *Prorocentrum lima*. Some edible bivalves are not killed by the toxins but become carriers, thus posing a serious health problem for man [1]. The toxins of Dinoflagellates can be released into the water or air (via water droplets), where they exert their harmful effects on man and fish. In fish, even small concentrations of these toxins are fatal, while in man, direct exposure can induce contact dermatitis, coughing, sneezing, and conjunctivitis. Another dinoflagellate, *Pfiesteria piscicida*, that is common in lakes, rivers and estuaries, contains a toxin that is fatal to fish while in man it can induce contact dermatitis, pain, burning, eye or respiratory irritation, confusion, problems of recall, and impaired cognitive function. The onset of the manifestations occurs within 2 weeks of exposure, and they can persist for weeks or months [9].

8.1.1 Seaweed Dermatitis

A Cyanophycea alga that causes a dermatological condition is *Lyngbya majuscola,* present in rivers, lakes, pools and oceans. It belongs to the Oscillatoriacea family and grows as greenish-blue, very long, slender filaments that look like hairs. It is common all across the globe and large blooms have been reported in both the tropics and subtropics; major blooms have been described in warmer climates in various localities such as Queensland (Australia), Florida and Hawaii. The alga covers sandy sea bottoms or lives attached to other algae. Not all races are toxic and indeed,

those in some zones may be toxic while those in zones a few miles away are innocuous. *Lyngbya* is abundant in tidal areas and down to a depth of 100 feet (30 m), and is therefore a danger to all bathers. Two toxins that cause painful dermatitis have been isolated and purified from this species, namely lyngbyatoxin A and debromoaplisiatoxin [1, 10].

In man, exposure generally induces skin complaints, more rarely gastrointestinal disorders [11], and there was one associated fatality [12]. Periodic outbreaks of dermatitis have been reported every 10 years or so since the early 1950s [13–16]. In the summer of 1958, *Lyngbya* caused a dermatitis epidemic (125 cases) among Hawaiians living in one coastal area of the island of Oahu (capital, Honolulu) [1, 17, 18]. Only a few minutes after bathing in the turbid algae-filled water, the onset of intense itching and burning sensations occurred, followed after 3–8 h by blisters leaving painful erosions, especially in the perineal region (the genitals and perianal area). The eruption affects the areas covered by the swimming costume; in males it is especially severe on the scrotum and in females on the breast. Histology demonstrated hyperkeratosis and intraepidermal vesicles with polymorphonuclear cells and red blood cells; in the superficial derma, an infiltrate of mononuclear cells, eosinophils and neutrophils was described [18]. Some cases of skin reactions to freshwater blue-green algae have also been reported [19, 20]. This dermatitis must be differentiated from "seabather's eruption". Suitable prophylaxis is for swimmers to remove their wet costumes as soon as they come out of the sea and shower abundantly using soap. Treatment is symptomatic, and topical steroids can relieve the inflammation process.

8.1.2 Dermatitis from Other Seaweed Species

Some French authors reported the observation in a fisherman of a simultaneous contact allergy to a bryozoan (*Electra pilosa*) and to *Sargassum muticum*, a brown seaweed (Phaeophyceae) that originates on the Japanese coasts of the Pacific [21]. This seaweed had spread to Europe about 15 years before, possibly when importing Japanese oysters. *S. muticum* colonies show an explosive growth from March to October, the maximum fertility period being in June and July. Apart from competing with the local marine species, they can damage small boats owing to their great size. At present, *S. muticum* is the only erect species on the European coasts that can grow to a height of 10 m. The reason why it can proliferate so widely is because it attaches to various supports and has a remarkable regenerative power (new growth can start from a small fragment that has broken off). This seaweed should be considered toxic as it secretes phenol compounds.

8.1.3 Dermatitis from Mucilaginous Aggregates

During the summer months from 1989 to 1992, large quantities of mucilaginous aggregates of algal origin appeared in vast zones of the Adriatic Sea. The marine organisms that can secrete mucilage are the Dinoflagellates and above all the

diatoms. As well as damaging the marine ecosystem, these aggregates can cause food poisoning in man through intoxication of the fish. Just swimming in infested waters should not be harmful, although mucilaginous aggregates attract pathogenic bacteria that are then incorporated in the gelatine [22].

Kokelj and colleagues [22] reported the case of a woman who developed intensely itchy erythemato-vesiculo-pustular lesions of the limbs a few hours after swimming in the Gulf of Trieste in August 1991. Histological examination of one of the lesions showed spongiosis, vasodilation and neutrophilic infiltration of the superficial derma. The dermatitis regressed after 6 days of topical corticosteroid treatment. Patch tests with samples of water containing the mucilage aggregates gave negative results in 10 healthy volunteers. The authors believe that this rare observation should be included among irritant contact reactions.

8.1.4 Protothecosis

Skin protothecosis is an exceptional infection induced by seaweed, that mainly affects subjects with an impaired immune system and features various clinical pictures. Most cases are caused by achlorotic algae of the *Prototheca* species [23–27]. These are unicellular, colourless (because they lack chlorophyll) micro-organisms classified as an achlorotic mutant of green seaweed of the *Chlorella* genus. *Prototheca* is a eukaryotic non micelial organism, spherical or round, ranging from 2 to 25 μ in size, that reproduces asexually by internal cleavage (endosporulation), forming morula with up to 20 endospores. It was isolated in 1894 and classified in 1916 [28].

Prototheca's natural habitat is tree mucilage and sewage; it can also be found in the soil, in lakes, ponds, in cats and dogs and in cow's milk. The organism has also been isolated from human nails, skin, expectorate and faeces without any infection being present [29]. It has also been isolated from tap water, swimming pools, soil, and foodstuffs such as shrimps, butter, potato peel and bananas [30].

Three species of *Prototheca* are currently known: *P. stagnora, P. wickerhamii* and *P. zopfii. P. moriformis, P. portoricensis, P. ciferii, P. ubrizsyi* and *P. segbwema* are identical to *P. zopfii*. In most cases, the causal infectious agent is *P. wickerhamii*, while there have been few reports of infection by *P. zopfii* [31–33].

Protothecosis has been reported in the literature in various parts of the world: Europe, Asia (Japan, China, Thailand, Vietnam), Africa, Panama, Oceania and the south-east of the United States. However, the infection seems to be most common in tropical areas [33–35].

Protothecosis most often manifests as lesions confined to the cutaneous or subcutaneous layer (66 %); in about 15 % of cases it presents as olecranon bursitis and in 19 % of cases as disseminated systemic disease. The latter form exclusively affects subjects with an impaired immune response.

The infection is transmitted mainly as a result of trauma. However, the pathogenic potential of these algae seems to be relatively low, and infection seems to be induced by a state of local or systemic immune depression. In fact, apart from a very

few exceptions, skin protothecosis is observed in subjects with a debilitating disease or immune deficiency. It has been reported to be associated with the acquired immune deficiency syndrome (AIDS), with immunosuppressive treatment and with alterations in the function of polymorphonuclear neutrophils [36, 37]. Cutaneous protothecosis can also be associated with an underlying disease, or immune suppression owing to kidney transplantation [38], a hematologic malignancy (acute myelogenous leukaemia, Hodgkin's lymphoma, and chronic lymphocytic leukaemia) or malignancy of the breast or uterus [30], diabetes mellitus [39], steroid administration, systemic lupus erythematosus, chronic obstructive pulmonary disease, congestive heart failure, myasthenia gravis, gout, arthritis, and rheumatoid arthritis. Forms of superficial and subcutaneous protothecosis may also be secondary to intralesional corticosteroid therapy [40, 41]. In laboratory animals, the infection has been reproduced only after pre-treatment with hydrocortisone [34]. Unlike cutaneous and systemic forms, olecranon bursitis affects immunocompetent subjects. In about 50 % of cases local trauma, such as a car accident, fall or surgical operation, has been shown to play a fundamental role in inducing the infection [32].

The first case of human protothecosis was described by Davies and Coll. in 1964 [31]. Of the 45 cases reported by Nelson and colleagues [34], 28 (62 %) presented cutaneous or subcutaneous infections. Most of these consisted of papular or eczematous lesions confined to the face and limbs. These lesions, single or multiple with a slow evolution, had a centrifugal spread. Other reported types of lesions include blisters, cellulitis, verrucous nodules, pustules, ulcerative papules and plaques, herpetiform and pyoderma-like lesions. The sites most often affected are exposed areas like the arms (forearms, wrists, and fingers and the dorsum of the hands) and the legs. Other sites include the face, neck and chest [39]. It is not known how long the incubation time of the infection is, but it is thought to be some weeks or months. As there are no specific clinical pictures, diagnosis is made by searching for the causal agent in the tissues, and confirming this in culture. As the micro-organism reproduces by endosporulation, the various stages are easily identified in the tissues. The cellular elements have a prominent hyaline wall that is little stained by haematoxylin-eosin, but responds better to PAS, mucicarmine or Gomori (methenamine-silver). The single cells (large nonbudding elements with spherical to oval contours) have a basophilic content demonstrated by haematoxylin-eosin and measure from 3 to 30 μ depending on the species. Cells in the initial sporulation phase show cleavage and are slightly bigger. Mature forms in advanced sporulation are the most characteristic, measuring over 20 μ and resembling morula.

The *Prototheca* species grows within 48 h in Sabouraud dextrose agar culture medium, at between 25 and 37 °C in the absence of cyclohexamide, forming smooth, yeast-like, creamy-white colonies. The individual forms can be identified by inoculating them in the culture medium (sucrose, trialose, inositol and propanolol) over 14 days. More rapid identification and differentiation of the species can be achieved with immunofluorescence tests of cultures and tissues.

The *Prototheca* species must be differentiated from some non-sporulating cells that can be very similar, like *Blastomyces dermatitidis* (8–15 μ), *Cryptococcus neoformans* (2–15 μ), *Paracoccidioides brasiliensis* (5–60 μ), and *Pneumocystis*

carinii. The different sizes of the sporongia are helpful to differentiate the *Prototheca* species from these non-sporulating organisms [42].

Histological examination demonstrates many isolated or aggregated organisms among the collagen fibres, within the histiocytes in the papillary and reticular derma, in the annexes and the epidermis. In haematoxylin-eosin stained sections, the organisms appear strongly basophilic, with a pale halo. The epidermis is hyperplastic and an inflammatory infiltrate is evident, scattered or organized as granulomas.

Clinical diagnosis is not easy. A skin trauma can favour entry of the organism. From the aetiological point of view, *Prototheca* must also be differentiated from unicellular green algae (being an achlorotic mutant of these), that can in exceptional cases cause human infection [43]. The two organisms have a strictly related size, shape and reproduction method and similar staining characteristics. Green algae cells are differentiated on the basis of the presence of cytoplasmic granules, which are lacking in *Prototheca*. However, these granules cannot be revealed by haematoxylin-eosin staining (which cannot therefore differentiate between the two organisms) but only by PAS or Gomori staining. In a recent study, immunohistological investigation using rabbit antiserum against *P. wickerhamii* was made of infected cutaneous human and animal tissue exhibiting protothecosis. The antiserum detected *P. wickerhamii* in human and feline protothecosis tissue, and did not react with *Candida albicans* in human kidney tissues showing candidiasis. This antiserum can therefore differentiate *P. wickerhamii* cells from the yeast-like cells of *C. albicans* and *P. zopfii* in target tissues [44].

Treatment of skin protothecosis is quite challenging, especially in immunocompromised patients. The lesions can persist for years and can also spread. Exceptionally, they may also resolve spontaneously [45]. There is no known elective treatment. Localized lesions can be surgically removed. Oral ketoconazole has been found efficacious in some cases; intravenous amphotericin B, alone or in association with oral tetracycline has had variable success. In cases reported recently, itraconazole [33, 46] and fluconazole [40] yielded good results. Treatment with amikacin combined with tetracyclines was also shown to have an effect [47].

8.2 Dermatitis from Bryozoans

Up to now, 4000 species of Bryozoans (from Greek *brion* = moss) have been identified. These belong to the animal kingdom and are very ancient invertebrates which appeared in the sea in the primary era. For a long time they were mistakenly taken to be algae or corals. They grow in colonies, and each colony (zooarium) consists of masses of units, ranging from a few up to thousands of individual animals. Each animal measures about 1 mm and appears as a tiny cell with a chitinous wall and a visceral portion starting with a buccal orifice surrounded by a crown of tentacles. Its ciliary movements attract food particles suspended in the water.

The colonies live attached to the sea bottom, and assemble as coral-like masses encrusting rocks (Fig. 8.2), shells or seaweed, or free-floating masses with

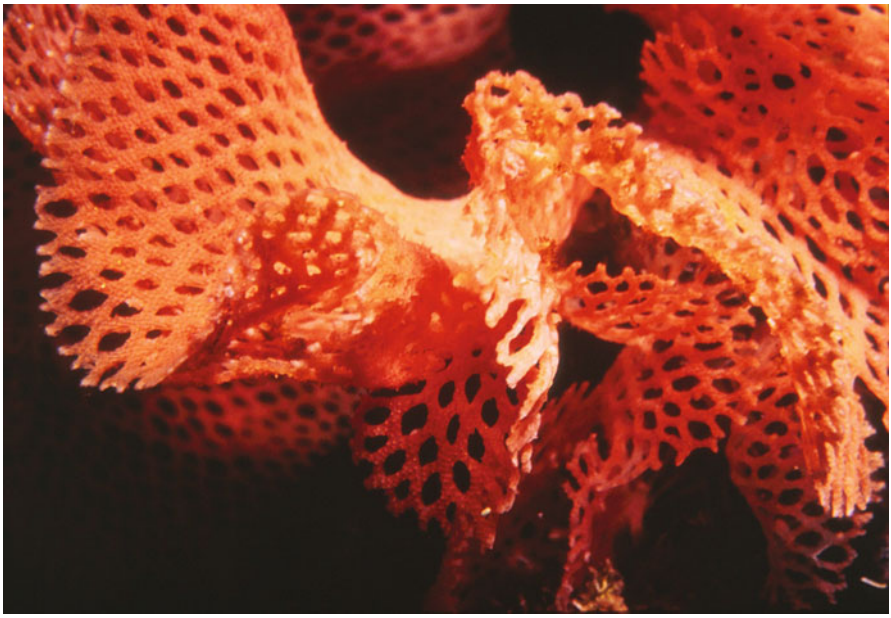

Fig. 8.2 *Sertella beaniana* (ribbon alga) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

filament-like or tree-like extensions like those of seaweed. Torn from the sea bed by fishing nets, they attach to mineral or organic surfaces and proliferate during the summer season, flourishing at temperatures of between 8 and 22 °C. Various Bryozoans can cause contact dermatitis [21, 48–50]. In most cases, *Alcyonidium gelatinosum*, a filament-like zooarium, is responsible, and occasionally *A. hirsutum,* that builds encrusting colonies or *A. topsenti*; in exceptional cases *Flustra foliacea,* a free-floating or encrusting zooarium, and *Electra pilosa,* an encrusting zooarium, can be implicated.

A. gelatinosum is one of the oldest animals on the planet and looks like a yellow-green-brown alga (hence the name "algue pain d'épice" given to this animal by fishermen from Le Havre). It lives in colonies attached to hard substrates (rocks, shells, gravel, stones) in filaments about 20–30 cm long. Each colony consists of a large number of hermaphrodite individual creatures. These produce larvae that then attach to the same filament or to other substrates, creating new colonies. The animal feeds on plankton and proliferates during the summer season, whereas it becomes rarefied during the winter as from October. *A. gelatinosum* is widespread in the Northern Hemisphere, above the 45th parallel of north latitude, and especially in the Atlantic, the Baltic, the North Sea, the Arctic and the North Channel. It is also present in the Southern Hemisphere, in the coral zones of the Pacific, in Australian seas and more rarely in the Mediterranean and the Adriatic Sea.

E. pilosa builds a zooarium of white colonies that encrust various substrates. It is common in most of the seas in the Northern Hemisphere (the North Sea, the

Channel, the Atlantic, the Mediterranean) at depths of between 15 and 18 m and it proliferates during the warm seasons [21].

Contact dermatitis from Bryozoans affects fishermen and is quite disabling. It was first observed in the North Sea (hence its first name "Dogger Bank Itch", from the Dogger Bank area in the North Sea, given to the disease by Bonnevie but now no longer used) [48], and then reported in the eastern part of the Channel [49–51], in the Bay of the Seine [52, 53] and in Polynesia. This occupational eczema typically affecting fishermen manifests in the form of an allergic mechanism of delayed type, that recurs each summer after the initial sensitisation. The onset can occur even on first exposure. Fishermen come in contact with "sea moss" or "sea mats" when they pull their nets on board the boat and find them jumbled in with the fish; sometimes large quantities are present and are then thrown overboard. The clinical picture of the dermatitis features both dry, fissuring and acute, exudative lesions. The hands and forearms are first affected through direct contact with the Bryozoans; the face and neck may also be involved through airborne contact (airborne allergic contact dermatitis) with drops of sea water containing the allergenic material. With successive exposure, the dermatitis may become generalized and manifest as blistering, oedematous eruptions. Although recovery generally occurs within a few weeks of avoidance of the allergen, progression towards exogenic photosensitivity can also be observed, confirmed by photobiological exploration. The dermatitis may also become chronic, showing relapse even without exposure to Bryozoans (chronic actinic dermatitis) [54, 55]. The allergen responsible is 2-hydroxyethyl dimethylsulphoxonium in the case of *A. gelatinosum* [56, 57]. Patch and photopatch tests can be made with fragments of live Bryozoans just after harvesting, with seawater containing the allergen and with aqueous and acetonyl extracts of sea moss. Histological tests have shown intraepidermal spongiosis and a perivascular inflammatory dermal infiltrate [52].

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Dermatitis Caused by Aquatic Worms

9

Domenico Bonamonte, Paolo Romita, Michelangelo Vestita, and Gianni Angelini

Worms are marine and land invertebrates with a long, soft, contractile body and no limbs. At present these organisms are classified in the phyla of Platyhelminthes, Nemertea, Nematoda, Annelida and many others (Table 9.1). The marine forms of these phyla have been investigated for toxins, and the chemical nature of some of those found has been identified [1].

The Annelid phylum, consisting of segmented worms, features organisms with an elongated body and pairs of bristles. The external body covering is a thin, non-chitinous cuticle. Some species have well-developed chitinous jaws. Annelid worms are cosmopolitan and can live in seawater, freshwater and earth.

The Annelida phylum includes four classes of worms [2]:

1. Hirudinea class: leeches.
2. Oligochaeta class: worms with few bristles, like earthworms.
3. Archiannelida class: primitive worms, that are rarely observed.
4. Polychaeta class: worms covered in bristles, that are the most common marine forms (Fig. 9.1).

The few venomous Annelid species are metameric worms belonging to the Polychaeta class; they are all marine animals. Nereistoxin, a tertiary amine with a

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Table 9.1 The phyla of some salt- and freshwater worms

1. Phylum: Platyhelminthes
Family: Schistosomatidae (cercariae)
Species:
Trichobilharzia ocellata
Trichobilharzia stagnicolae
Trichobilharzia physellae
Gigantobilharzia huronensis
Schistosomatium douthitti
2. Phylum: Annelida
A. Class: Hirudinea (leeches)
B. Class: Polychaeta
Species:
Hermodice carunculata (dogworm)
Aphrodite aculeata (sea mouse)
Nereis diversicolor
Lumbriconereis impatiens
3. Phylum: Nematoda
Species:
***Ancylostoma* spp.**
Onchocerca volvulus

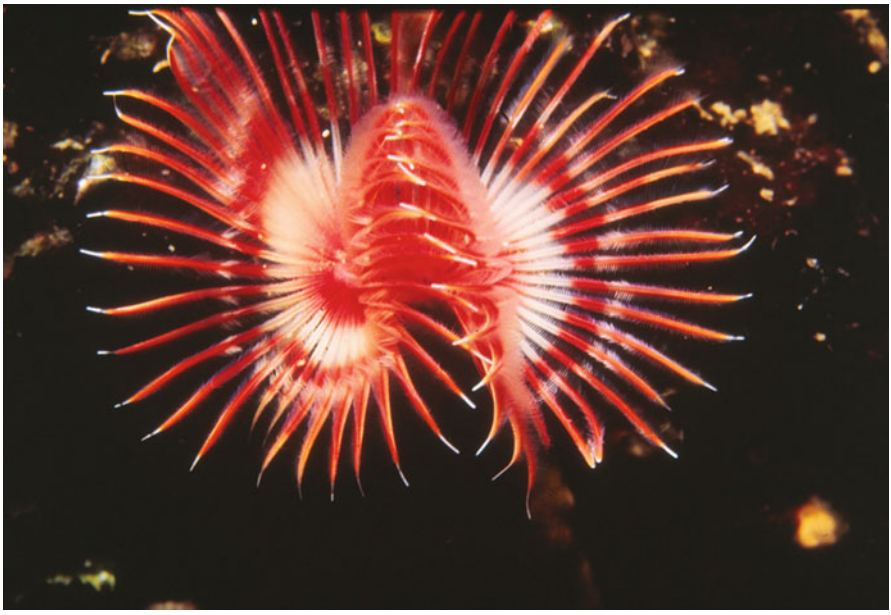

Fig. 9.1 *Serpula vermicularis* (Polychaeta) (Courtesy of Drs. Pablo Helman and Susanna Volpe, "Il quaderno blu", Provincia di Imperia Ed., 1995)

cyclic disulphuric group, has been isolated from *Lumbriconereis heteropoda* [3, 4]. The Nemertea, that are similar to Platyhelminthes but have more complex organs and apparatus, range in size from a few mm to several metres and live in seaweed and among rocks. They are equipped with a long, generally eversible proboscis: this

is everted to capture the prey, which is then killed by contact with a slimy liquid secreted by the animal. The substances nemertine, amphiporine, nemertelline and anabasin have been isolated in this liquid. The latter three are pyridinic toxins with a nicotine-like action [5].

Aquatic worms can induce injuries by means of three pathogenic mechanisms: bites with the chitinous mandibles (traumatic lesions) and envenomation or traumatic lesions through the corporal bristles. Bites commonly occur in mussel harvesters [6].

9.1 Cercarial Dermatitis

Cercarial dermatitis ("swimmer's itch" or schistosome dermatitis) is an acute inflammatory pruritic and non contagious eruption caused by skin penetration of free-living larval stages (cercariae) of trematodes, of the Schistosomatidae family (Platyhelminthes) [6–14]. The clinical picture, induced by non human-parasitizing schistosomes, is different from visceral and cutaneous schistosomiasis or bilharzias, caused by the human-parasitizing species *Schistosoma mansoni* and *S. japonicum*, which infect the gastrointestinal tract, and *S. haematobium*, which infects the urinary system.

Cercarial dermatitis is well known everywhere, being widespread in the East and West, in the Arctic, in tropical and temperate zones and in salt- and freshwater. As well as in bathers and underwater divers, it can be observed in subjects working with freshwater for irrigation (agricultural workers and rice growers) [15, 16].

The schistosomes that induce this form of dermatitis are blood parasites of birds and mammals, but in their ecological cycle, man can become a chance host. The cycle starts with the hatching of the eggs contained in the faeces of infested animals. Through contact with the ciliated miracidia from the eggs, some varieties of shellfish can become infested and act as intermediate hosts. After a period of incubation in Molluscs, the cercariae are released into the water; through their fork-like extremity these parasites then batten on specific warm-blooded animals used as hosts (sea birds, mice, sparrows), which in turn evacuate the eggs and complete the cycle. Occasionally, man can contract cercarial dermatitis and enter the life cycle of these parasites.

The most common of these are *Trichobilharzia ocellata*, *T. stagnicolae*, *T. physellae*, *Gigantobilharzia huronensis* and *Schistosomatium douthitti* [10]. The Mollusc intermediate hosts most often belong to the *Lymnaea*, *Physa*, *Planorbis*, *Polyplis* and *Stagnicola* species. Depending on the target host, three forms of cercarial dermatitis can be distinguished, two freshwater forms and a seawater form.

Dermatitis from Freshwater Cercarias This form, whose target host is a bird, has also been reported in Italy among female workers in rice fields [16]. This seasonal affliction has been reported in the Padania Plain during periods coinciding with the rice-picking season but technological changes in rice growing methods have now made it an exceptional observation. Summer cases among bathers in streams containing cercariae have also been described [16]. Freshwater cercarial dermatitis is well known also in North America, mainland Europe, Asia and Africa.

Dermatitis from Freshwater Cercarias This affliction is due to cercarias whose hosts are buffaloes, sheep and goats, and has been reported in workers in oriental rice fields (India, Malaysia, China) and Austral Africa.

Dermatitis from Saltwater Cercarias The target host of cercarias causing this dermatitis is a sea bird, while the intermediate hosts are marine Molluscs. This form has been described in bathers in infected waters in the USA, Australia and Hawaii. Cercarial dermatitis has also been reported in subjects exposed to shallow coastal waters, in particular on Long Island Sound (USA) where the condition affects clam diggers, giving rise to the name "clam digger's itch" [14]. Cercarial dermatitis has also been reported to affect the hands and forearms, attributed to cleaning an aquarium in which the subject kept native water snails [17].

The onset of clinical manifestations is as hypersensitivity phenomena in allergic subjects. The allergic reaction is elicited by the process of destruction of the cercarias, that occurs in the epidermis because cercarias seem to be unable to penetrate beyond the papillary derma. The organisms undergo histolysis within 3–4 days. The cercarial protein residues stimulate delayed type hypersensitivity reactions, that can be exacerbated by repeated exposure.

An initial stinging sensation is followed by the rapid development of wheals, which resolve in about half an hour leaving maculae. Within 10–12 h these turn into very itchy papules which reach their most severe form of expression by the second or third day. The papules resolve in 1–2 weeks but the dermatitis can be complicated by excoriations due to scratching, and secondary infections with the formation of pustules. Intense itching, that reaches a maximum after 48–72 h, is associated with pain and swelling of the affected areas. Headache, fever, and lymphangitis with adenopathy are sometimes present. By the 3rd and 4th day, skin biopsies show an amorphous eosinophilic mass on the site where the cercaria dissolved, and an intense lymphocytic infiltrate, followed by histiocytes in the medial and deep papillary derma.

Differential diagnosis of cercarial dermatitis is with insect bites from chiggers, mosquitoes, and fleas; stings from other marine coelenterates; "seabather's eruption"; and dermatitis from blue-green algae (seaweed dermatitis). Seabather's eruption is a hypersensitivity reaction to the larval forms of jellyfish, and causes a pruritic papular eruption over covered sites. The reaction to blue-green algae (*Cyanobacteria* toxin) can induce a pruriginous eruption, associated with irritation of the mucosa and gastrointestinal symptoms. In Africa, Asia, South America, and Puerto Rico, swimmer's itch must be differentiated from dermatitis due to human schistosomiasis, that induces an eruption and very similar symptoms, although they are milder and shorter lasting.

It can be challenging to find cercariae in a water body, because they can survive only for 24 h after leaving the snail [18], and also only some of the snails in a particular water habitat may be infested. Identification methods include filtration, centrifugation, phototropic and chemotropic entrapment, PCR-based approaches [19], and the use of sentinel mice [12].

Individual prevention is obviously important (after bathing it is important to change the bathing suit and rapidly dry the skin by energetic rubbing with rough towels to remove cercariae which have not completely penetrated the skin), as well as environmental clean-up (antiparasitic treatments). The efficacy of use of petrolatum and different chemical repellents still requires confirmation. Treatment of cercarial dermatitis is symptomatic. Mild dermatological complaints may be treated with cool compresses, antipruritic or drying lotions, oat meal or starch baths. Antihistamines may alleviate pruritus; aspirin may be helpful for the pain and swelling. It is important to prevent a bacterial super-infection. More severe eruptions require potent topical and systemic corticosteroids. Bacterial super-infections may require systemic antibiotics.

9.2 Reactions to Leeches

Leeches are freshwater segmented worms belonging to the Hirudinea class (from the Latin *hirudo* = bloodsucker) and the Annelida phylum. These dark green invertebrates have a slender body about 5–7 cm long. They attach to the skin and suck blood until they are gorged and have doubled their volume, whereupon they drop to the ground. Their saliva has anticoagulant, fibrinolytic and local anaesthetic properties, causing the victim to bleed freely without feeling pain.

In the ventral position at the cephalic level, leeches have a terminal sucker which attaches to the victim, and in the dorsal position they have five pairs of punctiform eyes. They have a cutaneous respiratory system and live in ponds and streams, feeding off the blood of vertebrates and especially mammals. There are sea and land leeches (the latter live in tropical rain forests). In infested waters, man can be bitten during the summer months [20].

With its bite, the leech injects an anticoagulant, hirudin, together with other antigenic substances whose nature is still unknown. In non sensitised subjects, the wound bleeds and heals slowly. In allergic subjects, the onset of urticarial, blistering or necrotic and even anaphylactic reactions may be observed [21]. Contact sensitisation is only exceptionally observed [22].

In some Middle Eastern and Oriental countries, leeches are shown off in large glass containers for sale in the market for medicinal purposes. They must not be forcibly detached from the skin as the jaw may remain in the wound; removal from the host is favoured by the application of heat (lighting a match under it), alcohol, strong vinegar, or saturated salt solutions [23].

Modern medicine has reinstated the use of leeches for some particular indications in microsurgery and plastic surgery, to prevent venous congestion and thrombosis of skin flaps [24, 25], and also for the drainage of large haematomas. Although many species of leeches are used, the most popular is the medicinal leech *Hirudo medicinalis*, whose largest members can reach about 12 cm when fully extended. Unfortunately, the use of leeches poses a risk of introducing wound infection, most often by *Aeromonas hydrophila*, a Gram-negative rod; occasionally, other microorganisms are involved (*Vibrio fluvialis*, *Serratia marcescens*) [26–30]. *Aeromonas* belongs to the normal gut flora of the leech: in fact, it is thought to be essential for

the leech to digest a blood meal, since proteolytic enzymes are virtually absent from the leech gut. Many plastic surgeons who use leeches administer antibiotic prophylaxis against wound infection. Multiple pseudolymphomas have occurred following the application of leeches to the legs [31].

9.3 Dermatitis from Polychaetes

Polychaetae (which means "many bristles") annelid worms are metameric, covered in bristles, and have a cylindrical body. Their segments form many somites or body units, each equipped with paddle-like appendages, or parapodia, that are covered with setae. Tentacles extend out from the region of the head. There are two major groups of Polychaetes: Errantia, that are free-moving animals, and Sedentaria, that live in burrows. The toxic species belong to the errant group.

There are estimated to be over 6200 species of these worms, present in all the seas, from the tidal zones up to depths of 5000 m. They burrow in the mud, corals, palings or under rocks. Few species live in the open sea. Most of these worms are 5–10 cm long, although different species range from only 2 mm to the giant Australian kind, that can measure 1 m or more. Many Polychaetes are extremely beautiful, being iridescent and red, pink or green or a combination of various colours. The Polychaeta venom apparatus includes bristles and jaws. The members of the *Chloeia*, *Eurythoe* and *Hermodice* species have mordant chitinous bristles projecting out of the parapodia.

When Polychaetes are at rest, the bristles are retracted and appear very short but when they are alarmed, the bristles are rapidly extended and the worm takes on the appearance of a bristly mass. The *Glycera* genus has a long extensible proboscis, equipped with fangs connected to toxin-secreting glands, and can inflict painful bites [32].

9.3.1 Reactions to Polychaetes

The best known toxic species are *Chloeia flava* (present on the coasts of Malaysia), *C. viridis* (the Caribbean), *Eurythoe complanata* (Mexico and the tropical Pacific), *Glycera dibranchiata* (the east coasts of the United States and Canada), *Eunice aphroditois* (tropical seas), *Hermodice carunculata* (the Gulf of Mexico) (Fig. 9.2).

In the Mediterranean, *H. carunculata* (the "dogworm") and *Aphrodite aculeata* (the "sea mouse") are widespread. The former is especially abundant in the Aegean and the seas around Sicily; its habitat is hard, dark substrates (grottoes, rocks, wrecks). It has an elongated body, of variable length and size, with setae at the sides of each metamere. Penetration of the setae into the skin causes intense, pruriginous and painful erythema and oedema, and loss of sensation of the affected part. The symptoms last for hours [33].

When a joint is involved, the onset of painful hydrarthrosis may arise, with diminished function. Unless the bristles are immediately removed (using a sticking plaster), they may be expelled through the development of a granulomatous or purulent inflammation.

Fig. 9.2 *Hermodice carunculata* (dogworm) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

The purely mechanical effect of the setae may be associated with a toxic action mediated by as yet unidentified biotoxins. These induce anaphylactic reactions affecting cardiac and respiratory function, above all, as observed in two professional scuba divers that accidentally came in contact with a dog worm, 8 miles to the east of Lampedusa [34].

The bristles of the sea mouse, that has a stout, virtually elliptic shape, have a similar action but sea mice prefer sandy and muddy sea bottoms with a downward slope.

9.3.2 Contact Dermatitis from Bait

Fishermen using lines, "Sunday" and leisure time fishing enthusiasts may, albeit rarely, present a peculiar contact dermatitis. We have observed one such case [35]. A 32-year-old civil servant and line-fishing enthusiast developed contact dermatitis of the fingers of the hands, that recurred for two consecutive years, lasting from June to September, the months when he could indulge his hobby most frequently. The affliction involved the fingertips, proximal nail folds and nails and manifested as desquamation, ragades and onycholysis (Fig. 9.3). The patient was in no doubt about the cause of the dermatitis, that was very painful: it was provoked by a sea

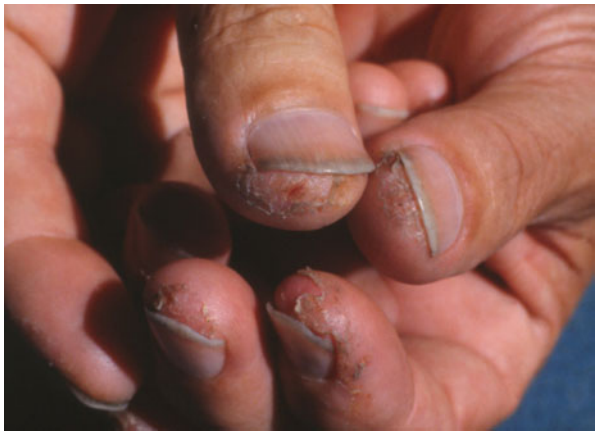

Fig. 9.3 Contact dermatitis to bait. Hypercheratosis and ragades of the fingertips with onycholysis

Fig. 9.4 *Nereis diversicolor*. Fishing bait on sale

worm used as bait. Each time, the onset of the affliction occurred 10–24 h after contact with this bait and regressed when he stopped using it. He had no problems when using other bait (shrimps).

The incriminated worm was *Nereis diversicolor* (sea Scolopendra), an annelid of the Polychaeta class that is very common in the North Sea, the Channel and the Mediterranean. The *Nereis* bait came from Normandy and is also sold in Italy in shops selling fishing articles, under the name "Saltarello Coreano" (it is widely cultivated in Korea) (Fig. 9.4).

Contact dermatitis brought on by bait is very rare and has been observed up to now only on the Mediterranean coasts. Some French authors reported 3 cases

Fig. 9.5 *Bernardo* hermit crab (paguro) and *Calliactis parasitica* (sea anemone) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Fig. 9.6 Threading the bait on the hook. The coelomic liquid of the annelid worm segment impregnating the fisherman's fingers induces dermatitis

induced by *N. diversicolor*, by a crustacean of the Paguridae genus (the hermit crab) (Fig. 9.5) and by a lugworm, respectively [36–38]. The first of the 3 cases was dubbed "escavenite" [36]. Other cases have been observed on the Ligurian Riviera [39] and in Spain [40], caused by *N. diversicolor* and *Lumbriconereis impatiens*.

While hooking fragments of the bait, the coelomic liquid impregnates the distal portion of the fisherman's fingers causing the above clinical picture (Fig. 9.6). This affliction is commonly considered to be a form of protein contact dermatitis, similar

to that provoked by some foods or other substances. Nereistoxin, a tertiary amine with a cyclic disulphate structure exerting a powerful insecticide action, has been isolated from some species of annelid Polychaetes [4, 5].

9.4 Dermatitis from Nematodes

The Nematoda phylum, of non segmented round worms, includes about 12,000 species that are widespread throughout the world. Most of these species live in damp soil and fresh or saltwater, while some are parasites of animals and plants. They vary in size from 0.05 to about 1 mm, but are mostly between 0.1 and 0.2 mm.

9.4.1 Larva Migrans Cutanea

In man, larva migrans cutanea (or "creeping eruption"), a dermatosis induced by the migration of parasites through the skin, is caused by nematode larvae, including the *Ancylostoma brasiliense* species. *Ancylostoma caninum*, the dog parasite, *Uncinaria stenocephala*, the European variant of the same worm, and *Bumostomum phlebotomum*, a bovine parasite, are more rarely implicated. This dermatosis can exceptionally be induced by other worms such as *Anatrichosoma cutaneum*, *Necator americanus*, *Dirofilaria repens*, *Spirometra miathostoma*, *Loa loa*, *A. duodenale*, *Strongyloides stercoralis* and *Gnathostoma hispidum* [41–43].

These Nematodes are natural parasites of dogs, cats and some wild animals. The affliction is most commonly observed in tropical and subtropical areas, particularly West, East and South Africa, Central America and southern parts of the United States. In Europe and in temperate zones in general, autochthonous cases of creeping eruption are less frequent [44–48], although in these zones it is possible to observe imported cases in subjects who have stayed in regions where the disease is endemic [49]. Of the 12 cases observed in our department only one was imported, seen in a nun who had been in Kenya (Fig. 9.7).

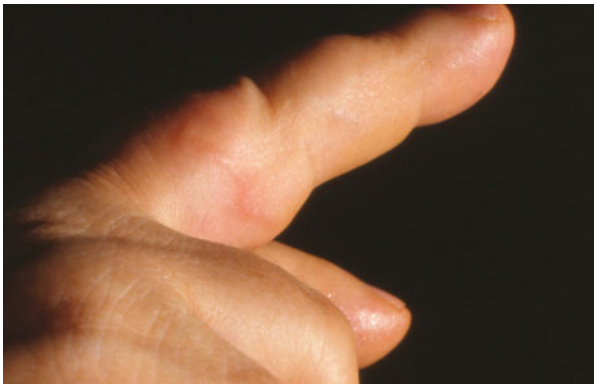

Fig. 9.7 Larva migrans cutanea

The parasite lodges in the bowel of the host animal. The fertilized eggs expelled with the animal faeces develop into embryos and thence into the various larva stages up to the infesting stage (strongyle or III stage larva). The latter enter the animal through the hair follicles or continuous skin solutions and travel in the circulation to the lungs, bronchi and trachea, and to the intestinal tract when swallowed.

Man can become part of the life cycle as a temporary host. The larvae are unable to penetrate beyond the derma, probably because they lack the necessary enzymes [50]. Hence, in man the larvae migrate within the epidermis or between the derma and the epidermis [51, 52]. In these areas, progression of the larvae varies from a few mm to some cm per day. The larvae migrate for biological purposes, since they need to reach the host intestine where the second phase of the life cycle will terminate and the parasites reach adulthood. Migration of a single larva is therefore limited in time; most die within a month, although a longer survival is possible (more than 6 months).

There are also cases of "larva currens" induced by larvae of *S. stercoralis* (which, from the rectum, then penetrate the skin), in which the speed of progression is 10 cm per day [53]. The skin sites most commonly affected are those which come in contact with the earth, i.e. the feet, hands and buttocks. Localization in the oral mucosa has also been reported [54]. Damp and sandy terrain, contaminated by the faeces of cats and dogs, is the ideal environment for maturation of the eggs and survival of the larvae. This disease most commonly affects bathers, agricultural workers, gardeners and sewage-farm workers.

The incubation time varies and may be as long as a few months. In most cases, 24–48 h after penetration of the larvae, the entry site shows an erythemato-papular lesion with one or more tunnel-like formations radiating out from it. The linear lesion is about 2–4 mm wide, of a variably intense reddish colour, and only slightly raised in comparison with the surrounding skin (Figs. 9.8, 9.9, 9.10, 9.11, 9.12 and 9.13). Itching, pain and pustular lesions are sometimes also present [55, 56].

The affliction is self-healing. The larvae stay in the skin for a time ranging from 10 days to 55 weeks, as reported in a review of 96 cases of creeping eruption [57]. Some larvae can also remain quiescent for a while before resuming their migration process [58].

Histological findings are generally aspecific, and the larvae are very difficult to isolate because they progress and are very often situated beyond the visible lesion. The derma shows an aspecific inflammation and the presence of eosinophils. An increase in circulating IgE can sometimes be demonstrated, together with a greater or lesser degree of eosinophilia [59]. Some cases featuring an eosinophilic pulmonary infiltrate (Loeffler's syndrome) have been observed [60] and one case of papulous eosinophilic folliculitis [61]. Immunological investigations to search for specific IgG in the patient's serum have now become an important diagnostic tool [48–54, 57–62].

Cryotherapy with liquid nitrogen or carbon dioxide snow is usually efficacious in very mild infestations, but it must be performed over a fairly wide zone beyond the site of progression apparent from the visible lesion. Good results are obtained using a 10–15 % suspension of topical thiabendazole (an imidazolic worm-killer)

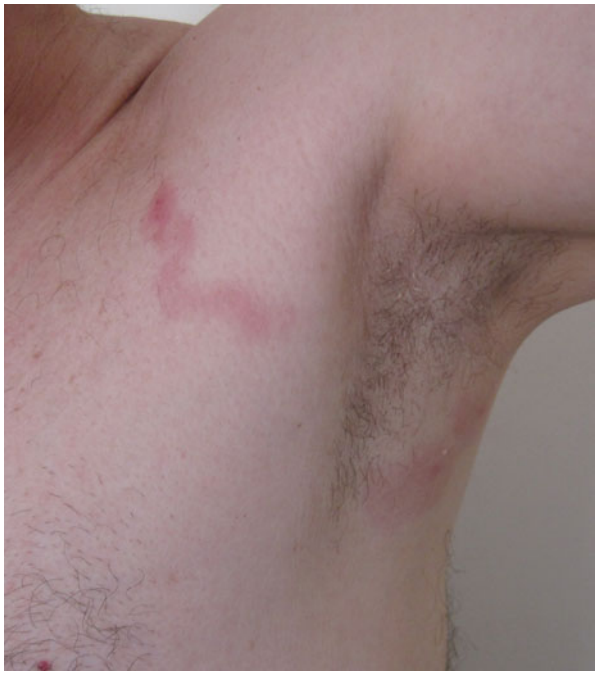

Fig. 9.8 Larva migrans cutanea

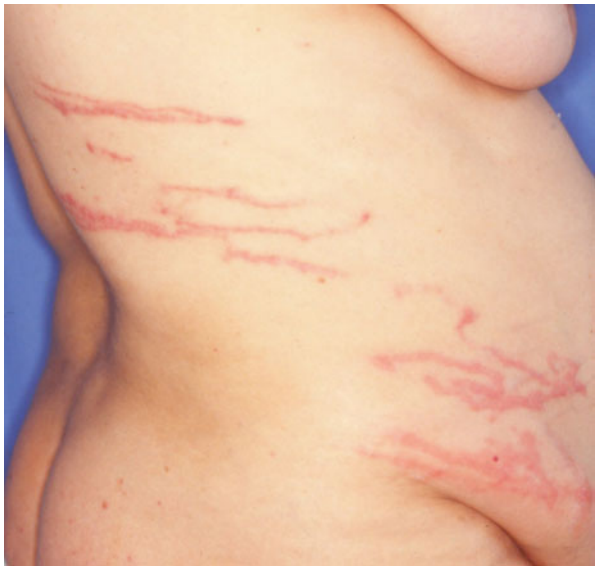

Fig. 9.9 Larva migrans cutanea

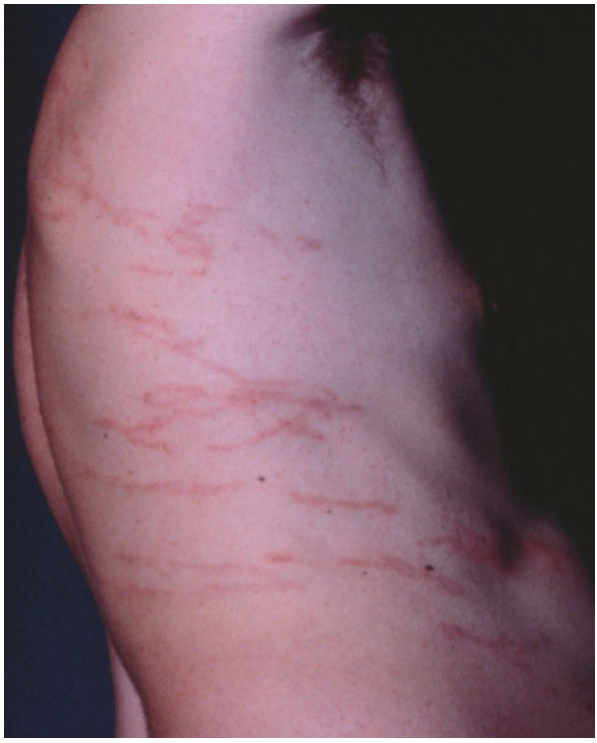

Fig. 9.10 Larva migrans cutanea

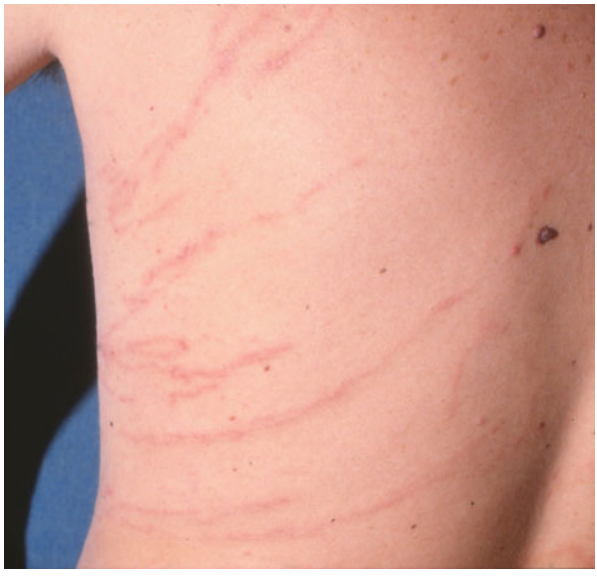

Fig. 9.11 Larva migrans cutanea

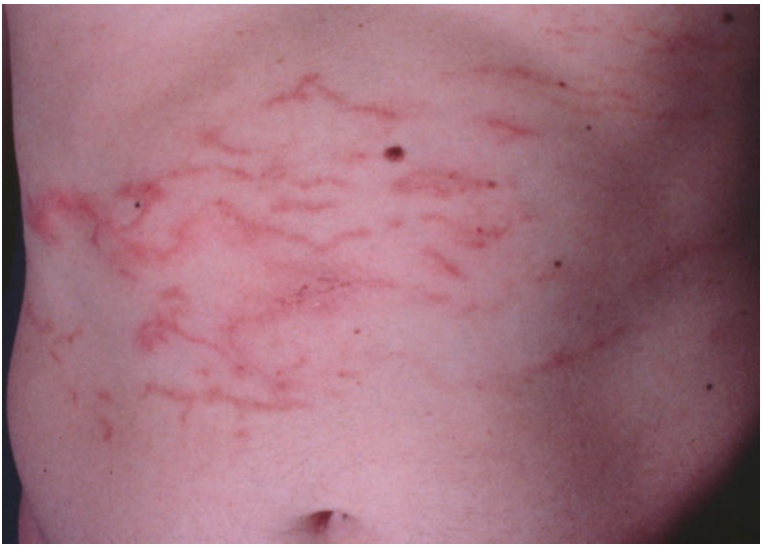

Fig. 9.12 Larva migrans cutanea (Reproduced with permission from Bonamonte and Angelini [56])

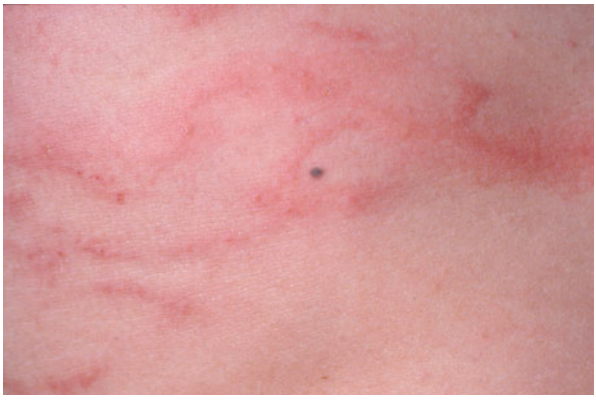

Fig. 9.13 Larva migrans cutanea

in eucerine, three times a day for at least 15 days, or a 2 % suspension in dimethylsulphoxide [59]. Slight scarification of the lesions and the application of thiabendazole and occlusive bandaging can enhance the efficacy of the treatment. Thiabendazole can also be taken orally, especially in cases with diffuse manifestations due to the frequent side-effects (nausea, vomiting, vertigo), at doses of 15–25 mg/kg/die for 7–10 days [50, 63]. Albendazole at doses of 400 mg/die for 3–5 days is a valid alternative. The latter drug can also be administered in a single dose (400 mg), although this is not always successful [64–67]. Another treatment option is a single dose of 12 mg of ivermectin, that heals the affliction in 80–100 % of cases [68].

9.4.2 Onchocerciasis

Onchocerchosis, or onchocerciasis ("river blindness"), is an infection induced by *Onchocerca volvulus*, a filament-like nematode that is a parasite only of man and the gorilla. The adult worms live in the derma and subcutaneous tissue; some are free while others collect in masses surrounded by a fibrous capsule (onchocercomata). The disease is transmitted by female Diptera of the *Simulium* genus (black fly), that deposit their eggs on plants and rocks washed with rapid-flowing water (streams, rivers, waterfalls). Mobile larvae hatch from these eggs and live in the running water, transforming into adult insects. Simuliidae are infected when they sting a parasitized individual and then pass the larvae on to another host, again through the sting mechanism.

Onchocercosis is a major parasitic disease affecting more than 40 million people, particularly in sub-Saharan Africa (Senegal, the Congo), Saudi Arabia, Yemen and Central and Southern America (Mexico, Guatemala, Venezuela, Colombia and Brazil).

The organs affected are the skin and eyes [69–85]. Skin manifestations start with intense, widespread itching, that can persist for a long time, caused by the migration of the microfilariae and lysis of the adult worms. After an incubation period of 3–36 months, an acute, pruriginous erythemato-papulous exanthema appears (with lesions 1–3 mm diameter) in various sites: the trunk and lower limbs in the African form, lower limbs in Saudi Arabia and Yemen, the head and chest in the American form. A chronic phase of diffuse lichenification follows, which may take on a hypertrophic and verrucous appearance. In a further phase, onchodermatitis present with hypotrophy or atrophy and hypo- and achromic lesions, producing the typical "leopard skin" picture. This delayed skin complaint manifests with onchocercomata, single or multiple nodular lesions generally between 2 and 5 cm in diameter, that are movable against the underlying skin layer but do not evolve into ulcers or suppuration. Chronic lymphatic obstruction of the inguinal lymphnodes can lead to hanging grain and elephantiasis of the genitalia [77]. In Central America, heavily infected young patients may develop erythema of face or upper trunk ("erysipelas de la costa"). Older patients may present purplish papules or plaques ("mal morado") which can lead to leonine facies. Ocular lesions (conjunctivitis, irreversible keratitis, uveitis, iridocyclitis, chorioretinitis, optic atrophy and glaucoma, blindness) are observed in cases with involvement of the head after long-standing infection (10–15 years).

Massive lymphadenopathy is also possible. Laboratory findings reveal eosinophilia, increased total IgE and ESR. Histological investigations demonstrate microfilariae lying lengthwise or winding through the papillary and superficial derma among the collagen fibres. Microfilariae can also be seen in the epidermis and above all in the onchocercomata, where adult worms are also present. Among the recommended immunological tests, it is important to search for direct antibodies to the specific antigen OV-16: these are present in the circulation before the microfilariae in the derma become apparent.

The diagnosis of onchocerciasis is not difficult in endemic areas, but requires microscopic visualization of microfilariae as they emerge from a skin sample (skin

snip) placed in saline. The Mazzotti reaction is an acute hypersensitive reaction to rapidly dying microfilariae within the skin and is elicited by oral administration of diethylcarbamazine. In the past, this reaction was used as a provocation test in cases of absence of microfilariae in skin samples.

Early lesions of onchocercal dermatitis must be differentiated from insect bites, scabies and contact eczema. The chronic lesions must be distinguished from chronic eczema with post-inflammatory pigmentary changes, leprosy and leukoderma of scleroderma. The differential diagnosis of elephantiasis is with other forms of filarial infestation; a false-positive skin sample can be obtained if the tissue is contaminated with blood filariae, in particular *Mansonella perstans* and *Loa loa*.

Treatment has drastically improved since the advent of oral ivermectin. It is effective in rapidly killing microfilariae and in preventing their escape from gravid females. Ivermectin causes few or no adverse reactions or Mazzotti reactions, while older drugs, such as diethylcarbamazine and suramin, were associated with severe hypersensitivity or toxic reactions. It is administered at a dose of 150 μg/kg per os. Usually, with this treatment microfilariae disappear from the skin within 1 week and from the eye within 3 months. Multiple doses of ivermectin kill adult forms. Nodulectomy and extraction of adult worms from onchocercomata of the head is a popular treatment in countries where these lesions are common; removal of head nodules reduces the risk of ocular disease. *Bacillus thuringiensis israelensis* H14 (NTI) is used in Africa to destroy the aquatic stages of *Simulium* black flies: this method has succeeded in reducing the disease transmission.

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Dermatitis Caused by Fish

10

Domenico Bonamonte, Angela Filoni, Pietro Verni, and Gianni Angelini

There are more than 500 species of vertebrate fish that are poisonous to man, while another 250 species have venomous organs or apparatus that can cause very painful, sometimes fatal wounds. Both poisonous (cryptotoxic) and venomous (fanerotoxic) (from the Greek *fanerós*=clear, evident) fish pose a serious economic and social problem, as the former are a handicap to the full exploitation of marine resources, while the spines and venomous sting apparatus of the latter are a danger to bathers, fishermen and all people engaged in water activities. The problem is aggravated by the fact that even on the rare occasions when the biotoxin can be identified, there are no known remedies able to neutralize the poisoning symptoms.

10.1 Actively Toxic Fish

Venomous fish have specialized organs, a venomous apparatus or glandular structures that can secrete toxic substances. These can be inoculated by means of a sting or a bite, and are intended to paralyse the prey. Man can inadvertently become the victim of these animals either in the water (mainly as a result of a defensive reaction and only very rarely of a direct attack) or outside, due to wrong handling of these fish [1–9].

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Table 10.1 Fish with toxic characteristics present in the Mediterranean Sea

1. Class: **Chondrychthyes** (cartilaginous fish)	
Order: Batoidea or Rajiforme (stingrays or trygonidae)	
A. Family: Dasyatidae	
Species:	***Dasyatis pastinaca*** (common stingray)
	Dasyatis violacea (purple stingray)
	Dasyatis centroura (thorny stingray)
B. Family: Myliobatidae	
2. Class: **Osteichthyes** (bony fish)	
A. Family: Trachinidae (weeverfish)	
Species:	***Trachinus araneus*** (weeverfish)
	Trachinus vipera (lesser weeverfish)
	Trachinus draco (greater weeverfish)
	Trachinus radiatus (radial weeverfish)
B. Family: Scorpaenidae (scorpionfish)	
Species:	***Scorpaena porcus*** (black sea pig)
	Scorpaena scrofa (large or red scorpionfish)
	Scorpaena ustulata (small scorpionfish)
	Scorpaena dactyloptera (seabottom scorpionfish)
C. Family: Muraenidae (moray eels)	
Species:	***Muraena helena***

Fig. 10.1 *Scorpaena notata* (scorpionfish) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

There are various species of venomous fish, belonging to two classes, those with a cartilaginous structure, the Chondrichthyes, and those with a bony skeleton, the Osteichthyes (Table. 10.1, Fig. 10.1) [1–14].

10.1.1 The Chondrichthyes Class

The Chondrichthyes (whose skeleton is cartilaginous) are one of the largest and most important groups of toxic marine organisms (second only to the Coelenterates in terms of the number of cases of human poisoning inflicted by their venoms). They are known by the generic name of stingrays, and have a flat

Fig. 10.2 Caudal spine of a stingray (Courtesy of Prof. Vidal Haddad Jr, Departement of Dermatology, Botucatu, University of São Paulo, Brazil)

body of rhomboid or trigonal shape (hence their other name trygonidae) and a long, whip-like tail with one or more sharp spines on the dorsal surface (Fig. 10.2). It has been estimated that upwards of 1,500 to 2,000 stingray attacks may occur per year in the United States alone. Most rays are seawater animals and only one family, the Potamotrygonidae (with about 20 species), lives in torrents or rivers in South America, Equatorial Africa and Laos. There are 6 different families of marine rays.

They are common inhabitants of tropical, subtropical and temperate seas, and vary greatly in size, ranging from 6 cm to 6 m or even more. They generally live on sandy or muddy bottoms, rarely deeper than 35 m, and have no migratory habit. Thanks to their flat bodies, rays pass long periods of time in shallow waters, burrowing half-hidden under a thin layer of sand with only their eyes protruding.

The venomous apparatus consists of a caudal, conical spine (one up to four) situated in the proximal part of the tail. It is saw-shaped and of a length ranging from 4 to 6 cm in Mediterranean species to over 40 cm in tropical species. The epithelium of the spine has a rich content of glandular structures and ducts that serve to secrete and inoculate the toxic substances. The caudal spine is caducous: after the formation of a new spine, the old spine is shed when the new one has grown to the same length. There are four different types of venomous apparatus; the above-described one belongs to the *Dasyatis* species and is notoriously the most dangerous. The spine is made of a hard material similar to bone, called vaodentine.

Most stingray injuries occur when bathers, waders, or fishermen accidentally step on the body of the ray as it lies partially covered by sand in shallow waters: pressure in this zone triggers a defensive mechanism whereby the fish arches its tail and projects the spine violently against the foot or ankle (Fig. 10.3). Exceptionally, if the victim is lying in the sand, the spine may strike the chest and in this case the wound can be fatal. Stingray wounds feature a laceration or puncture of variable depth; on penetration of the skin the toxic substances are released into the underlying tissue (Fig. 10.4). The damage is thus both mechanical and chemical. The venom, contained in two ventrolateral grooves on the underside of the spine and produced by holocrine glandular cells, consists mainly of protein structures with a

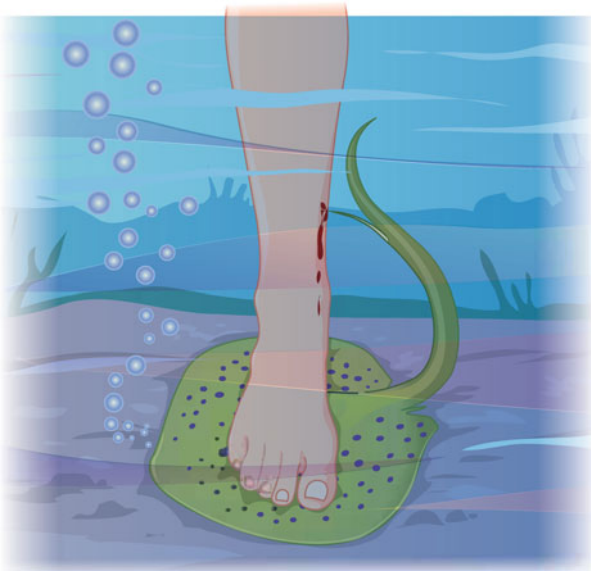

Fig. 10.3 Treading on the body of the ray causes violent projection of the spine against the victim's leg

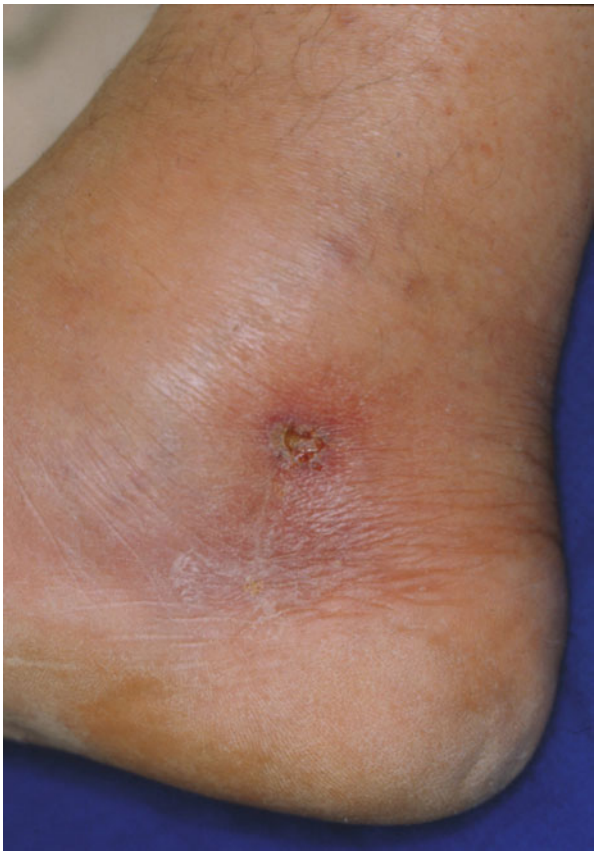

Fig. 10.4 Wound from stingray spine

high molecular weight. The pure extract contains serotonin, 5-nucleotidase and phosphodiesterase. The venom acts on the cardiovascular system (inducing vasodilation or vasoconstriction according to the concentration, atrioventricular blockage, cardiac arrest), the respiratory tract (depressing the respiratory centres) and the neurological system (bringing on convulsions).

Wounds inflicted by rays, unlike those caused by other venomous fish, are very wide and have jagged edges that sometimes need surgical treatment: a spine 4–5 cm long can inflict a wound 20–25 cm long. At the site of the lesion, an initial vasoconstriction is followed by intense erythema and in severe cases by perifocal necrosis. Local pain is generally immediate or develops within 10 min of the attack. It is disproportionately severe in comparison with the size of the wound, variously described as acute, throbbing or piercing, and can last 1–2 days. There may be a number of general symptoms (hypotension, sweating, vomiting, diarrhoea, tachycardia, muscular paralysis), that in very severe cases can even be fatal [15–21].

The best known, notoriously dangerous rays of the Dasyatidae family include the *Dasyatis brevicaudata* species (the largest ray in the world, that can attain a length of 4.5 m or more, a width of 2.2 m and weigh over 325 kg; many fatal inflictions have been attributed to this ray, that lives in the Indo-Pacific region), *D. dipterurus* (the most common ray in Central America, that is about 2 m long), *D. pastinaca* (the European ray, or "pastinaca marina", that is common in the Mediterranean, the northeast coasts of the Atlantic and the Indian Ocean, and can attain 2.5 m in length) and *D. americana* (that is about 2 m long and lives along the western coasts of the Atlantic).

Freshwater stingrays belong to a large group of predominantly marine elasmobranchs. There are about 20 species of potamotrygonids, that are commonly found resting on sandy or muddy bottoms in the shallow waters of some of the major rivers in South America, like the Atrato and the Magdalena in Colombia, the Orinoco and the Maracaibo in Venezuela, and the Amazon, the Paraná and the Paraguay in Brazil and Argentina [19]. They are also present in some rivers in Equotorial Africa (the Orinoco) and in Southeast Asia (the Mekong of Laos). These stingrays, that can reach a diameter of 1 m and weight of 30 kg, are equipped with one or more stings at the base of their tails, that are also covered by an epithelium with many glandular cells producing venom. In various areas in Brazil, accidents with freshwater stingrays are greatly to be feared because they are often associated with vast processes of cutaneous necrosis (due to the large quantities of hyalorunidases in their venoms), a high incidence of bacterial infections (caused by *Pseudomonas* species and S*taphylococcus* species), and induce a temporary or permanent physical incapacity [19, 22, 23]. Victims of such accidents include fishermen, who may inadvertently capture the animal in their fishing gear and bathers, especially during the dry season when the sand banks along the rivers under which they burrow are exposed, and offer a playground to the communities living nearby. Because freshwater stingrays are imported in Europe, Japan and the United States, aquarists can also fall victims to accidents with stingrays [24].

Fig. 10.5 *Trachinus radiatus* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

10.1.2 The Osteichthyes Class

10.1.2.1 The Trachinidae Family

Trachinidae, or weeverfish (Fig. 10.5), are relatively small fish (from *Trachinus vipera*, at about 10–12 cm to *T. draco* at 40–50 cm) of the Teleostei family, present along all the Mediterranean coasts and the North-East Atlantic (European coasts). All the species have spines on various parts of the body linked to cells that secrete a venom similar to snake-venom. The Latin name derives from the Greek *traknos* (stinging). In Italy these fish are also known as "pesce ragno" ("spider fish").

Weeverfish are among the most dangerous venomous fishes in temperate zones, and live in shallow waters or on the shore, half-buried in the sand with only the dorsal spines exposed. They have chameleon-like characteristics and blend with their surroundings. Weeverfish are sluggish and carnivorous and can survive outside water for a time; their spines are venomous even after death.

They have a dual venomous apparatus consisting of two opercular spines and 5–8 dorsal spines. The glandular tissue that secretes the venom is present at the base of the spines, while the excretory tubules terminate on the surface of the spine; the relative orifices are covered with a fine sheath to prevent release of the venom. When threatened, weeverfish blend even further with the background colour and remain immobile, only arching their dorsal spine for defensive purposes.

Accidental contact with a weeverfish is very common along Mediterranean shores, generally due to inadvertently treading on one (Fig. 10.6). Fishermen can

Fig. 10.6 Treading on a weeverfish

also be stung, while they are removing fish from their nets or lines (Figs. 10.7, 10.8, 10.9, 10.10, 10.11, and 10.12), as well as skin divers, since the spines are very strong and can pierce gloves and flippers. The chemical nature of the venom is little known; it has a strong anti-cholinesterase action and toxic activity on various organs, especially the heart. In fact, the rare fatalities are caused by cardiac arrest. Local pain is highly disproportionate, lasts 16–24 h and irradiates around the limb.

There are four known species of weeverfish, among which *T. draco*, that can attain a length of 45 cm, is widespread from Norway down to the Mediterranean and along the coasts of North Africa, and the smaller *T. vipera*, that is 15 cm long, lives in the North Sea and the Mediterranean.

10.1.2.2 The Scorpaenidae Family

Scorpaenidae, or scorpionfish, belong to the most numerous and geographically widespread family of toxic fishes, being present in all the warm and temperate seas on earth and even in the cold Arctic Sea. There are about 80 species with a venomous defensive and offensive apparatus. They are all shallow-water bottom dwellers, and have a short, brilliantly coloured body, very large eyes and mouth and large fins. Some of them can blend perfectly into the surrounding environment.

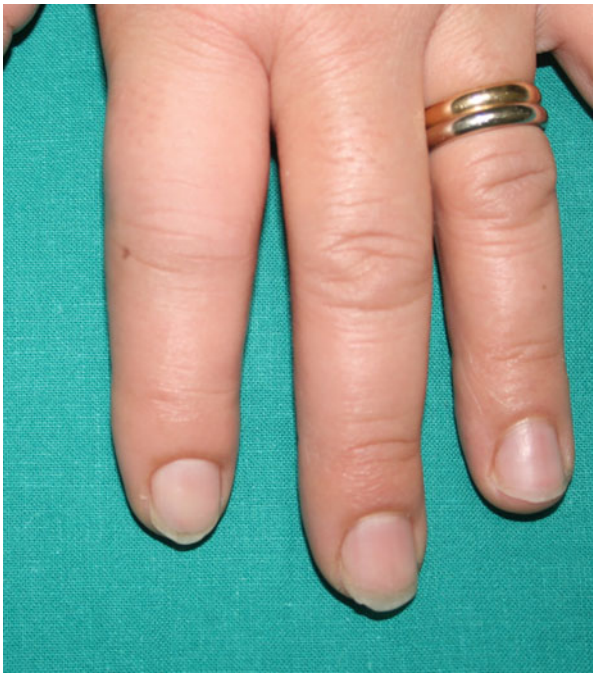

Fig. 10.7 Weeverfish lesion with oedema of the second finger

Toxic Scorpaenidae are subdivided into three groups, according to the shape of the venom organs: scorpionfish (*Scorpaena*), zebrafish (*Pterois*) and stonefish (*Synanceja*).

Scorpionfish live in bays, along sandy beaches, rocky coasts or coral reefs, from the tidal zone down to a depth of about 150 m. About ten different species have been reported to be endemic to the Mediterranean, the most frequently encountered being *Scorpaena porcus* (Fig. 10.13), a dark coloured fish about 20–30 cm long and *S. scrofa* (Fig. 10.14), that has a typical pink skin and attains a maximum length of 50 cm. Other species known to be particularly toxic include *Apistus carinatus* (this species is about 16 cm long and is common along the coasts of India, Indonesia, the Philippines, China, Japan and Australia), *S. guttata* (common along the Californian coasts) [25], *S. plumieri* (present on the Atlantic coast from Massachusetts to Brazil) and *S. mystes* (that lives along the coasts from Mexico to Peru).

The venom apparatus of these species consists of short, thick spines: 12 dorsal, 3 anal and 2 pelvic. The glandular tissue and tubular secretion structures are situated within the grooves of these spines. The tubular orifices again lie near the points of the spines and are enveloped in a thin sheath. The membrane ruptures on contact, enabling inoculation of the venom, a heat-labile protein compound with a high molecular weight and a serotonin-like effect.

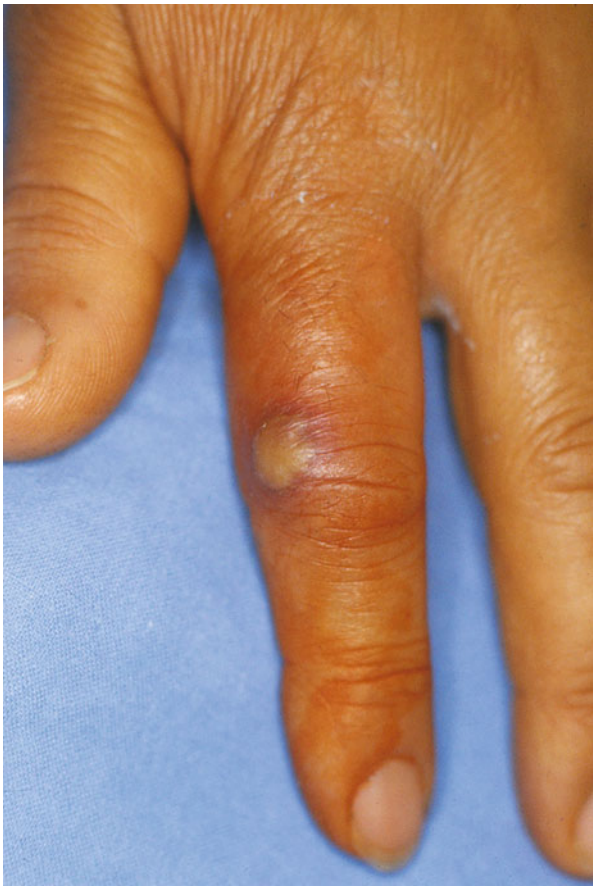

Fig. 10.8 Weeverfish lesion

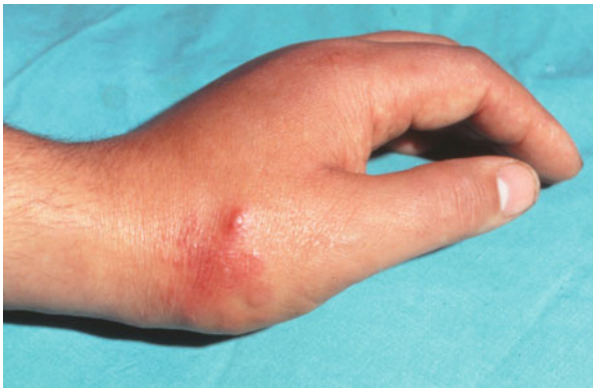

Fig. 10.9 Weeverfish lesion (Reproduced with permission from Bonamonte and Angelini [9])

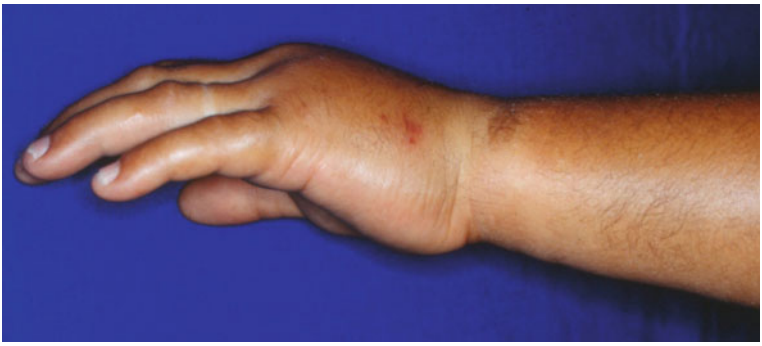

Fig. 10.10 Weeverfish lesion with intense oedema of the arm

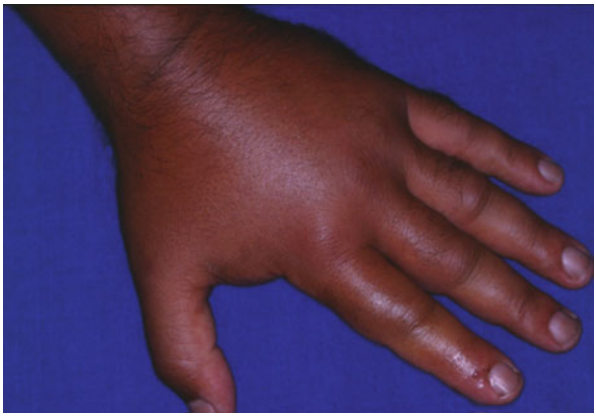

Fig. 10.11 Weeverfish lesion with intense oedema of the hand

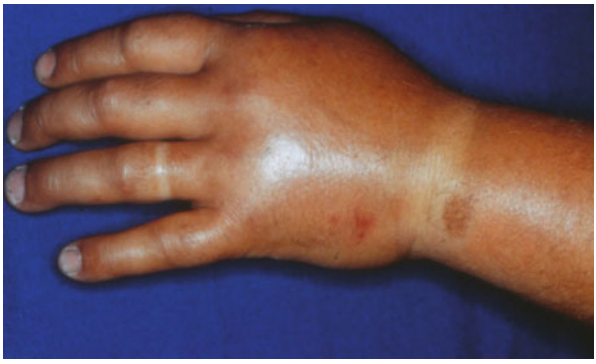

Fig. 10.12 Weeverfish lesion with intense oedema of the hand (Reproduced with permission from Bonamonte and Angelini [8])

Fig. 10.13 *Scorpaena porcus* (black scorpionfish) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Fig. 10.14 *Scorpaena scrofa* (red scorpionfish) (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

Scorpionfish spend long periods of time on the sea bottom, preferring rocky, irregular bottoms. Human contact with scorpionfish is generally accidental during fishing expeditions by boat or underwater, especially during harvesting procedures.

Scorpaenidae of the *Pterois* group (zebrafish), present in the Pacific, from the east coast of Africa to India, the Philippines and Australia, are among the most beautiful fish in existence. They have very long, feathery pectoral fins and lacy dorsal fins. As they swim, they wave their fins gently and look like birds in flight. They appear innocuous and inviting but one must resist the temptation to touch them: hidden under the lacy and feather-like fins are the slender venom spines. The venom apparatus is similar in shape and location to that of scorpionfish. The best known species are *Brachirus zebra* (that are 12 cm long and live in regions of the Indian and Pacific Oceans), *Pterois antennata* (30 cm long, present in the Indian and Pacific Oceans) and *P. volitans* (one of the most beautiful, spectacular fish among the coral reefs, to be admired from a distance: beware of contact!). Stings by lionfish, beautiful animals

that are very popular for saltwater aquariums, are starting to become common among aquarium enthusiasts. However, their harmful effects are very modest [26].

Scorpaenidae of the *Synanceja* type (stonefish) are commonly found in tidal pools and shoal reefs, lying motionless among the corals, under rocks or hidden in the sand or mud. They appear entirely unconcerned by careless human intrusions. They have the same number of spines in the same sites as the other Scorpaenidae, but these are short and thick and the venom apparatus is highly developed. Most of these species are widespread in Australia (*Inimicus barbatus*, 20 cm long), Japan (*I. japonicus*, 20 cm long), Indian and Pacific Oceans (*Chloridactylus multibarbis*, 10 cm long; *Synanceja horrida*, an extremely dangerous fish about 60 cm long; *S. verrucosa*, 30 cm long, also present in the Red Sea).

Stings from Scorpaenidae, whatever the species or type, cause such fierce, anguishing pain that the victim may lose consciousness. The general symptoms are much more serious after stings by the *Pterois* and above all the *Synanceja* species than from *Scorpaena*, but stings by the latter type are more frequent. Some fatal cases of stings by this genus have been reported.

10.1.2.3 The Muraenidae Family

There is still debate as to the toxicity of the Muraenida family, and especially the most widespread species in the Atlantic Ocean and Mediterranean, *Muraena helena* (Fig. 10.15). Moray eels have a long, cylindrical body flattened posteriorly, and a small head with a wide buccal aperture. They usually live on rocky sea bottoms at depths of more than 15 m. They have no spines on their bodies but their powerful jaws are equipped with a row of sharp, strong teeth, unconnected with glandular or secreting substances. The venom is, in fact, produced by unicellular glands lining the dome of the palate and is present only in the blood (haemoichthyotoxin). The

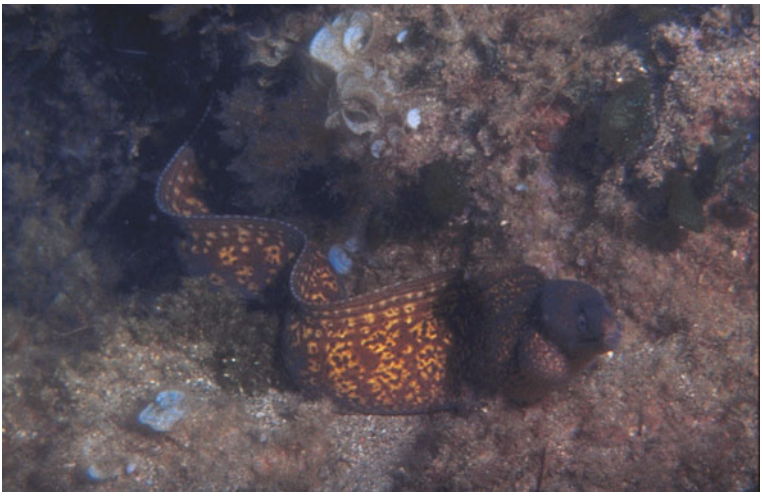

Fig. 10.15 *Muraena helena* (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio G.R.O. Sub, Catania, Italy)

toxin may be injected into the wound inflicted by a bite through contact with toxic saliva or by direct compression against the animal's palate.

The same type of blood toxin is present in all the Eel order, consisting of *Anguilla*, *Muraena* and *Conger*. This ichthyotoxin is a heat-labile protein and is not therefore harmful to man because it is inactivated by cooking. However, one must be careful to avoid lacerating wounds when handling the eel.

The traditional view that moray eels are voracious, vicious animals quick to attack is a myth, and probably derives from their fierce appearance as they repeatedly open their jaws wide in order to breathe. This sight, especially in an animal that has attained 1.5–2 m in length, can cause a diver to panic and thrash about frantically, which can be very dangerous because bigger moray eels tend to nestle inside grottoes and crevices, where the diver's movements should be carefully controlled.

Contact with a moray eel generally occurs while capturing and handling it. Moray eels are very muscular, resistant animals and do not surrender without a strenuous fight. When harpooned, the eel winds around the barrel of the weapon and tries to bite anything within reach. The battle between a fisherman and an eel is particularly difficult because the human has to observe long periods of decompression. A bite from a moray eel, especially a large one that was well-anchored within its lair, sometimes prevents a diver from being able to resurface, resulting in very dangerous, occasionally fatal consequences. Once the eel has been pulled on board the boat, it does not die quickly and so it is necessary to kill it fast to avoid furious bites, particularly as its slimy hide is very slippery.

The local pain from a bite is tearing and intense and may be associated with general symptoms such as breathlessness and collapse. Nevertheless, no fatal cases have been described in the literature.

The venom present in the blood that makes the eel so poisonous and venomous is fairly complex and has not yet been fully identified. It contains proteolytic enzymes (hyaluronidase, substances activating bradyquinines), haemotoxic (with a haemolytic action), neurotoxic and cytotoxic substances with a local action (curaro-like paralysing toxins) and small peptides with a hypotensive action.

10.1.3 Clinical Symptoms

The clinical symptoms of poisoning due to stings or bites from the various actively toxic fish are much the same; the severity of the signs is generally proportional to the type of venom and to the quantity inoculated. In any case, the appearance of the wound is no guide to the severity of the clinical picture.

The pain is instantaneous, constant and extremely fierce. It is worst in the case of weeverfish stings and to a lesser degree, those by rays or scorpionfish, and only slightly less intense after a bite from a moray eel. The pain irradiates around the whole limb within 30 min and persists unabated for 12–48 h. This is generally followed by further intermittent paroxysms. In all cases it is so violent as to provoke malaise, lipothymia and loss of function of the limb. Clearly, all these symptoms can seriously impair the underwater diver's ability to emerge correctly.

The wound generally appears slight and falsely reassuring. The type of wound can help to identify the precise species involved. An extensive, lacerated wound suggests a stingray, and is most frequent on the legs or arches of the feet, whereas a pointed, copiously bleeding wound localized on the feet or hands is likely caused by a weeverfish.

At the moment of the sting or soon after, a severe inflammatory reaction will develop, with ischaemic necrosis, pallor, cyanosis, purpura and blood-blisters. Extensive, hard and painful oedema will then ensue, followed by lymphangitis and later by satellite adenopathy. However, the signs of inflammation are often masked by the tissue ischaemia. Victims may also show purpura and local blood blisters. Gastrointestinal symptoms, headaches and arthralgia are frequently reported [27].

The tearing pain induces anguish, tachycardia, dyspnoea and hypotension. These signs of shock may be very pronounced, and can even lead to syncope and death. Neurological symptoms are sometimes present, with vertigo, paraesthesia, contracture or muscular spasm, convulsions and delirium [26]. Reynaud's phenomenon has also been observed, a few weeks after a sting from a weeverfish, on one finger only, the site of the sting [28].

In the Mediterranean, the evolution is always favourable and the risks are more closely linked to its effect on underwater swimming activities. The most frequent contact is with weeverfish; an encounter with a stingray is less common whereas contacts with scorpionfish are relatively frequent but have a more benign evolution.

10.1.4 Treatment and Prevention

Envenomation by fish is a common, serious problem; in fact, the number of venomous fish is higher than that of venomous reptiles [27]. The clinical manifestations, as well as the treatment, are relatively uniform. Treatment must be immediate and expert, carried out at the site of the accident. The principal aim is to limit the spread of the poison as much as possible. The wound should be washed immediately with sterile saline or warm water, if available, and with seawater, as a last resort [29]. If possible, all accessible fragments of spines are to be extracted, but without lacerating the tissues. If the wound involves a limb, the spread of the poison can be circumscribed by a haemostatic ligature, although this must not block arterial flow and must be released for 90–120 s every 10 min.

Sucking out the poison is not entirely risk-free, even if the poison is largely inactivated by the digestive juices, and in any case is not very efficacious. If available, it is better to use a "poison-aspirator" for this purpose. This is an easy-to-use, painless first-aid kit consisting of a syringe-shaped mini-pump that, in a fraction of a second, can provoke a depression that can extract much of the poison and soothe the pain. As the pump is portable and can be applied to all people, it is an essential item in any first-aid kit. However, in no way can it be considered a substitute for prompt hospital admission for the necessary general and local symptomatic treatment.

To denature and inactivate the venom (which is heat-labile and is destroyed at 50° C), the affected part (generally a limb) should be immersed in water as hot as possible (approximately 42–46° C), to which a disinfectant may be added. Soaking should be continued for 1–2 h or until maximum pain relief is achieved. The pain, however, may peak again after removal of the affected limb from the hot water, probably because the vasodilation caused by the hot water counteracts the vasoconstrictive effect of the venom [27, 30]. The hot soaks may be repeated if the pain returns. Obviously, because the wound or limb may be partially anaesthetized, the person administering the first aid must first test the water temperature. As hot water is not always available on a beach, a useful source of hot water in an emergency may be hot seawater from a motorboat's cooling system. At the site of the event, the general treatment must aim to soothe the pain. Local injections of 1–2 % lidocaine without adrenaline can be given. Longer acting anaesthetics like procaine and bupivacaine can be used to gain a longer period of pain relief. Intravenous calcium gluconate, potent analgesics or morphine, and tranquillizers may be useful. Corticosteroids are useful to relieve the symptoms both of shock and of the poison.

In practice, the administration of antihistamines does not seem to be very effective, while no sensitisation mechanisms seem to be triggered by contact with fish venoms and so no signs of anaphylaxis are observed.

Once in hospital, the wound will be cleaned, incised and debrided to remove spines, and if necessary, surgical sutures will be applied. The patient may need rehydrating, oxygenation and cardio-circulatory intensive care. Analgesic drugs will be administered for a long period. In general, the conditions do not justify the use of heparin.

Antitetanus shots must be given if indicated, and systemic antibiotics are recommended if the wound occurred more than 6 h before or if it is extensive. The choice of antibiotic must take into account the bacteriology of the seawater environment where the accident occurred, and later the results of culture. Antibiotic treatment of infections of wounds received in saltwater should include cover against *Vibrio* species. The most indicated drugs are intravenous ciprofloxacin, imipenem-cilastatin, third-generation cephalosporins, tobramycin, and trimetoprim plus sulfamethoxazole.

Only for severe reactions to stonefish stings in Australia is an antivenom available (produced by the Commonwealth Serum Laboratory, Melbourne, Australia), that must be administered by slow intravenous infusion (one vial for 1–2 spine punctures, two vials for 3–4 spine punctures, three vials for more than four spine punctures) [18].

The only prevention measures are to avoid the temptation to walk barefoot in shallow waters, instead wearing plastic sandals and, above all, a mask, wetsuit and fins for underwater diving. These fish should never be picked up by hand, even if they are lying on the beach or the bottom of the boat, as the spines remain poisonous for many hours after death. There is no danger at the fishmonger's, because there is a legal obligation to remove the spines and stings of venomous fishes before displaying them for sale. But if in any doubt, better safe

than sorry! Instead, owing to the fact that the venom is heat-labile, a meal of these fish can be enjoyed in all safety.

10.1.5 Catfish Stings

Catfish live mainly in freshwater in Eurasia, North and South America, Africa and Australia. They belong to the super-order of Ostariophysia and the order of Siluriformes. Most of these fish (there are 30 families and about 2400 species) live in tropical rivers and streams; some live in temperate zones (Ictaluridae, Siluridae, Diplomistidae, Bagridae), while only two families, Plotosidae and Ariidae, live in the sea [31]. They are called catfish because of the long, fleshy barbels that grow from their snout. There are various shapes and sizes of catfish: in South America, especially in the Andes and Amazon rivers, the species are very tiny (13 mm in Bolivia), whereas in the Amazonas they may attain 3 m.

Some fishes of the Pygidiidae family are "parasites" of bigger catfish, living and depositing their eggs in the gills. These strange fish, present only in South America in the rivers of the Andes, have no scales and are slender, transparent or brownish, ranging in length from 3 mm to 5 cm. They are unusual in having an elective tropism for mammalian urine, including human urine. They swim against the flow of urine and enter the urethra, the vagina and rectum while the mammal is urinating into the water. These fish (called candirú or carnero by the natives of South America) probably mistake the flow of urine for the jet of water expelled from the gills of large catfish. The best known species is *Urinophylus erythrurus*, so-called for its urinotropic tendencies and the fact that it feeds off blood [15, 32].

The venom apparatus of catfish consists of a single, robust cutting spine (sometimes with jagged teeth running along it) in the dorsal and pectoral fins, and axillary venom glands. The most common marine species are *Galeichthys felis* (in the Gulf of Mexico), *Clarias batrachus* (the Indian Ocean) and *Bagre marinus* (North and South America). *Noturus furiosus* is common in the rivers of North Carolina and *N. miurus* is present in the Mississippi.

The pain from a catfish sting is instantaneous and piercing, and may be localized or irradiate around the whole limb. Some tropical fish (*Plotosus*) provoke violent pain that persists for 2 or 3 days. The affected part immediately becomes pallid. This pallor (the venom has a potent vasoconstrictive effect) is followed by cyanosis and then by erythema and oedema; the latter is very severe in some cases and is associated with torpor and gangrene of the damaged zone. Shock may also ensue. Supervening bacterial infection of the wound is a common problem, as is the retention of spine fragments. Some fatal cases of stings from tropical catfish species have been reported. It should also be borne in mind that catfish are common in aquariums and that it is dangerous to handle them [2, 33, 34]. Catfish cause about 80 % of the human injuries occurring in both marine and freshwater environments on the Brazilian coast. Generally speaking, however, these common injuries are much less serious than those induced by scorpionfish and other fish that can be harmful to humans [35].

10.1.6 Soapfish Dermatitis

Among actively toxic fish, some produce toxins in the skin glands to repel attacks. Apart from fish, toxic secretions are also produced by Opistobranch molluscs and, among land animals, by amphibians.

The discovery of toxic skin secretions in fish was made thanks to chance observations of irritations on the hands after touching these fish, and to having seen that other fish die if placed in the same tank. Many tropical fish belonging to various families are toxic. From the *Ostracion lentiginosus* species of the Ostraciontidae family, a toxin called pahutoxin (from the Hawaiian name "pahu", after the species that produces it) has been isolated [36]. This fish is called a boxfish by the Americans (analogously, the Italian name is "pesce cofano"), owing to its box-shaped body. Pahutoxin is a choline ester with β-acetoxypalmital acid and in aqueous solution it foams like saponin. It has a strong haemolytic action on other fish but is not toxic to man, who may, however, develop contact dermatitis.

Ichthyotoxins from the skin secretions of other fish, although chemically unlike pahutoxin, also have a haemolytic action. There are many toxin-secreting fish of the Grammastidae family, known as soapfish because they produce large quantities of foam when they are put in a tank or otherwise disturbed. This toxin, called grammistine, seems to be a mixture of peptides with tertiary or quaternary amine groups. A well known species found in the Virgin Isles and Puerto Rico is *Rypticus saponaceus*, contact with which induces acute dermatitis together with itching and burning sensations.

10.1.7 Fish Equipped with an Electric Apparatus

Electric fish are among the most interesting of the harmful aquatic animals. Many plants and animals give off an electric shock, and there are approximately 250 species of fish equipped with electric organs. Electricity is an essential part of the metabolic activity of living creatures. In most cases, however, the amount of current emitted is so small that it can be detected only by means of highly sensitive instruments. In land animals, the air acts as a good insulator and these small discharges are not therefore usually noticed. Instead, water is an excellent conductor, and aquatic animals and some fish possess specialized organs that discharge electricity through the water at very high voltages.

Only a few fish produce electricity as high as 650 V, such as the electric eel *Electrophorus*; most emit discharges ranging from some millivolts to several volts. High discharges are only emitted in exceptional circumstances as a defence mechanism or to stun their prey, whereas weak discharges are emitted continually as an electrolocation system and for social communication. The electric organs of such fish function through particular cells (electrocytes or electric cells) arranged in series, that are synchronously excited by spinal nerve signals to generate small voltage gradients running in the direction of their linear arrangement. As each stack of electrocytes is hermetically enclosed by insulating tissue, the voltage of

each electrocyte contributes linearly to the whole sum, just like a series of small batteries [37].

The electrolocation process resembles that of a sonar: the animal sounds out the surrounding environment by emitting signals and monitoring their feedback. In this way, such animals can operate in total darkness. The fish generates a current field that is triggered by the anterior part of the body and converges at the tail extremity. An object with a different impedance (opposition in an electric circuit) in the surrounding water distorts the electric field and so alters the model of electric current intensity on the body of the fish. In this way, by monitoring the local variations in electric activity, the fish can perceive the nature of surrounding objects.

The best known and most closely studied aquatic organisms belong to the Electrophoridae and Torpedinidae families. The latter family has only a single species, *Electrophorus electricus*, an eel that inhabits the streams and swamps of South American jungles. It is the most powerful of the electric fishes and can produce electric shocks of up to 650 V, with an average of 40 W, enough to light up an electric bulb. When this current is discharged into the water, it sets up an electric field that is sufficient to stun a man or even a horse. At rest, *Electrophorus* gives off no electricity, but when it is swimming it emits a discharge of about 50 V/s. It can give out a steady series of discharges for 20 min, rest for 5 min and then start again: it can truly be said to be one of the most efficient batteries in the world!

The Torpedinidae family, of the Rajiforme order, includes 30 species. These fish have an oval, flattened body and a large, short and strong robust tail. The kidney-shaped electric organs are arranged dorsally in pairs, one on each side, and can emit current up to 200 V. In emergency situations, torpedo rays give off shocks at a relatively high voltage and amperage. These diminish progressively in power and a rest period is required to restore the starting electric potential. In the past, torpedo rays were used in electrotherapy: the Greeks called these fish “narke” (lethargy), from which the terms narcosis and narcotic are derived. Ancient Roman doctors used torpedo rays to inflict an electric shock on their patients.

Among the best known species, *Narcine brasiliensis* lives inshore along the western Atlantic coast (Florida, Texas, Brazil, Argentina), while *Diplobatis armata* and *Torpedo californica* inhabit the coast of southern California.

Three species of torpedo rays live mostly burrowed in sandy or muddy bottoms at shallow depths in the Mediterranean: *Torpedo torpedo* (Fig. 10.16), *T. marmorata* and *T. nobiliana*. The first two attain a maximum length of 60 cm and live along the coast at depths ranging from a few meters to about 100. The third species is the largest and can attain 1.80 m and a weight of about 70 kg: this is the most dangerous species for man.

Injury occurs by means of direct or indirect contact during capture and handling of the animal. In fact, if a diver touches his metal rod after harpooning a torpedo ray, he will suffer an electric shock that is more or less proportional in power to the size of the animal. The shock is not generally strong enough to cause direct skin or nerve lesions, apart from a slight state of stupor induced by very large animals. The greatest danger to the diver may be abnormal, incorrect emersion due to loss of

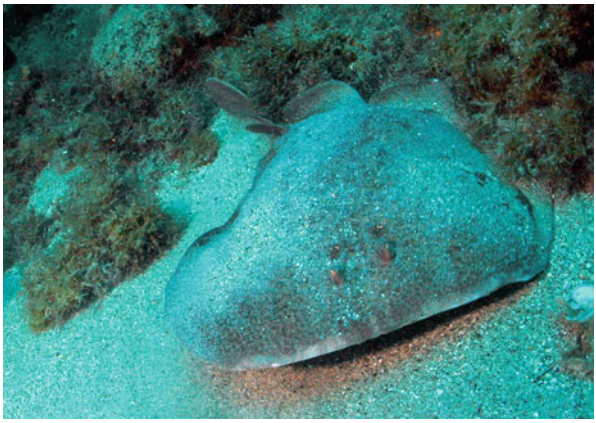

Fig. 10.16 *Torpedo torpedo*. (Courtesy of Drs. Filippo Massari and Fabrizio Frixa, Fotoarchivio)

awareness or panic caused by the unexpected shock occurring in an unfavourable environment.

10.2 Passively Toxic Fish

Poisonous fish are also known as passively toxic fish; in other words, they do not produce toxins for defence or offence purposes but acquire them from the environment where they live. They are not therefore poisonous in themselves but only when eaten. In these cases, the exogenous origin of the toxin has not always been ascertained. Moreover, strangely enough, in the same environmental conditions some species are poisonous while others are not, or else some individuals of the same species may be poisonous and others not; again, species living around a particular island, for instance, may be poisonous whereas others of the same species living near a different island a few miles away may not. In any case, these kinds of fish are known to populate the tropical regions in particular.

10.2.1 Ciguatera Fish Poisoning

The term "ciguatera" seems to derive from the Cuban word "cigua" for a poisonous marine snail (*Livona pica*, the West Indian top-shell), coined by the early Spanish settlers [38]. Ciguatera is now used to refer to a disease resulting from the ingestion of one or more of the 400 species of warm-water, shore or reef fish living in latitudes between 35°N and 35°S, in particular in the South Pacific and Caribbean [39, 40]. There are more than 50,000 cases per year worldwide, having an incidence of up to 2 % of the population. The fish most commonly associated with ciguatera belong to more than 400 species of 57 different families, including Lutjanidae (snappers), Scaridae (parrot fish), Serranidae (groupers), Scombridae (king mackerel),

Muraenidae (moray eels: the most toxic), Sphyraenidae (barracudas), and Carangidae (jacks) [41].

It is now known that the toxins causing ciguatera fish poisoning, the poliether ciguatoxins, maitotoxins and scaritoxins, originate from bentic Dinoflagellates such as *Gambierdiscus toxicus*, that are eaten by herbivorous fish. These, in turn, are the prey of carnivorous fish that, when eaten by man, can induce severe gastrointestinal, neurotoxic and cardiovascular symptoms. Ciguatoxins are concentrated in the bowel, gonads and viscera. It is impossible to predict the acquisition of toxins in fish, nor are there seasonal variations in the prevalence. Ciguatoxins excite Na^+ channels, while maitotoxin activate voltage-independent Ca^{2+} channels [42–46].

Worldwide, the Cook Islands in the Pacific are the zone with the highest incidence of ciguatera [47]. In recent years, however, not only has an increase in the incidence of ciguatera been observed in endemic areas, but also a higher incidence in subtropical regions and a spread of Dinoflagellates in temperate zones, ciguatoxic fish being found on the European coasts and in the Mediterranean [48, 49]. In the last few years there have been at least three ciguatera outbreaks in the Canary Islands, that coincided with new toxin-producing Dinoglagellates of the genus *G. excentricus* and *G. silvae* [50, 51].

In the past, the only endemic zone in the Atlantic Ocean was the Caribbean but recently cases have also been reported along the West African coast (Cameroon, Senegal) [52], in Korea [53] and in China [45]. Also recently, there have been outbreaks in New York due to eating contaminated imported fish (from the Centers for Disease Control and Prevention, 2013) and in Germany [43], where 61 cases were reported between 2000 and 2013, attributed to travel in endemic areas [54].

Ciguateric fish are indistinguishable from non toxic fish, by texture, smell, or taste. Moreover, ciguaterotoxins are indistructible by heating, freezing, or gastric acids, and virtually non perishable after freezing. Intoxication can therefore occur anywhere as a result of eating contaminated imported fish.

The symptoms usually appear within 1–6 h after the ingestion of poisoned fish, although exceptionally the onset may be within a few minutes or after as many as 30 h. The first symptoms are numbness or tingling of the lips, tongue, throat and extremities, a metallic taste and a dry mouth or hypersalivation. In 80 % of patients there is a cold sensation reversal, in which the patient perceives a cold temperature as a hot sensation, and vice versa: this sign is considered pathognomic for ciguatera poison [41]. In many cases, especially of milder poisoning, the first symptoms are gastrointestinal (sudden abdominal colic, nausea, vomiting, and profuse diarrhoea). These are followed at a later stage by myalgia, ataxia, vertigo, visual disturbances and pruritic skin eruptions. The gastrointestinal symptoms resolve within a few hours, whereas paraesthesia and myalgia can persist for weeks, months or even years. Cardiovascular symptoms are uncommon but can be severe (Table 10.2). Ciguatera poisoning after eating moray eels (*Gymnothorax* species) has a particularly rapid and severe onset due to the high concentration of toxins in these animals. Exposure does not confer an immunity.

Table 10.2 Symptoms of ciguatera poisoning

Gastrointestinal	Nausea, vomiting, abdominal pain, profuse watery diarrhoea
Cardiovascular	Bradycardia, hypotension
Neurological	Paraesthesias, vertigo, headache, fatigue, numbness, ataxia, lethargy, myalgia, diffuse pain, cold allodynia, coma

Table 10.3 Treatment of ciguatera poisoning

Agent	Indication
Intravenous fluids	Volume replacement
Atropine	Bradycardia
Pressors (dopamine, epinephrine, dobutamine)	Hypotension
Mannitol	Neurological symptoms[a]
Pregabalin	Neurological symptoms
Antihistamines	Pruritus

[a]Efficacy still unproven

The only preventive measure is to avoid eating warm-water reef fish, especially those from zones where ciguatera poisoning is known to occur. When eating the fish, the risk of poisoning can be reduced by refraining from eating the internal organs and limiting the amount of initial ingestion. Although the great majority of cases is due to direct ingestion, in a few cases ciguatera has been passed on through sexual contact or breast milk [55].

Treatment is supportive (Table 10.3) [43]. In many cases intravenous fluids serve to replace gastrointestinal losses. Atropine is indicated in cases developing bradycardia, and temporary electrical pacing may be required in cases with refractory symptoms. If there is severe hypotension, pressors must be used. The action of mannitol in reducing the duration of neorological symptoms has still to be assessed in dedicated trials [56]. There have been few reports of the use of amitriptyline, nifedipine and gabapentin [57], while pregabalin was reported to be efficacious in two cases of ciguatera poisoning [58].

10.2.2 Tetrodotoxic Poisoning

More than 50 species of tropical scaleless fish of the Tetraodonitiformes order are poisonous; they include puffer fish, porcupine fish, and molas or sunfish, that all belong to families living in the waters around Japan and Southeast Asia. The flesh of puffer fish (Japanese fugu) is particularly relished in Japan, where, despite the stringent regulations, cases of tetrodotoxin poisoning occur every year, and about four deaths. There have also been cases described in Thailand and many other Indo-Pacific countries. Tetrodotoxin (an aminoperhydroquinazoline) is one of the most potent non protein substances known. It is concentrated in the ovaries, viscera and skin. The greatest concentration occurs from May to June in Japan. The toxin induces neurotoxic and cardiotoxic symptoms. Its origin is unknown; it may possibly be synthesized by *Pseudomonas* bacteria and aquired through the food chain.

Between 10 and 45 min after eating the fish, dizziness and ataxia develop, with possible numbness, sweating, hypersalivation, and hypotension. In general, no gastrointestinal symptoms develop. As to signs and symptoms, on the skin, erythema, petechiae, blistering, and desquamation appear. Death due to respiratory paralysis normally ensues within 6 h. No specific treatment or antidotes are available.

10.2.3 Scombrotoxic Poisoning

This "histamine syndrome" is linked to eating scombroid fish (tuna, mackerel, bonito and skipjack), and canned non-scombroid fish (sardines, pilchards), whose red flesh can be decomposed by the action of bacteria (*Proteus morgani*), decarboxylating muscle histidine into histamine, saurine, cadaverine and other toxins that have not yet been identified.

Toxic fish induce a warning tingling or smarting sensation in the mouth while eating. After a few minutes, or within 24 h after ingestion, the onset of skin symptoms may be observed (pruritus and urticaria), as well as intestinal (abdominal colic, nausea, vomiting, diarrhoea), neurological (flushing, burning, headache), cardiological (hypotension) and respiratory symptoms (bronchial asthma). In the blood and urine of affected patients exogenous histamine can be demonstrated [59]. Treatment consist of anti-H1 and anti-H2 antihistamines, corticosteroids and bronchodilators.

10.2.4 Other Fish Poisoning Syndromes

Paralytic shellfish poisoning can be provoked by bivalve molluscs (mussels, clams, oysters, cockles, and scallops), that acquire neurotoxins like saxitoxins from Dinoflagellates of the *Alexandrium* species (*Gymnodinium catenatum*, *Pyrodinium bahamense*), present in the waters between latitudes 30°N and 30°S.

These Dinoflagellates are particularly abundant during the warm seasons and induce a red tide; their presence is revealed by the discovery of an unusual number of dead fish and sea birds. The symptoms develop within 30 min after ingestion and include perioral paraesthesia, gastrointestinal symptoms, ataxia, visual disturbances and paresis (that can evolve to respiratory paralysis within 12 h) in 8 % of cases. Modest gastrointestinal and neurological symptoms have been associated with molluscs contaminated by neurotoxic brevetoxins from microalgae *G. breve*, that act on sodium channels. These algae also produce red tides [60].

In the Far East (China, Taiwan, Hong Kong, Japan and Thailand) the raw bile and gallbladder of various species of freshwater carp (*Ctenopharyngodon idellus*, *Probarbus jullienii*) are believed to have medical properties. The onset of gastrointestinal symptoms (pain, vomiting and water diarrhoea) may occur within 2–18 h after drinking raw bile or eating the raw gallbladder of these fish. Liver and kidney

damage can also ensue, that may progress to hepatic failure and oliguric or non-oliguric acute renal failure. The hepatonephrotoxin has not been identified but it is heat-stable and may be attributable to the carp's diet [61].

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Cutaneous Infections from Aquatic Environments

11

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Various skin disorders can develop after exposure to aquatic environments. Pathogenic organisms can be introduced through stings and bites, or wounds inflicted by aquatic life forms. In addition, preexisting wounds can be passively infected as a result of exposure to contaminated waters. Table 11.1 lists the pathogenic organisms most commonly associated with waterborne skin infections [1–3].

11.1 Infection by *Mycobacterium marinum*

Mycobacterium marinum lives in aquatic environments, where it causes disease in many poikilothermic fish species living in fresh- or saltwater; the organism has a wide geographic distribution in the water world [4]. It was first isolated in 1926 by Aronson from tubercles in various organs of marine fish found dead in the Philadelphia Aquarium [5]. This organism was identified as a causal agent of human disease only in 1951, when it was identified from skin lesions in swimmers in a contaminated swimming pool in the city of Orebro, Sweden [6]. The term "swimming pool granuloma" was coined to denote these lesions and the causal agent was classified as *M. balnei* [7], and then, when the two mycobacteria were later seen to be identical, as *M. marinum* (Fig. 11.1).

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Table 11.1 Skin infections by waterborne pathogenic organisms

Organism	Clinical features
Mycobacterium marinum	Swimming pool granuloma (very rare today)
	Fish tank granuloma (associated with aquariums, or in pet shop workers)
Mycobacterium ulcerans	Necrosis of dermis and subcutaneous tissue with ulceration (Buruli ulcer)
Rapidly growing mycobacteria	Post-surgical infections
	Skin and soft tissue infections
Erysipelotrix rhusiopathiae	Erysipeloid
Aeromonas species	Cellulitis, fasciitis
Chromobacterium violaceum	Macular lesions and abscesses
Edwardsiella tarda	Cellulitis, abscesses
Shewanella species	Deep ulcers and hemorrhagic blisters of legs
Vibrio vulnificus	Cellulitis
Streptococcus iniae	Cellulitis
Pseudomonas species	Swimmer's ear
	Hot tub folliculitis
	Trench foot

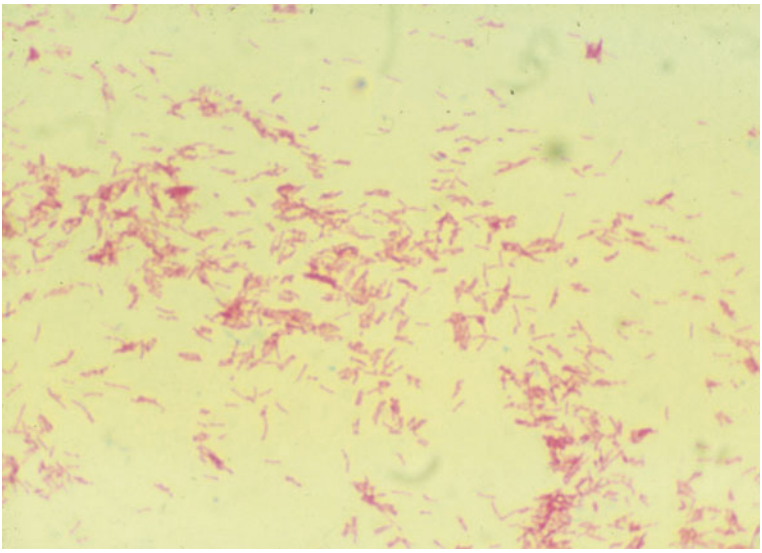


Fig. 11.1 *Mycobacterium marinum*

Lastly, in 1962 Swift and Cohen reported two cases of *M. marinum* infection from a tropical fish tank; the term "fish tank granuloma" was introduced at this stage [8]. Since those reports, "swimming pool granuloma" has essentially disappeared thanks to the introduction of proper chlorinization of this reservoir. Various other activities may implicate a potential risk, including cleaning household aquariums, skin diving [9], dolphin training [10] and a number of fishing and boating activities [11].

Table 11.2 Classification of mycobacteria

"Typical" mycobacteria
Mycobacterium tuberculosis
Mycobacterium bovis
Mycobacterium leprae
Nontuberculous mycobacteria
Group I (photochromogens)
Mycobacterium kansasii
Mycobacterium marinum
Mycobacterium ulcerans
Group II (scotochromogens)
Mycobacterium scrofulaceum
Mycobacterium flavescens
Group III (non chromogens)
Mycobacterium avium
Mycobacterium intracellulare
Mycobacterium xenopi
Mycobacterium triviale
Mycobacterium terrae
Group IV (fast growing)
Mycobacterium fortuitum
Mycobacterium abscessus
Mycobacterium chelonae

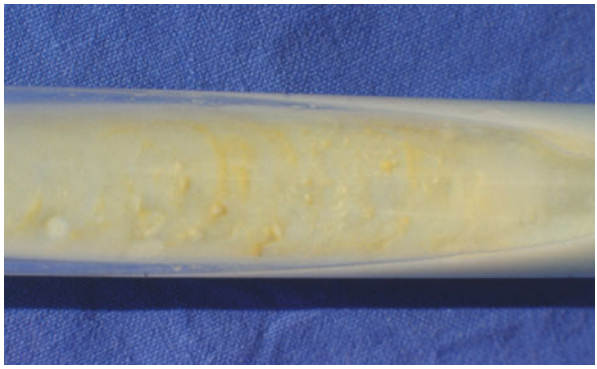


Fig. 11.2 Yellow photochromogenic colonies of *Mycobacterium marinum* in Löwenstein-Jensen culture medium

This mycobacterium belongs to the first of four groups in Runyon's classification (Table 11.2) [12]. It is photochromogenic (cultures turn yellowish-orange after photoexposure) (Fig. 11.2) and in culture medium (Löwenstein-Jensen) it grows slowly over 3–4 weeks at 30–32 °C rather than 37 °C. Thus, unless it is suspected and searched for in appropriate culture medium, the bacillus may not be identified [13–15]. *M. marinum* is alcohol- and acid-fast.

While endemic in fish, *M. marinum* infection in humans through contact with contaminated water or fish is comparatively rare [8, 16–32]. In a retrospective survey carried out in 21 Spanish laboratories from 1991 to 1998, 39 bacteriologically confirmed cases were noted [32]. Culture-confirmed *M. marinum* infection was reported in 66 patients from 1996 to 1998 in France, with an infection incidence of

about 0.04 cases per 100,000 inhabitants per year [33]. The annual incidence in the USA is 0.27 confirmed cases per 100,000 inhabitants [34].

In the last years, significant updates on the pathophysiology of *M. marinum* have been reported. A dynamic host-pathogen interaction has been shown: metabolically active bacteria are controlled by the host immune system and products of specific bacterial genes interfere with the host's effort to eradicate the bacteria. In more detail, the ESX-55 system of the mycobacteria is responsible for the secretion of various proline-proline-glutamic acid (PPE) and proline-glutamic acid (PE)-polymorphic GC-rich repetitive sequence (PGRS) proteins. Animal model studies suggest that such proteins interact with host immune components and possibly subvert critical innate immune pathways, establishing a moderate, persistent infection [35–39]. *In vitro* observations on infected human macrophages further suggest that these proteins strongly modulate the human macrophage response and actively suppress T-lymphocyte receptor signaling-dependent innate immune cytokine secretion, thus allowing bacterial survival [40]. In particular the PPE38 protein, expressed on the cell-wall surface, seems to be involved in bacterial surface properties such as cord formation, sliding motility and biofilm formation, as well as in the induction of pro-inflammatory cytokines in infected macrophages [39]. Additionally, some authors have presumed that these proteins are a source of antigenic variation which allows the pathogen to evade antigenic-specific host responses [38]. Given the above data, it is easy to understand why immune system impairment is a significant factor in the establishment of *M. marinum* infection at the pathogenic level [41].

Owing to the growth temperature of *M. marinum*, the infection is primarily localized at the coolest region of the body, which is the skin. Less commonly it involves deeper structures, such as joints, tendons and bones [42–45].

As already pointed out, dissemination of the infection more commonly occurs in immunocompromised hosts, like transplant recipients and subjects on corticosteroid therapy [46–49], while it is rarely reported in individuals with a relatively intact immunity [50, 51]. As of recent date, *M. marinum* infection has gained a relevant role as an opportunistic infection in patients treated with anti-tumor necrosis factor (TNF)-α or other biological drugs [52–56]. However, recent reports support a safe re-exposure to anti-TNF-α therapy after elimination of the bacteria through correct antibiotic therapy [57].

The infection is now linked in particular to activities such as maintenance of domestic aquariums, and is occasionally reported in occupational environments (among fishermen, laboratory technicians, workers in charge of maintenance of fish tanks at aquariums, zoos or pet shops), although one case was observed in an industrial plumbing mechanic with no direct aquatic exposure [23].

M. marinum invades the tissues through preexisting broken skin. The sites most commonly affected are the knees, elbows, arches of the feet and backs of the hands in swimming pool granulomas, and the backs of the hands in fish tank granulomas. One case of sporotrichoid infection of the face has also been reported, in a 2-year-old child, probably caught from fish in an aquarium [27].

The initial lesion, generally single, presents as a reddish or reddish-blue nodule, of a soft consistency and variable diameter, that may even be as large as 5–6 cm. Ulceration or colliquation may develop and the lesion will then rupture and exude pus, or else it may remain as a verrucous surface lesion. Multiple or disseminated

lesions on the trunk or limbs are rare [17, 20, 21], except in subjects with an immune deficiency. Sporotrichoid forms are frequently observed, with several nodules running along the lymphatic drainage lines. Mild involvement of regional lymph nodes is a rare possibility. The infection may resolve spontaneously within a few months, but generally persists for many years.

Concerning the histopathology, it is widely known that a histologic diagnosis of *M. marinum* infection can be difficult [58] because various aspects tend to vary according to the age of the lesion. In particular, a nonspecific inflammatory infiltrate may be observed in the first 6 months; after this period, a granuloma with epithelioid and multinucleated cells is much more likely [28, 59]. Various patterns can be observed: sarcoid-like granuloma, granuloma annulare, or rheumatoid-like nodules are frequent pictures [60–63]. Epidermal changes (hyperkeratosis, acanthosis, pseudo-epitheliomatous hyperplasia, intradermal neutrophilic abscesses and ulcerations), as well as dermal fibrosis (in chronic lesions) and small vessels proliferation are important findings that are generally present in such cases [58, 63]. In histological preparations, alcohol-acid-resistant bacilli can be identified using Ziehl-Neelsen or trichromic staining.

M. marinum infection does not confer immunity so re-infection is possible. The clinical history is very important for diagnosis, as well as identification of the mycobacterium by biochemical tests (Table 11.3), and molecular biology methods are a must. Intradermal tests with PPD prepared from *M. marinum* will be positive.

There is currently no consensus on the optimal treatment of *M. marinum* infection. Therapy is usually medical in nature, although adjunct surgical procedures, cryotherapy and electrodessication may be needed to control resistant or deeper infections. The duration of therapy varies widely in the literature, ranging from 2 to 12 months overall: most authors recommend extending treatment for 1–2 months following clinical resolution,. Spontaneous resolution is possible but rare; complete regression can take up to

Table 11.3 Differential features of some mycobacteria inducing skin lesions

Species	*M. tuberculosis*	*M. marinum*	*M. ulcerans*	*M. fortuitum*	*M. chelonae*
Growth rate	L	I	I	R	R
Optimal growth temperature	37 °C	30 °C	30 °C	37 °C	37 °C
Growth 25 °C	–	+	+	±	±
Growth 45 °C	–	–	–	–	–
Pigment	N	P	N	N	N
Niacin test	+	V	–	–	–
Reduction of nitrates	+	–	–	+	–
Tween hydrolysis (10 days)	±	+	–	+	V
Catalase 68 °C	–	+	+	+	+
Urease	+	+	–	+	V
Pyrazine amidase	+	+	–	+	+
Growth NaCl 5 %	–	V	–	+	V
Growth MacConkey Agar	–	–	–	+	+

Rate of growth = *R* (rapid: non >7 days); *I* (intermediate: 8–14 days); *L* (slow: more than 14 days)
Pigment = *N*: non photochromogenic; *P*: photochromogenic
V = variable

Table 11.4 Drugs most widely used in the treatment of *Mycobacterium marinum* cutaneous infection according to the literature [66]

Antimycobacterial agent	Dosage[a]	Duration
Minocycline	50–100 mg/2/die	2–6 months
Doxycycline	50–100 mg/2/die	4–5 months
Clarithromycin	250–500 mg/2/die	3–6 months
Ofloxacin	200–300 mg/2/die	1–2 months
Ciprofloxacin	250–500 mg/2/die	2–3 months
Rifampicin	600–900 mg/die	2–5 months
Rifamycin	250 mg im/2/die	2–5 months
Rifabutin	450–600 mg/die	2 months
Sulfamethoxazole plus trimethoprim	400 mg + 80 mg/2/die	1–2 months
Ethambutol hydrochloride	15–25 mg/kg/die	2–6 months
Isoniazid	5–10 mg/kg/die	1–2 months

[a]If unspecified, administration is per os

2 years [64]. Various antibiotics are reported as effective options but randomized controlled trials comparing different antibiotics regimens are lacking. Widely used molecules include tetracyclines (mostly minocycline and doxycycline), sulfamethoxazole plus trimethoprim, rifampicin, and ethambutol. Less common alternatives are clarithromycin, levofloxacin and amikacin [33, 41, 59, 65, 66]. Other drugs such as newer macrolides and fluoroquinolones (sparfloxacin) offer feasible approaches [33] (Table 11.4), even if both success and failure have been reported for each of these molecules. Monotherapy with minocycline, doxycycline and clarithromycin has proven successful in most cases, especially for superficial cutaneous infections. Combination therapy, often with clarithromycin plus rifampicin and/or ethambutol, is preferred for more severe forms characterized by deep tissues involvement.

11.1.1 Personal Experience [67]

From 1987 to 2011 we observed 15 patients with cutaneous *M. marinum* infection, 12 males (80%) and 3 females (20%; male to female ratio 4:1), of ages ranging from 15 to 55 years (mean: 39.9). The infection was occupational in 11 subjects (3 of them worked at institutional aquariums, 8 in shops selling aquariums) and extra-occupational in 4 patients (all of whom tended home aquariums). One of the latter four patients was in the 8th month of pregnancy at the time of observation [67].

Each patient had a documented history of former minor trauma, such as abrasion or a superficial wound, acquired while handling fish, shellfish, or alternatively caused by infected foreign bodies within the aquarium, like wood splinters or stones. The median incubation time after the traumatic inoculation was relatively long, ranging from 3 to 24 weeks (mean: 6.6). The interval between the lesion onset and our observation was in the range of 1–6 months (average 4.3 months).

Four patients (20.7%) presented with a single papulo-verrucous plaque (Figs. 11.3, 11.4, 11.5, and 11.6) and 11 (73.3%) had a sporotrichoid distribution of nodular lesions (Figs. 11.7, 11.8, 11.9, 11.10, 11.11, 11.12, 11.13, 11.14, 11.15,

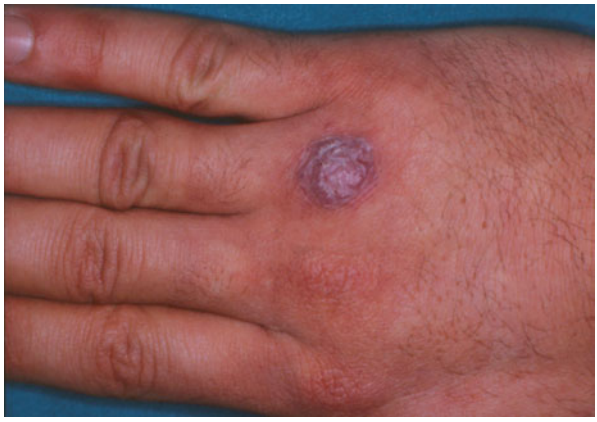


Fig. 11.3 Fish tank granuloma

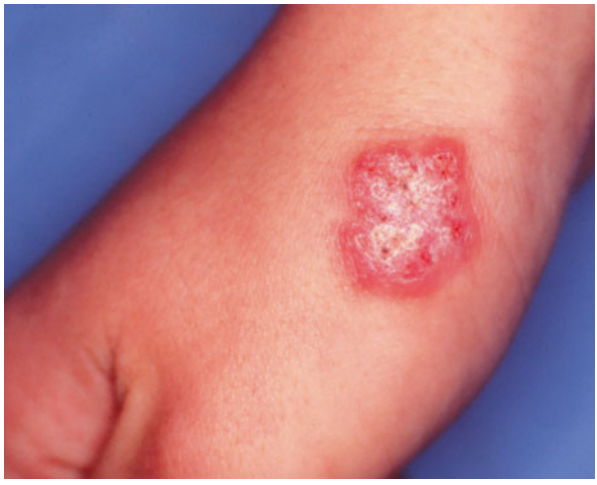


Fig. 11.4 Fish tank granuloma

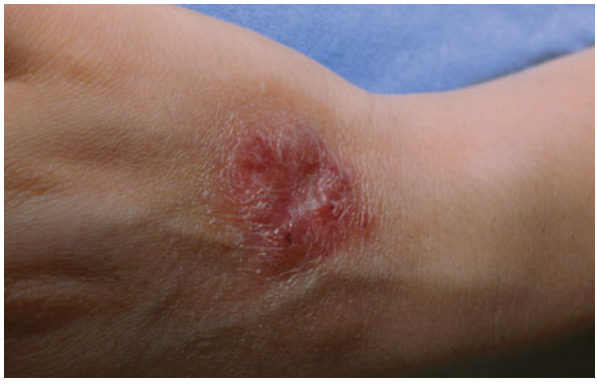


Fig. 11.5 Fish tank granuloma

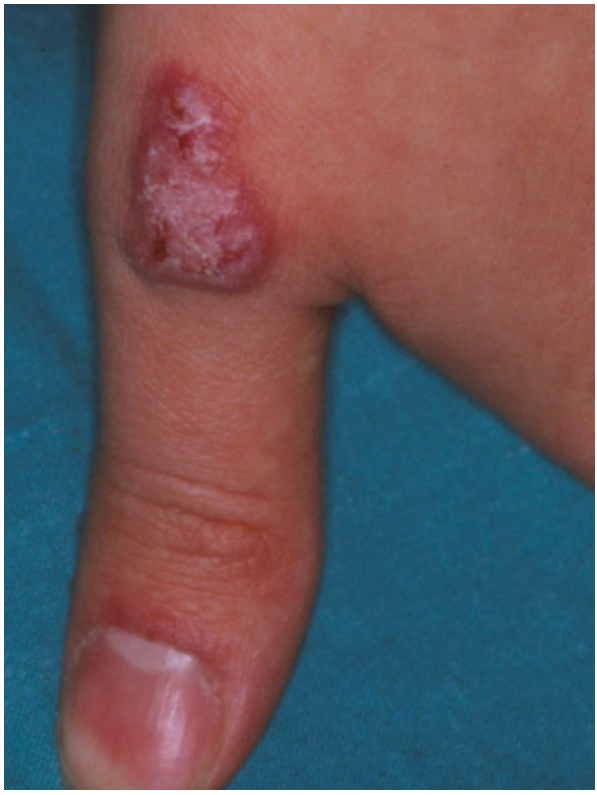


Fig. 11.6 Fish tank granuloma (Reproduced with permission from Bonamonte and Angelini [30])

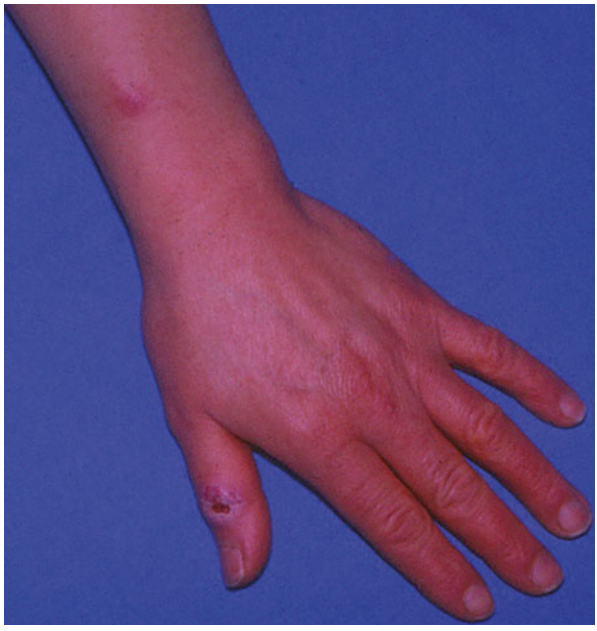


Fig. 11.7 Sporotrichoid fish tank granuloma

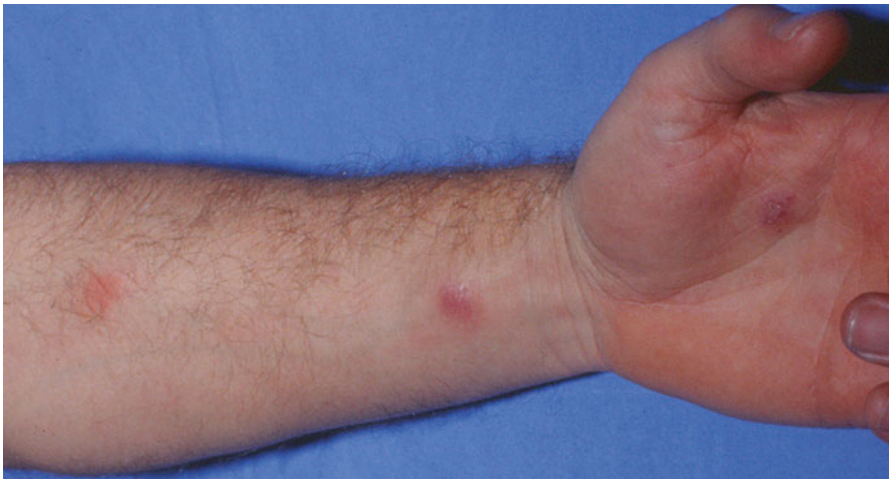


Fig. 11.8 Sporotrichoid fish tank granuloma

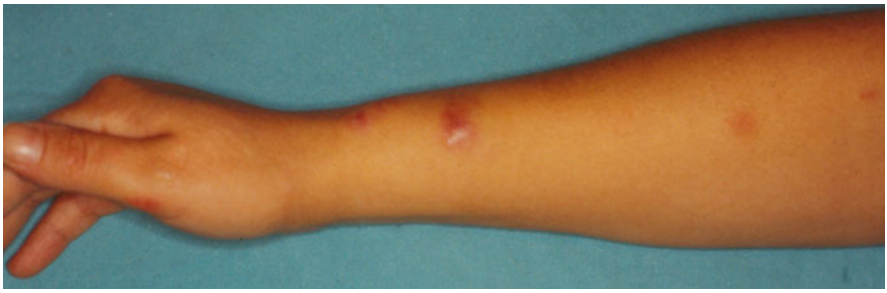


Fig. 11.9 Sporotrichoid fish tank granuloma

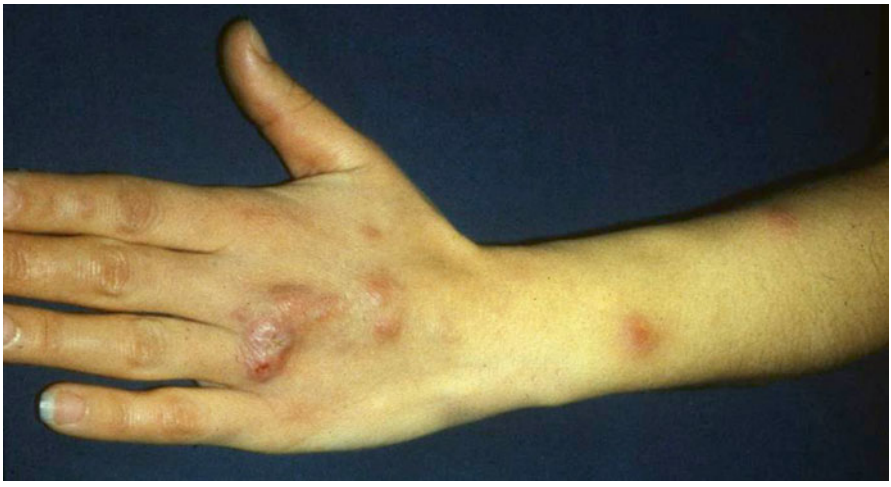


Fig. 11.10 Sporotrichoid fish tank granuloma

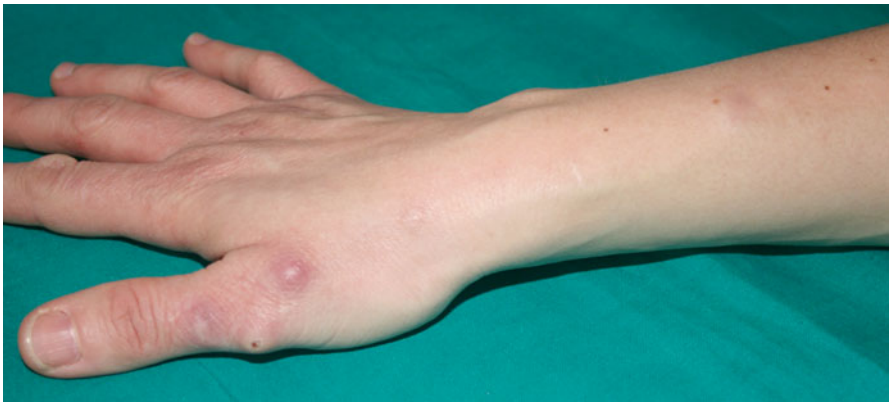


Fig. 11.11 Sporotrichoid fish tank granuloma

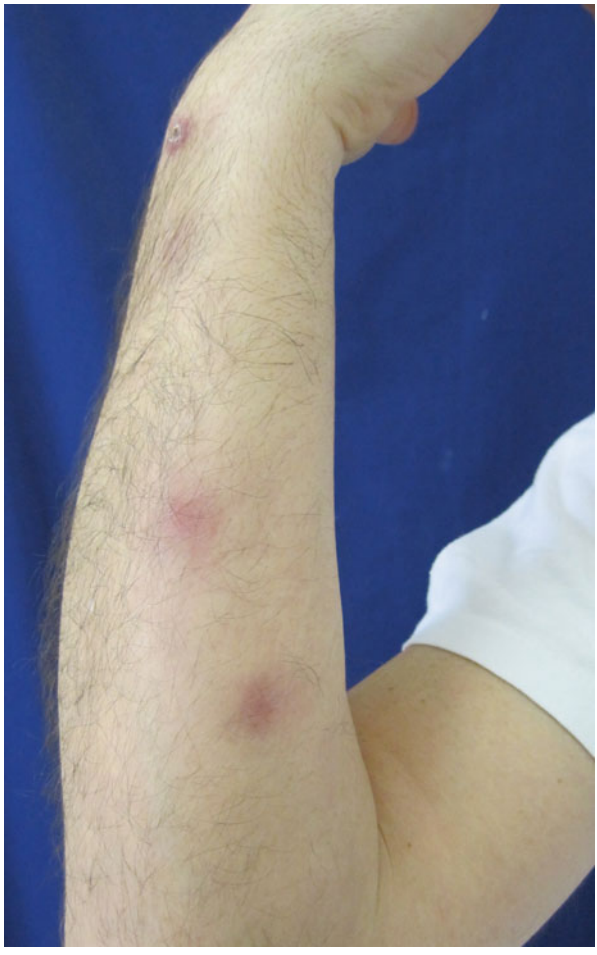


Fig. 11.12 Sporotrichoid fish tank granuloma

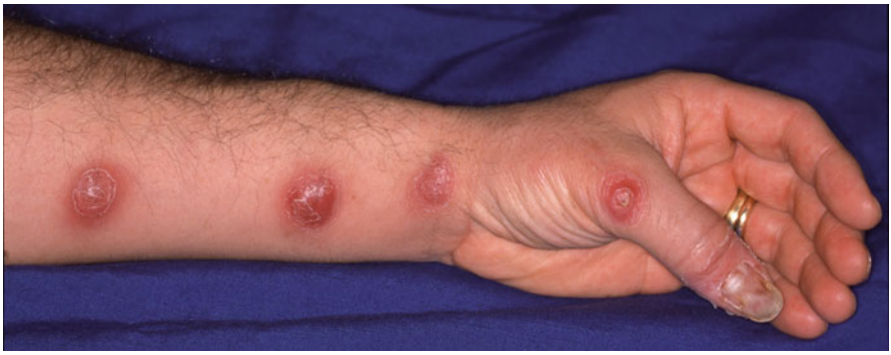
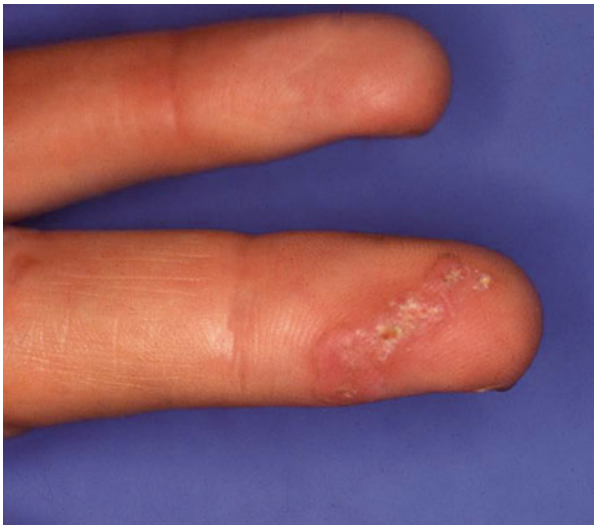


Fig. 11.13 Sporotrichoid fish tank granuloma (Reproduced with permission from Bonamonte and Angelini [30])

Fig. 11.14 Fish tank wound



11.16, and 11.17). The anatomic distribution was typically on the upper limbs, first involving the hand, fingers and dorsum (right hand in 13 cases, left hand in 2 cases), in 12 cases later spreading centripetally up the whole arm, trailing up lymphatic vessels. In 3 of these 12 sporotrichoid cases, the first observed lesions were ulcerated nodules that caused mild pain, unlike in the remaining cases, where the infection was painless. Associated systemic symptoms, localized adenopathy, deep structures involvement like tenosynovitis, bursitis, and arthritis, were not present in any of the 15 cases. All patients were immunocompetent and referred no history of transplantation or immunosuppressive therapy.

An interesting finding emerged from the history of the 12 sporotrichoid pattern cases: nodular lesions, arranged in rosary-like chains, appeared one after the other at regular 1–2 week intervals. Moreover, each lesions first involved the cutis deep structures, presenting as a prominence covered by healthy skin, and then later the overlapping epidermis was affected [67].

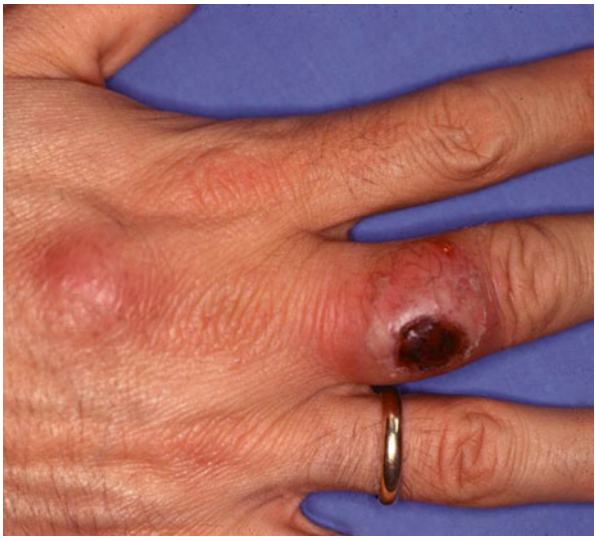


Fig. 11.15 The same case as in Fig. 11.14. Sporotrichoid fish tank granulomas, one with an ulcerative evolution (Reproduced with permission from Bonamonte and Angelini [31])

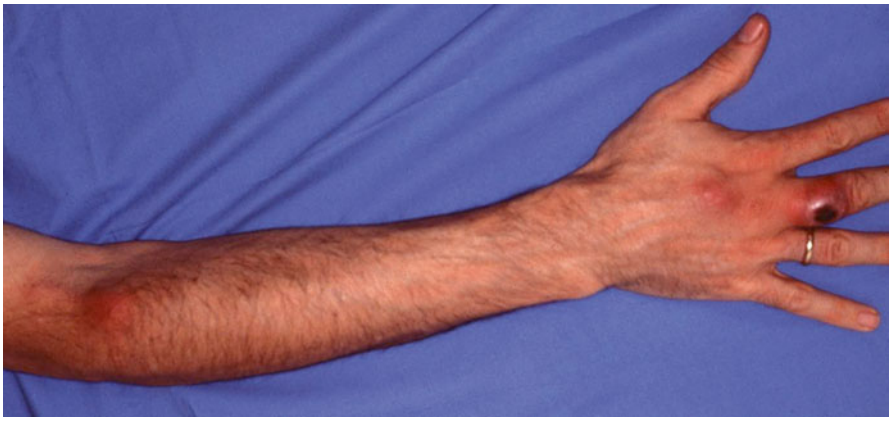


Fig. 11.16 The same case as in Fig. 11.14 with sporotricoid granulomas

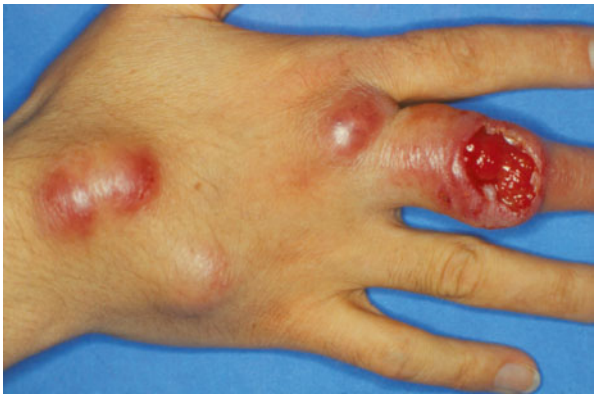


Fig. 11.17 Sporotrichoid fish tank granulomas with an ulcerative evolution

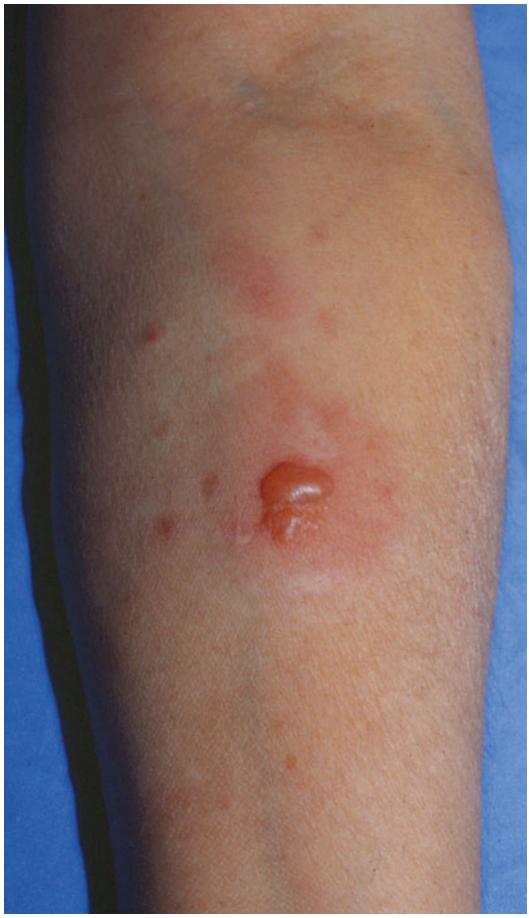


Fig. 11.18 Strongly positive reaction to PPD from *Mycobacterium marinum*

Culture tests of skin biopsy fragments in Löwenstein-Jensen at 30 °C indicated *M. marinum* growth in 13 of our 15 cases (93.3 %); according to the literature, positive rates of cultures range from 70 to 80 %. However, in the two culture-negative cases, the history, intradermal skin tests with PPD of *M. marinum* and PCR tests were positive, lesions were classic sporotrichoid, and minocycline therapy was efficacious. Culture in Löwenstein-Jensen at 37 °C yielded negative results in each case. In all cases PPD skin tests resulted strongly positive for *M. marinum* (Fig. 11.18); the lesions featured an induration area measuring 10–15 mm in diameter, and were moderately positive for *M. tuberculosis* (Fig. 11.19) [67]. Even if none of our patients had a history of a positive tuberculin skin test result, the positive PPD results could be interpreted as cross-reactivity, consistent with studies showing a close genome relationship between *M. marinum* and *M. tuberculosis* [68]. Deep tissue involvement was not revealed in any of our cases, likely because of the brief time lag between the disease onset and the clinical diagnosis. In 7 of the 15 patients the PCR test was performed, yielding positive results in each instance.

Biopsies were taken in all subjects. Epidermal changes were present in 46.6 % of cases and included hyperkeratosis (three cases), acanthosis (seven cases) pseudoepitheliomatous papillomatosis (four cases) and lymphocyte exocytosis (two cases). We demonstrated superficial and/or deep dermal involvement in every case. A tuberculoid granuloma, with lymphocytes, histiocytes, neutrophils, giant cells but no sign of central caseation (Figs. 11.20 and 11.21),

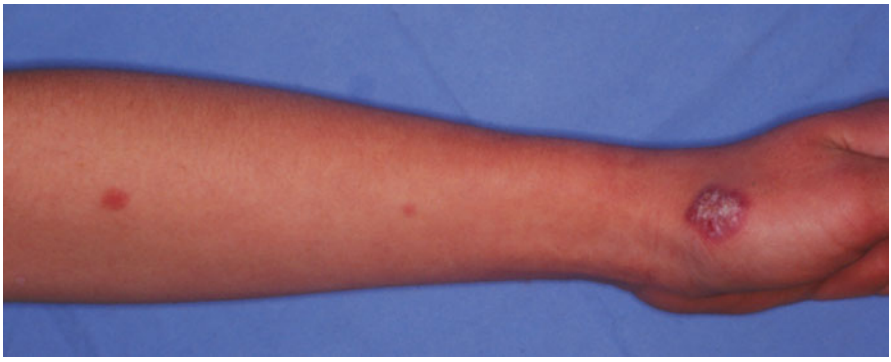


Fig. 11.19 Fish tank granuloma with intensely positive PPD to *Mycobacterium marinum* and weakly positive PPD to *Mycobacterium tuberculosis*

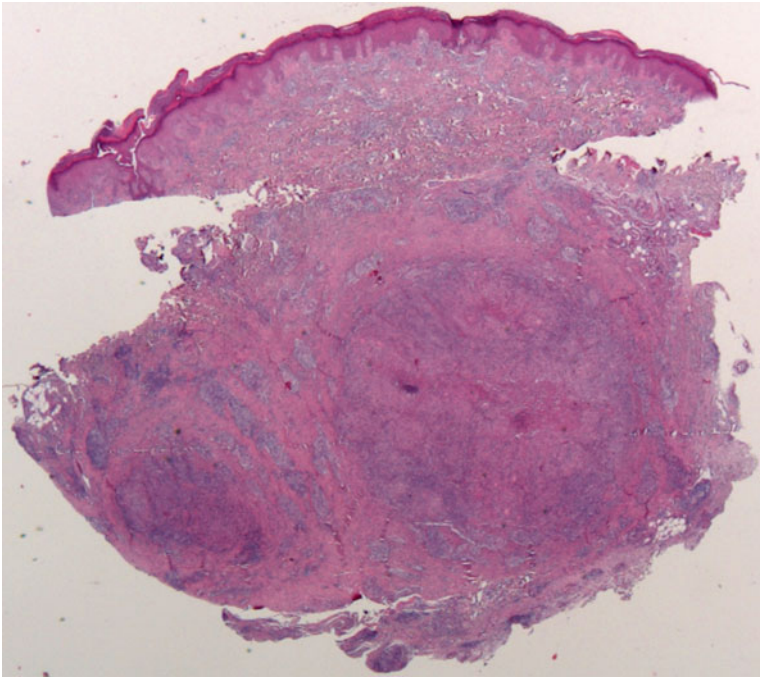


Fig. 11.20 Granulomatous inflammation of deep dermis and subcutaneous tissue (Hematoxylin-eosin – ×10) (Reproduced with permission from Bonamonte and Coll. [67])

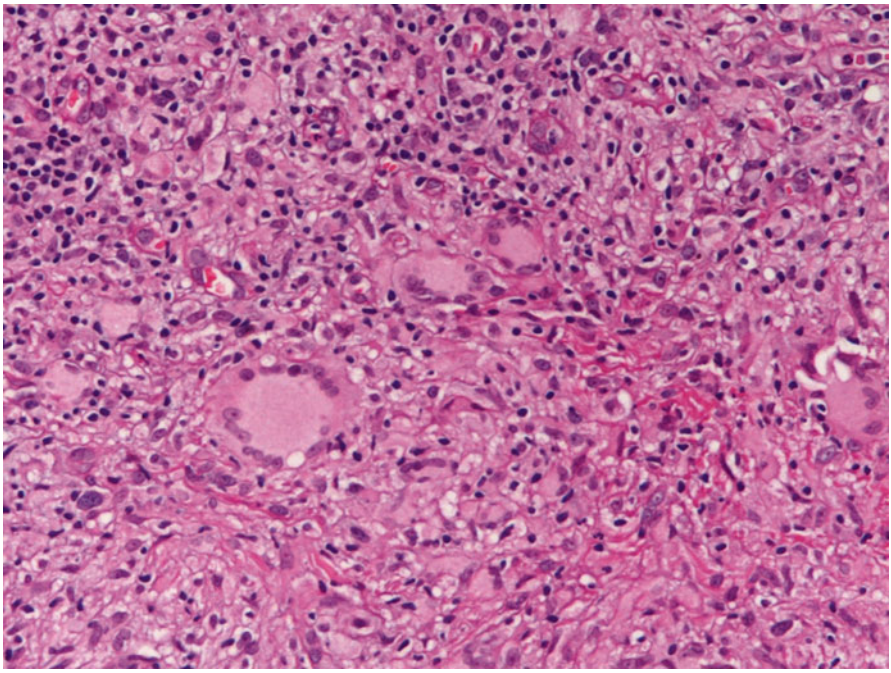


Fig. 11.21 Tubercoloid granulomatous infiltrate with lymphocytes, hystiocytes, and giant cells (Hematoxylin-eosin – ×100) (Reproduced with permission from Bonamonte and Coll. [67])

was found in one case (6.7 %), in which the sampled lesion was 5 months old. In the remaining 14 cases, in which histology was performed on lesions that were 3–12 weeks old, a nonspecific dermo and/or hypodermic mononuclear-cell (lymphocytes, histiocytes, plasma cells) infiltrate was evidenced, with little or no tendency towards a tubercular-like granuloma formation (Fig. 11.22). Other observed features included dermal fibrosis (one case) and mild blood vessels proliferation (three cases). Ziehl-Neelsen stain highlighted acid-fast bacilli only in the histologically demonstrated tuberculoid granuloma case (6.7 %). Additional laboratory tests, done for differential diagnosis purposes in particular with other mycobacteria, fell into the normal or negative range in every case [67].

We collected two dead aquarium fishes for testing purposes: notably, acid-fast bacilli were present in Ziehl-Neelsen stained sections from the two examined aquarium fishes and PCR was also positive in the single fish tested.

As to treatment, 13 patients responded completely to minocycline monotherapy 100 mg twice daily in 2–3 months. In one patient, who had already been treated with sulfamethoxazole plus trimethoprim for 30 days with no apparent benefit, the infection finally resolved after a switch to isoniazid (600 mg/die) and rifampicin (900 mg/die) for 2 months. Mean duration of treatment was 2.7 months. It should be noted

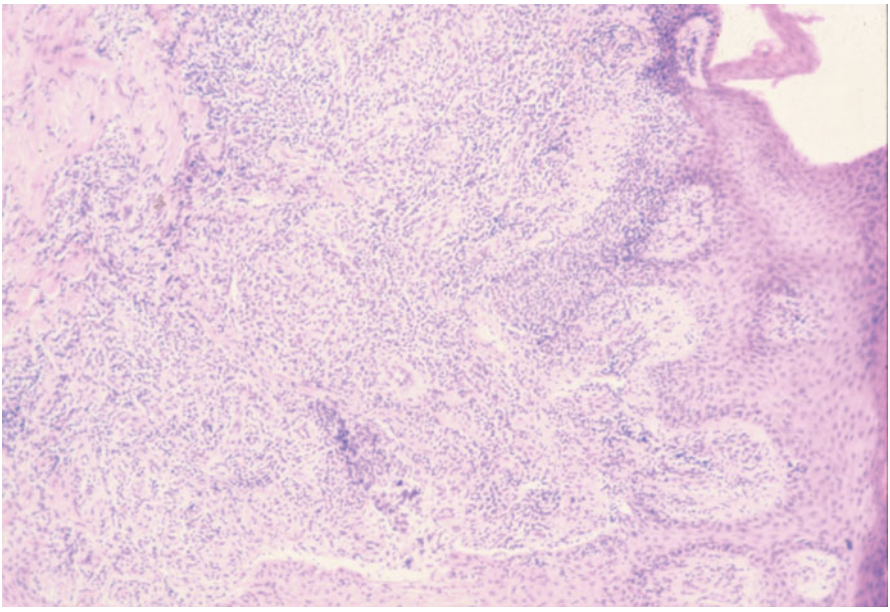


Fig. 11.22 Aspecific granulomatous infiltrate (Hematoxylin-eosin – ×40)

that therapy, that was antiobiogram-guided in all patients, was continued for at least a month after lesions clearance. None of the patients required surgical debridement. In the 8th months pregnant patient, regardless of the antibiogram sensitivity to tetracyclines, we did not administer the drug, given the well-known contraindications. Other viable options were either ineffective, as per antibiogram, or unfit for use during pregnancy. However, a spontaneous regression of the infection was observed through weekly follow-up, with complete resolution 1 month post-partum. End of follow-up in all the patients ranged from 12 months to 2 years and did not reveal relapse in any case [67].

In conclusion, the diagnosis of *M. marinum* infection relies on a detailed history, as well as microbiologic and PCR-based investigations. From a preventive point of view, the use of adequate concentrations of free chlorine in swimming pools, spas and hot water tubs is advisable, as recommended by the Center for Disease Control and Prevention [69, 70]. Furthermore, fish tank-related infection may be prevented by the use of waterproof gloves during maintenance and by the appropriate care of skin lesions on the upper limbs [71]. For the latter, however, chlorine derivatives show a limited activity against mycobacteria [72], whereas phenol, formaldehyde and glutaraldehyde derivatives are effective.

Recently, fish tank water sterilization by UV filters, which easily inactivate mycobacteria, has been introduced on the market, and a vaccine against *M. marinum* infection in fish has also been designed [73, 74].

11.2 Infection by *Mycobacterium ulcerans*

This disease is essentially cutaneous, even if it can be accompanied by bone involvement. It is characterized by the presence of ulcers with an undermined border and indolent course. No general signs are present. Due to its notable frequency in one region of Uganda, Buruli, it is better known as the Buruli ulcer, as instanced on the World Health Organization (WHO) Consulting Group web site: www.who.int/buruli. In the literature, the infection has also been reported by other eponyms: Bairnsdale ulcer (referring to the first focus, in Australia), Kakerifu ulcer and Kasongo ulcer (for the foci in Congo), and Kumusi ulcer (foci in New Guinea-Papuasia) [75].

After tuberculosis and leprosy, infection by *M. ulcerans* is the third most common mycobacterium infection in immunocompetent individuals [76]. In 1977, WHO recognized the infection as an important emerging disease, and in 1998 a world campaign to fight the infection was launched.

The disease had first been recognized as a specific entity in 1937 in Bairnsdale, South-East Australia, and the first Australian observations were published in 1948 [77], when a new alcohol-acid-resistant bacillus was isolated from the borders of cutaneous ulcers, that grew in culture at temperatures ranging between 30 and 33 °C, named *M. ulcerans* [78]. The first African report was in Uganda, and in 1972 the name Buruli ulcer was proposed [75]. The infection was then reported in many inter-tropical nations, Africa, South-East Asia (Malaysia, Indonesia, India, Sri Lanka, China), Latin America (Mexico, Peru, French Guyana) and Oceania (New Guinea-Papuasia) [79–86].

On numerous occasions, infection by *M. ulcerans* appeared 2–3 years after a severe ecological perturbation. It manifests as circumscribed endemic foci around aquatic systems (rivers, lakes, irrigation systems, marshes). *M. ulcerans* takes up to 6–12 weeks to grow at temperatures of 25–33 °C. Many conventional decontaminants can render the organism non viable, while the best culture media of the species must include egg yolk or a reduced oxygen tension. Molecular biology techniques have been developed to make a rapid identification of the organism [14].

Children over the age of 2 years, male or female, are the most frequently affected, likely because they have not yet developed an antimycobacterial immunity, as well as being more prone to contact with germs while playing. In adults there is a prevalence in women. Cases reported in tourists in endemic zones suggest a geographic risk as well as the need for conditions favoring the introduction of the mycobacterium into the organism: skin microtrauma, bites or stings by aquatic insects, bites by fish, wounds from shellfish claws, although never in marine saltwaters [75].

After an incubation of 6–12 weeks, the infection presents as one or more subcutaneous cold, well circumscribed nodules that do not adhere to the deep skin planes and are indolent and only mildly pruriginous. The legs are most commonly affected and less frequently, the arms. In children, the face and trunk can also be involved. Some forms can be extremely severe, showing an edematous onset, and are termed fulminant. They manifest as a hard, hot edema affecting a limb segment. The lesions

evolve slowly, the nodules fluctuate and ulcerate within 4–6 weeks. The ulceration is characteristic, featuring rounded or polycyclic margins while the base is covered by an adherent greyish-yellow patina that, when cleaned, appears granulomatous and erythematous. The ulcer margins are thickened, devitalized and undermined. There is generally only one ulcer but sometimes satellite, communicating ulcers can form around it. The lesions extend horizontally and can affect the entire limb, penetrating deep down to the muscles and tendons. These ulcers are painless or only slightly painful, and paradoxically, the patient's general conditions are good, with no fever nor loco-regional adenopathy.

The disease evolves over three phases: the above-described deep, horizontal extension, that lasts several months, is followed by a non uniform stabilization phase, while in the third and last phase there will be centripetal scarring. A superimposed infection of the lesions can occur, and it also poses a risk of tetanus. Even if this skin mycobacteriosis is not considered fatal, it can cause disabling scars, with tendon retraction, anchylosis, post-scarring lymphedema; amputation of the limb could even be necessary. In some disease foci a bone infection is also reported (osteomyelitis and even bone necrosis), that develops as a result of contiguity with the skin lesions or through the bloodstream [87].

The histology of the nodular and ulcerative lesions is peculiar. It initially reveals a necrotic eosinophilic vasculitis penetrating down to the deep derma and hypoderma; ischemia progressively affects the epidermis, and blistering appears, originating the ulceration process. During the ulcerative phase, the hyperplastic epidermis tend to become deeply invaginated, while a lymphohistiocytic infiltrate appears in the derma. The hypoderma is affected by the same massive eosinophilic necrosis and arteriovenous thrombosis may occur. In necrotic zones, Ziehl-Neelsen or auramine staining demonstrates the mycobacteria. In the chronic phase there will be a granulomatous infiltrate, with macrophagic epithelioid and giant cells. Finally, fibrohyalinose will replace the necrosis and lead to healing.

A direct search for the mycobacterium in the lesions is possible only in 30–65 % of cases, whereas the same search on biopsy samples seems to be more sensitive. Culture is also frequently negative, whereas gene amplification tests are rapid and sensitive.

M. ulcerans is the only mycobacterium that secretes a toxin with strong cytotoxic and immunosuppressive properties against the T lymphocytes. This same toxin, mycolactone, also inhibits local macrophagic phagocytosis, which explains the weak inflammatory reaction in the course of extensive necrosis.

Medical treatment offers no benefit in the case of extensive ulcerations [76]. Preulcerative lesions can be successfully treated by surgical excision, followed by monotherapy with rifampicin or heat therapy. Post-surgical antimycobacterial treatment can prevent relapse of the infection and metastases. However, many antimycobacterial agents are inefficacious; to control complications of the ulcers, rifampicin and clarithromycin are valid drugs. The ulcerations can be treated by superficial debridement and subsequent skin grafting [76].

The administration of the BCG (Bacillus of Calmette and Guérin) vaccine can confer some immunity also to infection by *M. ulcerans*: in fact, it has been noted that the disease incidence is notably reduced in vaccinated children. It should be borne in mind that *M. ulcerans* has a phylogenetic but not phenotypic affinity to *M. marinum* [88].

11.3 Infection by Rapidly Growing Mycobacteria

Rapidly growing mycobacteria (RGM) are known to cause cutaneous and subcutaneous infections as well as pulmonary, extra-pulmonary and systemic/disseminated disease. The main source of RGM is drinking water [89]. They can also be isolated from rivers and lakes, seawater, waste water from hospitals, animal drinking troughs, hot drinking water distribution systems, raw milk and soil [90]. It should be noted that RGM are robust bacteria, that are resistant to the standard disinfectants (e.g., chlorine) used in water treatment processes and in the hospital setting [91].

11.3.1 *Mycobacterium abscessus*

The most common source of the infection is tap water. An easy access point for this mycobacterium is also any skin piercing (e.g., tattooing) [92].

The skin infected by *M. abscessus* is erythematous, edematous, hot and painful; blisters and pustules can also be present, together with fever, chills, muscle aches, and a general feeling of malaise. Post-traumatic wound infections cause localized abscesses that can give rise to sporotrichoid pictures via a rising lymphatic spread [93]. Even if they are rare, infections by *M. abscessus* have been reported in fish handlers or individuals exposed to saltwater [94, 95], yielding sporotrichoid pictures similar to those of *M. marinum*.

The infection is diagnosed on a search for the bacillus in culture or molecular amplification tests. In localized infections, clarithromycin can be administered. This same antibiotic, together with azithromycin, is elective treatment also for disseminated forms, even if the risk of potential resistance makes it wise to combine these with other drugs such as amikacin, imipenem or cefoxitin.

11.3.2 *Mycobacterium fortuitum*

The onset of primary cutaneous and soft tissue infection due to *M. fortuitum* is most often following post-traumatic and surgical wounds, mesotherapy injections, venous catheterization in a healthcare setting, and at injection sites [96–100].

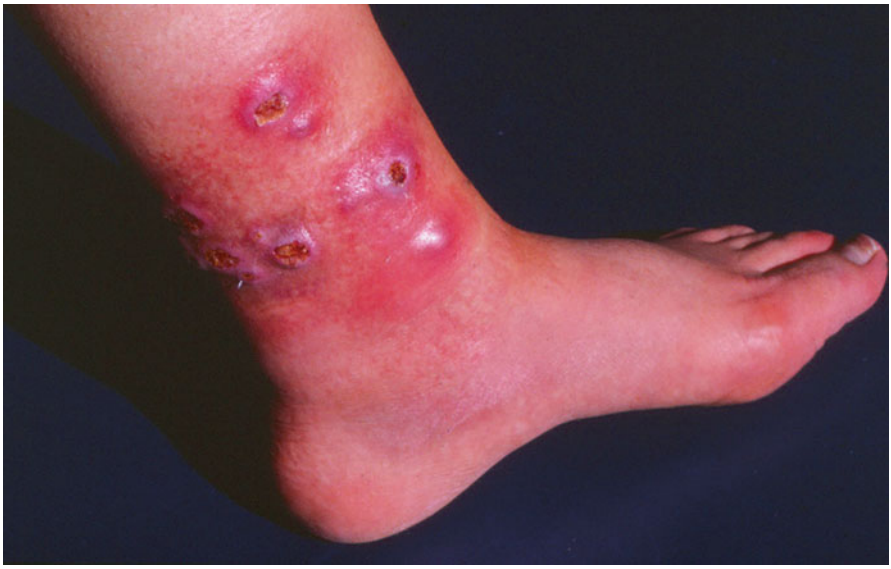


Fig. 11.23 Erythemato-ulcerative nodules from *Mycobacterium fortuitum*

Typically, the infection begins with erythematous-papulous lesions, that progress within weeks or months to purplish, fluctuating, painful nodules that evolve to ulcers (Fig. 11.23). Satellite adenopathy is rare.

Infection by *M. fortuitum* generally has a chronic, progressive course, although a spontaneous regression is sometimes observed. *In vitro s*usceptibility tests are important for treatment decision making. The most active drugs are macrolides (clarithromycin), quinolones, and sulfonamides but at least 4 months of therapy, with at least two agents, will be needed. Surgical drainage is indicated in cases of extensive disease and abscess formation.

11.3.3 *Mycobacterim chelonae*

Contaminated water is a natural reservoir and source of infection in man. *M. chelonae* prevalently infects immune-impaired subjects, such as HIV/AIDS patients. Cutaneous infections have been observed in hemodialysis and peritoneal dialysis patients, kidney and liver transplant patients, and individuals with tattoos [14]. The skin manifestations are like those induced by *M. fortuitum* (Fig. 11.24).

M. chelonae isolates show resistance to cefoxitin but are susceptible to clarithromycin, tobramycin and imipenem. However, susceptibility *in vitro* is not always correlated with a treatment efficacy *in vivo*. The choice of antibiotics (several drugs in combination), the treatment duration and the clinical outcome will depend on the host immunity status. Excision and drainage of the skin abscesses is a valid aid.

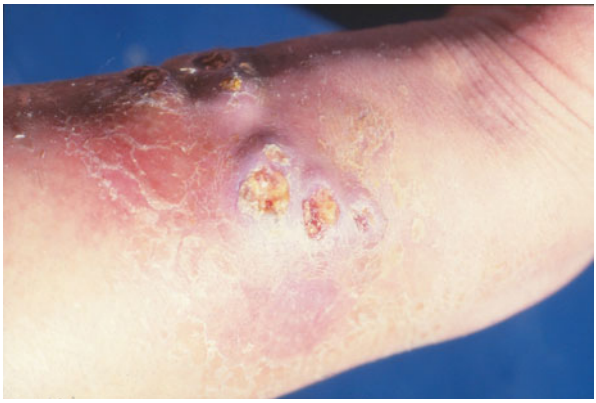


Fig. 11.24 Erythemato-ulcerative nodules from *Mycobacterium chelonae*

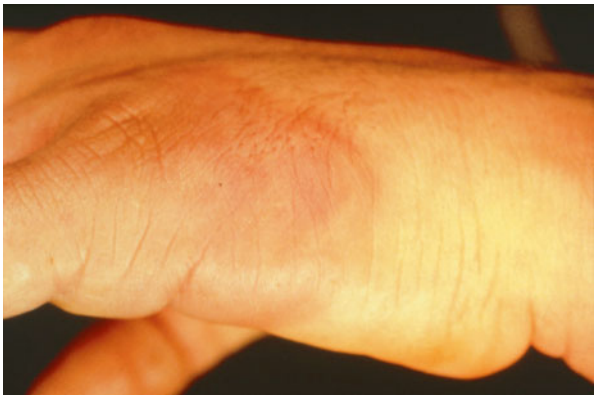


Fig. 11.25 Erysipeloid: erythematous raised lesion with centrifugal extension

11.4 Erysipeloid

This dermatitis, also known by the name of Baker-Rosenbach's erysipeloid, is an acute, rarely chronic infection induced by *Erysipelothrix rhusiopathiae,* the aetiological agent of "swine erysipelas" [101, 102]. *E. rhusiopathiae* is a Gram-positive, non spore-producing and non mobile bacillus, which usually has long filaments. It can survive in the environment for long periods and also lives in the sea. The infection is common not only in pigs but also in horses, chickens, ducks, sheep, turkeys and other animals and in salt- and freshwater fish. Although it is widespread all over the world in animals, man rarely contracts it. Most of the cases reported were occupational, being most often observed in fishermen and butchers. It has also been described in housewives pricked by fish or chicken bones.

The onset of erysipeloid is generally in the late summer when animal infections are most common. About 3 days after contagion, the puncture zone develops a dark erythematous raised area with an irregular centrifugal extension and distinct, raised polycyclic margins (Fig. 11.25). The sites most commonly involved are the hands and forearms but all exposed areas may be affected. In 10% of cases, fever

develops; pricking and itching sensations and pain may also be present. The area affected will spread wider over the following days and reach a maximum diameter of 10 cm. It resolves spontaneously in 2–3 weeks without any desquamation or suppuration phenomena [103–106].

Apart from this modest, localized form, a generalized skin condition can be observed in rare cases, as well as systemic forms complicated by septicaemia and endocarditis. Differential diagnosis must be made with erysipelas, a febrile streptococcal infection that spreads rapidly, and with cutaneous leishmaniasis [107, 108]. The disease does not confer immunity and re-infections are therefore possible. The bacterium responsible can be cultured from a biopsy sample obtained from the margins of the skin lesions, or from peripheral blood in systemic forms. However, isolation and identification is still not easy as the organism lies deep in the skin and culture (enriched with blood and incubated in an atmosphere containing 5–10 % CO_2) times are rather long. Some progress has recently been made in molecular approaches for diagnosis and for taxonomic and pathogenic studies of *Erysipelothrix.* Two different PCR techniques for diagnosis of the swine infection have also been described, one of which has been successfully used in human samples [109].

E. rhusiopathiae is sensitive *in vitro* and *in vivo* to penicillins, cephalosporins, tetracyclines (chlortetracycline, oxytetracycline), quinolones, clindamycin, erythromycin, imipenem and piperacillin. It is resistent to vancomycin, chloramphenicol, gentamicin, streptomycin, and trimethoprim-sulfamethoxazole. First choice drugs are penicillin and cephalosporins: a 7-day course is appropriate, and a clinical improvement is seen already after the first 2–3 days of treatment [101].

11.5 Infected Wounds

Seawater is a dilute suspension of bacteria, many of which are harmful to man and can cause various infections (external otitis, gastroenteritis, pneumonia). Wounds from any causes occurring in the sea can therefore easily become infected. The microorganisms isolated from infected wounds include bacteria present in seawater (vibriones, *Pseudomonas*, *Aeromonas* species, *Chromobacterium violaceum, Edwardsiella tarda, and Shewanella* species) and bacteria from normal skin flora (staphylococci, streptococci) [3].

11.5.1 *Aeromonas* Species

Aeromonas species (in particular *A. hydrophila*), that are Gram-negative rods found in warm, fresh and brackish waters worldwide as aquatic animal commensals and pathogens, give rise to wound infections typically occurring also after marine injuries from animals such as alligators, fish, snakes, or from freshwater leech bites [110, 111].

The body parts affected are generally the extremities or other regions immersed in contaminated waters during the warm months. Within 24 h, the wounds show

erythema, edema and purulent exudation. This may be followed by fever and chills and the onset of invasive infections, including necrotizing fasciitis, necrotizing myositis, and osteomyelitis in immunocompromised patients.

Most *Aeromonas* species are resistant to penicillins and first-generation cephalosporins. In addition to drainage and debridement of the wound, the infection must be treated with a combination of an aminoglycoside and either a fluoroquinolone or a third-generation cephalosporin.

11.5.2 *Chromobacterium violaceum*

This is an aerobic, Gram-negative bacillus widely distributed in soil and water in tropical and subtropical regions [112]. The bacillus grows rapidly in the usual culture media, producing purple colonies; strains of non pigmented *C. violaceum* are rarer, but the two forms may coexist in the same infection. The entry point is generally a wound or a fish bite, after exposure to brackish or stagnant water. The wound will become purulent, with a bluish exudate and regional swelling, usually of an extremity. In a few days, the onset of invasive septicemia can be observed, especially in immunocompromised subjects, with high fever and macular disseminated skin lesions that evolve to abscesses. Treatment is with aminoglycosides, fluoroquinolones, tetracyclines, imipenem, and trimethoprim plus sulfamethoxazole. The bacillus is resistant to penicillins and cephalosporins [3, 112].

11.5.3 *Edwardsiella tarda*

This is a Gram-negative rod of the family of Enterobacteriaceae, that is well known as a fish pathogen. Various cases of skin wounds that have evolved to abscesses after exposure to seawater have been described, especially after a catfish sting [113, 114]. As well as surgical drainage, treatment of all extra-intestinal cases relies on intravenous injection of a combination of Gram-negative anti-bacilli agents.

11.5.4 *Shewanella* Species

These are Gram-negative saprophytic bacteria that belong to the normal microflora of the marine environment in temperate and tropical regions worldwide. In culture they produce yellowish-brown mucoid colonies that emit hydrogen sulfide.

The most common clinical manifestations are deep ulcers, hemorrhagic blisters, generally on the legs, together with otitis externa, otitis media, and bacteremia. The ulcers can evolve to necrotizing fasciitis and osteomyelitis, while an ensuing septicemia is associated with endocarditis and meningitis. Pneumonia, cholecystitis, and peritonitis can follow the aspiration or ingestion of seawater. Triggering causes include trauma in seawater, the ingestion of raw seafood, preexisting ulcers on the legs, and immune system impairment [115].

Molecular amplification tests (PCR) are needed for a correct diagnosis. *Shewanella algae* is resistant to penicillins and first- and second-generation cephalosporins. Most species are sensitive to aminoglycosides, third-generation cephalosporins, and fluoroquinolones. In cases of invasive forms, a combination of several drugs is recommended, administered intravenously for 2 weeks followed by 2–4 weeks of oral therapy.

11.5.5 *Vibrio vulnificus*

This is a Gram-negative bacterium (of the Vibrionaceae family), that is pathogenic and highly virulent. It can cause three different types of infection: acute gastroenteritis from eating raw or under-cooked shellfish, invasive septicemia after ingesting raw shellfish (especially oysters), and necrotizing wound infections following marine injuries [3, 116].

Vibrio vulnificus is a halophilic, rod-shaped, motile bacterium that often flourishes in warm seawater estuaries, or brackish environments with a salinity of 0.5–2.5 % [117]. It is usually observed in temperate or subtropical seacoast regions or countries, such as the United States and East-Asia. Skin infections are uncommon, generally occur in the summer months, and are potentially fatal. Man is predisposed for several reasons, including occupational and recreational exposure to fish and shellfish (*V. vulnificus* can be isolated in the gut of oysters and other shellfish, and of fish that inhabit oyster reefs).

A necrotizing skin infection or septicemia following a marine injury, or the ingestion of, or exposure to raw seafood or seawater, especially in the summer months, should prompt suspicion of an *V. vulnificus* infection [3]. Aspirate from the skin lesions and blood cultures can demonstrate the characteristic bacillus. Antibiotic treatment must be instituted immediately due to high case fatality rates (CFR): a 24 h delay in starting therapy has been associated with a 33 % CFR and delays of more than 72 h with a 100 % CFR [118].

The US Centers for Disease Control and Prevention (CDC) recommend third-generation cephalosporins, specifically ceftazidime, plus doxycycline as the initial empiric treatment in suspected cases. In children, in whom doxycycline and quinolones are contraindicated, and in cases of antibiotic sensitivities, aminoglycosides and trimethoprim plus sulfamethoxazole can be used. Early surgical debridement of the wound and monitoring for compartment syndromes are indicated and help to reduce the mortality rate.

11.5.6 *Streptococcus iniae*

This Gram-positive beta-hemolytic is recognized to be a major fish pathogen that can cause outbreaks of invasive disease in farm-raised fish.

The first human cases of *S. iniae* invasive infections were reported in 1996 in subjects who had recently prepared fresh, whole, farm-raised fish [119]. The patients had handled live or freshly killed fish, and developed cellulitis within 16–24 h of an

injury incurred while handling the fresh fish, especially tilapia. In all cases the *S. iniae* isolates were sensitive to various antibiotics, such as aminoglycosides, cephalosporins, macrolides, penicillins, and trimethoprim plus sulfamethoxazole [119].

11.5.7 General Management of Marine Injuries

All traumas and even minor abrasions incurred in a seawater environment should be regarded as potentially contaminated by the commonest sea microbes, such as the *Vibrio* species. All wounds must be treated with normal sterile saline solution. Devitalized tissues must be surgically excised. Foreign bodies must be removed. Wounds should be left open to heal by secondary intention. Tetanus prophylaxis is indicated after all marine injuries [3].

Travelers with known risk factors for more severe marine infections, including those with open wounds, liver disease, an impaired immune system, diabetes mellitus, hematological disease, and AIDS, should be warned of the risk of contracting a marine infection after exposure to sea fish, seawater, live or freshly killed seafood, and ingesting raw or undercooked seafood, especially oysters. Travel medicine practitioners should be alert to the risk of onset of infection after an injury sustained in seawater, especially *V. vulnificus* in the Gulf of Mexico, *C. violaceum* in the Western Pacific, and *Shewanella* species in the Mediterranean and Western Pacific. Antibiotic treatment should be instituted at the first clinical signs of impetigo, cellulitis, erysipelas, pyodermas or necrotizing soft tissue infections [3].

11.6 *Pseudomonas* Dermatitis

Pseudomonas dermatitis has been reported after exposure to contaminated water in heated swimming pools, whirlpools, and hot tubes, or related to wearing a diving suit, or leg waxing [120–130]. Other pathogenic events for this dermatitis that are probably underestimated are exposure during a shower/bath [131, 132], or to contaminated bathing sponges or bathing suits [133].

In the majority of cases the causal agent is *Pseudomonas aeruginosa*, a Gram-negative, asporogenic, aerobic, mobile bacillus. It can survive at temperatures ranging from 4 to 42 °C, but not at pH values below 4.5. The most frequently reported serotypes are 0:9 and 0:11 and, less frequently, 0:4 and 0:8 [120–123, 132]. Major reservoirs include freshwater and humid terrains, but it may also be present on plants and in artesian wells. *P. aeruginosa* does not generally belong to the normal skin flora because it is unable to withstand dryness [134]. A simple occlusion does not seem to foster the growth of skin colonies of *P. aeruginosa*, whereas they can grow after prior hydration and then occlusion of the skin, bringing on skin manifestations [135].

The water temperature, pH and chlorine content are important factors for the development of skin infections, since *P. aeruginosa* can survive in warm and alkaline waters, that are physical-chemical conditions with lower chlorine levels [136, 137].

Usually, the dermatitis presents as maculous, pruriginous, follicular and papulopustular lesions on the lateral surface of the trunk, in the axillary folds, hips, buttocks, and suprapubic region. The onset of the lesions occurs a few hours or days after exposure, and they may show a pale green fluorescence under Wood's lamp [138]. Owing to the release of exotoxins, the skin eruptions can be accompanied by general signs such as malaise, fever, nausea and vomiting, diarrhea, painful otitis, a sore throat and sore eyelids, painful swelling of the mammary glands with axillary adenopathy [130, 132]. The affliction is usually self-limiting and resolves in 7–15 days. A case of "whirlpool-dermatitis" with "hot hands" has recently been reported: a 15-year-old boy suffered the onset of painful nodules on the palms and pustules on the forearms, 2 days after bathing in a new whirlpool. In children and adolescents such nodular lesions can also involve the soles of the feet ("hot foot syndrome") [139]. In immunosuppressed subjects, the infection can evolve to ecthyma gangrenosum, with nodules or progressive cellulitis [140, 141]; if untreated, it may persist for 2 weeks or more.

From the pathogenic standpoint, the typical skin distribution of the eruption can be explained by a possible specific apocrine tropism of *P. aeruginosa* [140] or, in cases linked to wearing a diving suit, by hydration and occlusion mechanisms [127]. Apart from the possible apocrine tropism of the bacterium, some authors believe that an occlusive enhancement during the hours after exposure, linked to wearing clothes that normally adhere to the typical sites of the eruption, can transform a superficial infection into manifest disease [132]. It is well documented in literature that not all members of a family exposed to the same water will develop the disease [132, 142]. A relapse may occur in cases of continued exposure.

Differential diagnosis of *Pseudomonas* dermatitis must be made with insect stings, other infectious folliculitis forms and scabies. The bacillus can be isolated in wells and tap water, kitchen sinks, bidets, showers, and the deep end of swimming pools.

Should the eruption persist, or severe general symptoms develop, and in immunesuppressed subjects, antibiotic treatment must be administered: the first-line antibiotic is ciprofloxacin 0.5–1 g daily. In children and adolescents ciprofloxacin is not recommended but piperacillin 4 g/tazobactam 0.5 g twice daily can be prescribed [139]. In milder cases, topical use of antibiotics, such as gentamycin or polymyxin may be sufficient [130].

Apart from the clinical forms reported above, *P. aeruginosa* can induce other skin infections such as balanitis, omphalitis, "green nail syndrome", as well as wound infections [143].

For prevention purposes, pool maintenance staff should have an adequate knowledge of appropriate chlorine and pH levels and monitor them daily. The free chlorine residual level must be 0.6 mg/l or higher with a pH of between 7.2 and 7.8, or 1.5 mg/l or higher with a pH of between 7.8 and 8.2. To eliminate *Pseudomonas*, some authors recommend hyperchlorination, with a chlorine residual level maintained at 5 mg/l or higher for at least 72 h [123]. In Germany, the Federal Environment Agency publishes special hygiene requirements for public bathing establishments and their surveillance: for whirlpools, for example, a free chlorine content of 0.7–1 mg/l and a pH value of 6.5–7.8 are required [130].

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Aquatic Animals Inducing Mechanical Injuries

12

Vidal Haddad Jr.

12.1 Introduction

Injuries and envenomation caused by aquatic animals are nowadays a common event and they are caused by poisonous, venomous, and traumatogenic animals. The main aquatic animals that can cause trauma in humans are included in the Phyla Cnidaria (corals), Echinodermata (sea urchins), Crustacea (crabs and mantis shrimp) and Chordata (fish and reptiles) [1–5].

It is important to know that in the early stages of the injuries there will always be emergency situations for the victim, due to the pain and bleeding associated with the wounds. The pain can be very severe. Occasionally, there is risk of death of the victim.

12.2 Invertebrate Aquatic Animals

12.2.1 Phylum Cnidaria (Jellyfish and Portuguese Man-of-War)

The cnidarians present as main characteristics a gelatinous body and tentacles used to capture food. They pass by a dimorphic life cycle, with a free form of sexually reproduction (the medusa or jellyfish) and other fixed form that reproduces asexually, the polyps. Regarding the human injuries, there are four important classes: Anthozoa (corals and anemones, without the medusa stage) and Hydrozoa, Scyphozoa and Cubozoa (Cubomedusae).

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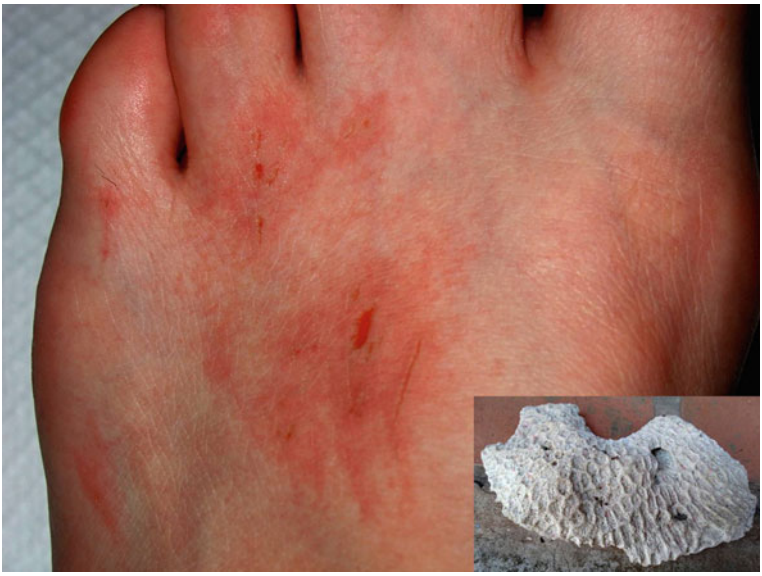

Fig. 12.1 Abrasions and wounds caused in a bather that crashed against a coral reef in a dive. In the detail: calcium carbonate body structure of a coral (Photos: Vidal Haddad Junior. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

If the injuries caused by jellyfish present typical lesions to help the identification of the agent by the Health professionals, the injuries caused by some hydrozoans, true corals and anemones show pain or burning sensation without a typical pattern. The skin marks are irregular, presenting an erythematous plaque with a rounded/oval shape or papules/vesicles dispersed in the area of contact [1–7]. These patterns of lesions are observed in divers that had contact with the underwater substrate.

True corals present minor toxicity, but can provoke extensive and deep wounds in bathers (Fig. 12.1) [1–7]. Cuts by corals predispose foreign body granulomatous reactions due the retention of fragments of the exoskeleton of the cnidarians, which is composed by calcium carbonate. Other serious complication is the bacterial infections after the traumas, which include the possibility of infections by highly pathogenic organisms, as *Vibrio vulnificus*.

The cuts and abrasions caused by corals, even superficial and small, need be intensively cleaned with soap and water. It is important the use of topical antibiotic (mupirocin or fusidic acid). If there is obvious infection, the care must be redoubled. The lacerated/deep/extensive injuries must have intensive care cleansing and systemic antibiotics (cephalexin or amoxicillin/clavulanate) for 10 days [1–7].

12.2.2 Phylum Echinodermata (Sea Urchins)

The echinoderms are marine animals that present varied body formats. The sea urchins show a round body covert by hollow traumatogenic spines composed of calcium carbonate.

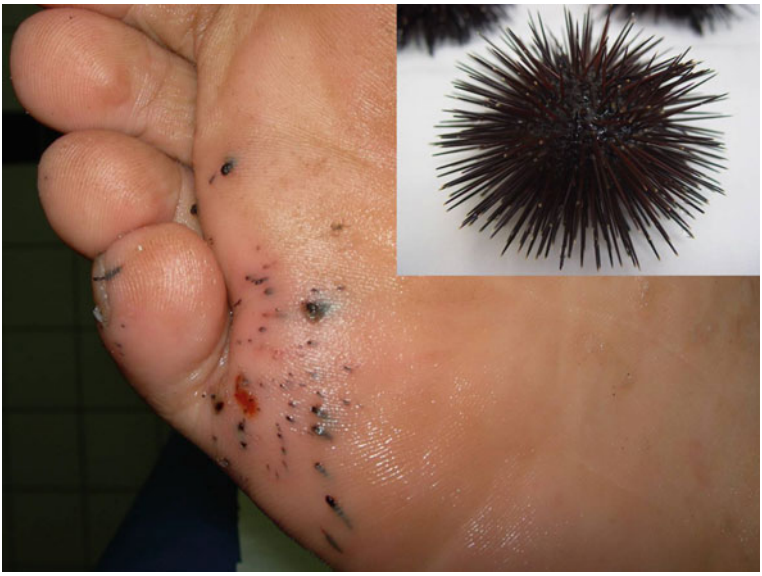

Fig. 12.2 Spines of a black sea urchin introduced at the foot of a bather. This species (*Echinometra lucunter*) does not cause envenomation, and injury presents traumatic nature (Photos: Vidal Haddad Junior. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

The majority of the injuries caused by sea urchins are traumatic, without envenomation (Fig. 12.2) and the spines can be visualized as small black, white, purple or green spots on the skin (Fig. 12.2). It is possible to extract fragments up to 3.0 cm of the site, but most of them are small pieces and sometimes there are only pigments at the site of entry of the spine. When the injury is mainly traumatic, the pain is moderate and it only occurs after compression [1, 2, 8–10]. The preferential affected regions are the plantar areas (Fig. 12.2). The spines can carry secondary infections, including tetanus. Most the spines is spontaneously eliminated, but the permanency of them may provoke nodules with erythematous and verrucous surfaces (foreign body granuloma) [1, 2, 8–10].

The bathers are the major victims of this type of injury, but it is common to see scuba divers presenting spicules or late nodules. The bathers present spines in the feet and suffer injuries when walking in shallow waters and small lakes between the stones of the beaches.

The removal of sea urchins spines of is made through a superficial scarification with a hypodermic needle of large caliber with use of the same needle for withdrawal of spines after local anesthesia. The fragments are brittle and can be difficult to remove, but it is fundamental to extract the large fragments to decrease the possibility of formation of granulomas. Many fragments are expelled by a local inflammatory reaction. All the venomous animals of this phylum have thermolabile venom, encouraging the use of immersion of the affected site in hot water, around 50 °C for 30–90 min, especially if there is spontaneous pain. This measure can be useful in injuries caused by venomous sea urchins and the starfish "crown of thorns". The envenomation caused by the irritating secretions of sea cucumbers should be

washed thoroughly and any secretion need be removed from the contact sites. When there is ingestion and oisoning, the gastric lavage and the symptomatic treatment are important [1, 2, 8–10].

12.2.3 Phylum Annelida (Leeches and Polychetas)

Leeches are worms that are included in the subclass Hirudinea. They are large worms, which can measure up to 15 cm, presenting wide distribution around the world. These worms are hematophagous presenting oral and caudal suckers and jaws with sharp teeth to attach to the victims and feeding. Allergic processes and infections may also occur in the point when the worm was fixed [1–5].

The marine worms (especially the marine brush worms or fire worms) have chitinous jaws with teeth and/or irritating body bristles. They can inflict painful bites in humans and the penetration of the bristles can provoke cutaneous edema, papules, itch, pain and skin necrosis.

The place bitten for a marine worm must be repeatedly washed with clean water. Topical antibiotics are useful to prevent bacterial infections.

12.2.4 Phylum Mollusca (Octopuses and *Conus* Snails)

The mollusks are organisms that can present a shell to protect their soft body, but not all have shells. Cephalopod mollusks are marine animals and include squids, octopuses, cuttlefish, and nautiluses. Octopuses present a horny "beak" used to capture prey that can inflict lacerations to victims (especially fishermen and divers).

An injury caused by the "beak" of an octopus in the hand of a patient provoked an area of induration and erythema about 8.0 cm which persisted for weeks [11]. Suckers of tentacles of octopuses can cause traumatic purpura by the strong suction (Fig. 12.3) [12].

12.2.5 Phylum Crustacea (Blue Crabs, Crabs, Shrimps, Prawns, Barnacles, Lobsters and Mantis Shrimp)

The crustaceans do not cause envenomations by inoculation of toxins. The traumatic injuries are the rule, mainly lacerated wounds caused by their claws. The injuries are not severe and rarely provoke great lacerations or intense bleeding. The mantis shrimp is a large and aggressive crustacean (up to 30 cm), who's sharp claws can cause serious injuries, receiving the name of *thumbspliter* in points of the Caribbean [1–4]. It is possible to observe cuts caused by barnacles, which live fixed to rocks and woods and have sharp edges, provoking incise wounds mainly in the hands and foot of the victims [1–4].

The treatment of injuries caused by crustaceans is done by intense washing the wound, tetanus vaccination and topical or systemic antibiotics if infection occurs.

Fig. 12.3 Ecchymosis caused by the suckers of an octopus on the arm of a researcher, when the animal's capture (Photo: Rafael Gregati. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

12.3 Injuries by Vertebrate Aquatic Animals

12.3.1 Phylum Chordata (Fish and Reptiles)

12.3.1.1 Traumatogenic Fish

Marine Fish

Although any fish can cause injury to humans through spines, stingers and teeth, some species are more related to traumatic injuries. The marine environments present fish of large sizes, which can cause severe injuries in fishermen and divers. In these cases does not occur envenomation, but there may be lacerations, severe bleeding and late bacterial and fungal infections. In this group are included the sharks (various species), barracudas (*Sphyraena* genus), the needlefish (Belonidae family), the swordfish (*Trichiuris lepturus*) and the triggerfish (*Balistes* sp.) [1–5].

The mechanisms of aggression are through collisions with the bodies of the fish, bites and wounds caused by spines and stingers. Although implicated in human deaths and exploited exhaustively by the media fears, attacks (a questionable term under behavioral point of view) by large sharks are unusual episodes, even in some areas, like the Australia, USA Pacific coast, South Africa and the metropolitan area of Recife town, northeast Brazil, where they are highly publicized. Injuries inflicted by large shark bites are usually a serious accident and can cause death, especially

Fig. 12.4 The tiger shark (*Galeocerdo cuvier*) is one of the species associated with attacks in humans. In the detail: scar after the bite of a tiger shark in a fisherman (Photos: Vidal Haddad Junior. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

those performed by the species *Carcharinus leucas* (bull shark), *Galeocerdo cuvier* (tiger shark) and *Carcharodon carcharias* (great white shark) (Fig. 12.4) [1, 3, 13].

The traumatogenic fish are the groupers and snappers (*Epinelephus*, *Lutjanus* and *Mycteroperca* genera), which includes the Jewfish or Golliath Grouper (*Epinelephus itajara*), a giant up to 450 kg weight and the snook (*Centropomus* sp.) that has sharp blades in both sides of the operculum [1–5, 14]. Other potentially vulnerant fish are the swordfish (*Xiphias* genus), the sailfish (*Istiophorus* genus) and the blue and the white marlin (*Makaira nigricans* and *Tetrapturus albicus*). These fish present a highly six traumatogenic "beak", used for capture prey and for their defense [15].

Freshwater Fish

The piranhas are the main fish associated with traumatic lesions in freshwater environments (Fig. 12.5), but despite the folklore surrounding them, there are no documented attacks of shoals to humans. There are various genera of piranhas in South America. The *Serrasalmus* genus occurs in all regions of Brazil, but the most important genus is the *Pygocentrus*, present especially in the Amazon region and in the Brazilian Pantanal. The rare attacks caused by shoals appear to be associated with this genus. Piranhas are voracious carnivores that act as decomposers in the Nature and are really attracted by blood in the water and agitation of the victim, but attacks by shoals

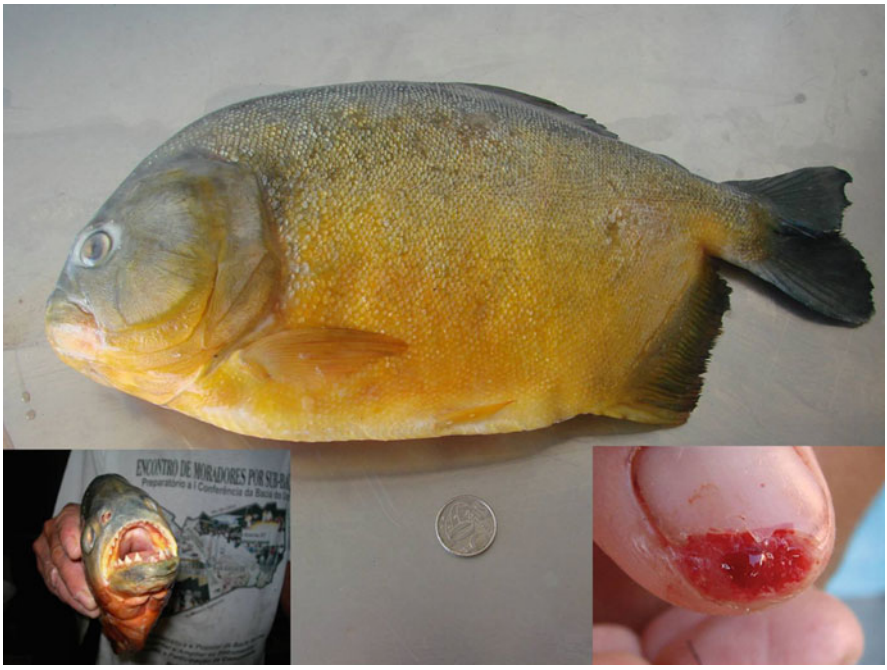

Fig. 12.5 Red piranha (*Pygocentrus nattereri*) and details of the teeth of the fish and bite at the thumb of a amateur fisherman (Photos: Vidal Haddad Junior. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

are rare. The real profile of attack by piranhas shows single deep bites in humans. The bite is oval or rounded and causes laceration and bleeding (injury in piecemeal) (Fig. 12.5). These bites are seen in areas of bath formed by the damming of some rivers and ponds, and occasionally in amateur and professional fishermen [1, 3, 16].

In truth, almost all species of fish have the potential to cause injuries in the hands and feet of fishermen, especially in the amateur fishermen. The injuries are more probable to occur caused by the "sportive" fish, as catfish and great fish with sharp teeth [4, 5].

The piraíba is the largest freshwater fish in South America and can reach 3 m in length and over 200 kg in weight [4, 5]. These fish are accused of devouring human beings in the Amazon region, especially children swimming in deep waters. There are descriptions of human beings devoured by big catfish in Asian rivers and even in Eastern Europe, through documented cases of children swallowed by the wels catfish or sheatfish (*Silurus glanis*), the large European catfish capable of measuring 5 m and weigh 350 kg [1, 3].

The true *candirus* also belong to Siluriform order (catfish). These fish are hematofagous and have a cylindrical and elongated body, with thin and sharp teeth [4, 5]. They parasitize the gills of larger fish and probably due to the sensitivity to the smell of ammonia or blood in the water, the candirus may be attracted and invade the urethra or other human natural orifices (Fig. 12.6). The fish then fix its intraopercular

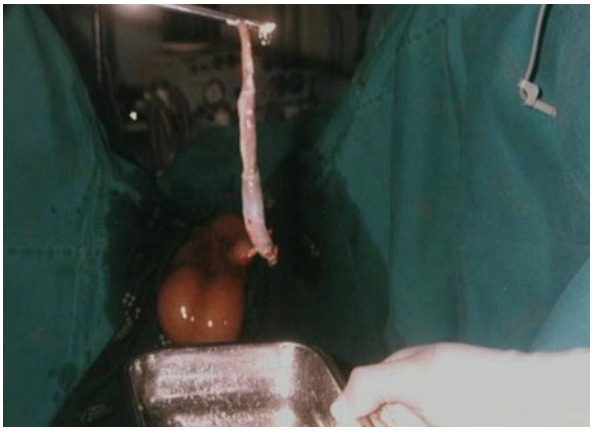

Fig. 12.6 This rare image shows an extraction of a small catfish (candiru) of the urethra of a bather, in the Amazon region (Photo: Anoar Samad, Manaus, Brazil. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

"claws" (the odontoideos) and cannot retreat them, dying and causing obstruction and uremia or severe bleeding that can cause the death of the victim. Treatment is always surgical and candirus are much feared by riverside communities and swimmers in Amazonia [1, 3].

The electric eel (*Electrophorus electricus*) is capable to apply electric shocks up to 600 V in animals and humans in the water. Although the voltage is hardly capable of killing a human being, this can drown by contractures and muscle stiffness due to electric shock. The fish is feared on the occurrence areas in the Amazon [1, 3].

12.3.1.2 Alligators, Crocodiles and Snakes

The reptiles have aquatic and semi-aquatic location. All species of crocodiles and alligators may cause human injuries due to their teeth, tail and the speed of the movements in the water. Most accidents and attacks occur in Amazon, Nile River and Indo-Pacific, due the species *Melanosuchus niger* (the jacaré-açu or black alligator), *Caiman crocodilus* (the jacaretinga or speckled caiman), *Alligator mississippiensis* (the American alligator), *Crocodylus niloticus* (the Nile crocodile) and the *Crocodylus porosus* (Saltwater, Estuarine or Indo-Pacific crocodile) (Fig. 12.7) [1, 3, 17].

Injuries caused by crocodiles and alligators are very severe, provoking lacerations and tearing of tissues, profuse bleeding and serious infections, caused by the animal's mouth flora (Fig. 12.7). The attacks are mainly reported in fishermen pulling the net or diving to get objects, bathers or people working in the river banks. The injuries caused by crocodiles and alligators have the same spectrum of the injuries caused by the sharks, and are potentially fatal, due the complications described above, needing similar therapeutic approach.

There are various venomous and non venomous snakes that live in aquatic and semi aquatic environments. The anacondas of the Boidea family are not aggressive snakes as represented in movies or in the legends, but occasionally can wound humans, in provoked situations. These snakes have a large size (up to about 7 m) and the ability to suffocate their prey and then swallow them whole, but they rarely attack humans [1, 3].

Fig. 12.7 The lesions caused by crocodilian's bites are highly destructive and cause severe bacterial infections. The images are of a caiman and a bite in a fisherman with perforations, lacerations and secondary infection (Photos: Vidal Haddad Junior. Published with kind permission of © Vidal Haddad Jr., 2016. All Rights Reserved)

Conclusions

Aquatic animals can provoke traumas of diverse severity, since minor wounds to fatal lesions. The injuries can present important bleeding and aggression to internal organs just after the contact and late complications, which also can be severe, as infections by bacteria and retention of fragments of rays and stingers [1, 3, 18–21]. All the lesions caused by aquatic animals should be examined with attention.

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Aquatic Skin Diseases from Chemical and Physical Causes

13

Domenico Bonamonte, Pietro Verni, Paolo Romita, and Gianni Angelini

Apart from the diseases due to biotic noxae described up to now, there are various other dermatological conditions connected in some way with salt- or freshwater contact or with aquatic activities (Table 13.1) [1, 2]. No analysis will here be made of clinical forms favored, induced or aggravated by exposure to the sun, that is of course inevitable in subjects involved in aquatic activities for long and even short periods, nor of those caused by non aquatic biotic agents.

13.1 Aquagenic Urticaria

This form of urticaria, first described by Shelley and Rawnsley in 1964 [3], is induced simply by skin contact with the water, regardless of its physical and chemical properties (source, salt content, temperature) [4–11]. The affliction is often misdiagnosed. The onset is generally observed in young adults, with a mean age of 18 years, and is five-fold more frequent in the female sex [7, 12–14]. Sometimes, several members of the same family are affected [3, 15–17]. There are no data available on the evolution and duration of the disease, although many patients have referred a very long course, even 20 years.

The onset of the urticarial affection occurs 3–10 min after any type of skin contact with water; it reaches a peak in about 30 min and dies down again after a further

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Table 13.1 Some skin diseases of aquatic origin

General
Sunburn
Aquagenic urticaria
Aquagenic pruritus
Cold urticaria
Contact dermatitis
Swimming costume
Diving equipment
Dry skin (swimmer's xerosis)
Aquagenic skin wrinkling
Seawater
Immersion syndrome
Abrasive effect
Surfer's nodules
Otitis externa
Aquagenic urticaria
Freshwater
Swimming pools
Mycosis
Verrucae
Chlorine irritation
Chapping in atopic subjects
Aquagenic acne
Greenish hair tinge
Hair bleaching
Chemical conjunctivitis
Otitis externa
Swimming pool granuloma
Jacuzzi/hot tubs
Folliculitis induced by *Pseudomonas*
Sauna
Miliaria
Tinea versicolor
Shower
Aquagenic pruritus
Sub-aqua activities
Otitis externa
Intertrigo
Staphylococcal infections
Burns
Linear abrasions from wetsuit folds
Pruritus and erythema from decompression
"Napkin rash" type dermatitis

30–60 min. The exposed skin sites are generally refractory to stimuli for several hours. The raised lesions are not clinically distinguishable, as regards shape and distribution, from those of cholinergic urticaria (with which they can coexist), being punctiform, with a diameter of 2–3 mm, surrounding the hair follicles (Fig. 13.1). These small wheals, that are intensely itchy, appear on the areas in contact with the water and if the whole body is exposed, mainly on the neck and trunk, and to a lesser

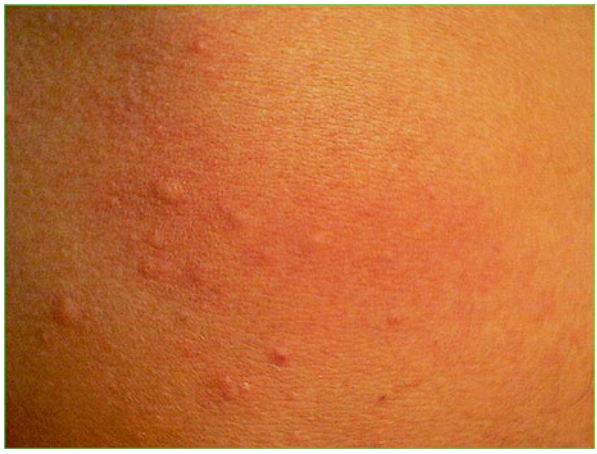

Fig. 13.1 Aquagenic urticaria: erythemato-oedematous punctiform wheals

degree, the shoulders and sides. The palms of the hands and soles of the feet are not affected. Alcohol and other organic solvents applied to the skin do not cause wheal formation [17]. Systemic reactions are rarely reported [18, 19].

The pathogenic mechanism is unknown. Several mechanisms seem most likely to be implicated. An interaction of water with a component within or on the stratum corneum or sebum, that may generate a toxic compound, has been suggested: absorption of this substance would lead to degranulation of the perifollicular mast cells and histamine release [3]. However, removal of the stratum corneum seems to aggravate the reaction, while pretreatment with organic solvents enhances wheal formation in contact with water [6]. Czarnetzki et al. have hypothesized the existence of a water-soluble antigen at the epidermal layer that, when absorbed in the derma, causes the release of histamine by mast cells [7]. Other authors have recently reported that 5 % saline was more effective than distilled water in eliciting the urticarial eruption. They proposed that the salt concentration and/or water osmolarity may influence the pathogenic mechanism of aquagenic urticaria, possibly by enhancing the solubilization and penetration of a hypothetical epidermal antigen, in the same way as has been postulated for the enhancement of organic solvents [20]. As regards the ionic concentration of water, Gallo and Coll. reported six young women with urticarial rashes triggered mostly by sea bathing, characteristically localized on the inferior facial contours and neck. The patients underwent challenge tests with tap water and with a hypertonic NaCl water solution (3.5 %, iso-osmolar with seawater) at room temperature, by means of applying soaked compresses for 20 min to the mandibular region or neck, and a positive response was elicited [21, 22]. The authors concluded that what they observed may be a distinct subtype of aquagenic urticaria with a peculiar, sometimes exclusive, localization [21, 22]. Another proposed chemical mediator in aquagenic urticaria is acetylcholine, in view of the ability of the acetylcholine antagonist, scopolamine, to suppress wheal formation when applied to the skin before water contact [6]. Methacholine injection testing is negative in patients with aquagenic urticaria, while it is often positive in cholinergic urticaria [16]. Serum histamine levels will differ from case to case [16].

Table 13.2 Provocation tests of some types of physical urticaria

Physical urticaria	Diagnostic test
Aquagenic urticaria	Wet compresses (35 °C) at room temperature to the upper body for 30 min
Cold urticaria	An ice-cube in a thin plastic bag applied to the forearm for 5–10 min
Cholinergic urticaria	Exercise test until sweating Warm bath (43 °C)
Heat urticaria	Heated cylinder (50–55 °C) applied to the upper trunk for 30 min

Table 13.3 Skin reactions directly (*) or indirectly (°) (pseudo-aquagenic reactions) due to contact with water

Reaction	Stimulus
Aquagenic pruritus (*)	Water
Aquagenic urticaria (*)	Water
Cholinergic urticaria (°)	Bathing or swimming in hot water
Acquired cold urticaria (°)	Cold water
Localized heat urticaria (°)	Hot water
Symptomatic dermographism (°)	Shower jet, towel friction
Polycythaemia rubra vera (*)	Water

The standard diagnostic test is application of 35 °C water compresses to the patient's chest for 20–40 min. It is best to use a thermometer on the site of the test to make sure of the correct temperature, in order to be able to differentiate between aquagenic, cholinergic, cold and heat urticaria (Table 13.2). A possible association with dermographism, another type of physical urticaria, should be taken into account. If only itching develops, without skin lesions, then a diagnosis of aquagenic pruritus can be made.

Differential diagnosis must also be made with other complaints induced by water, even if not always directly (Table 13.3). Apart from aquagenic urticaria, other cases of urticaria from physical causes develop only after contact with certain types of water, which is not the true cause. Pre-treatment of the skin with vaseline or lanolin prevents the eruption, perhaps by preventing the formation of the causal molecule [23].

The treatment of choice is antihistamines, although variable responses are obtained [16, 19]. Refractory cases can treated with ultraviolet (UV) radiation (psoralen plus UVA and UVB therapy), either alone or in combination with antihistamines. It has been hypothesized that the effect of UV therapy is mediated by inducing a thickening of the epidermis thereby preventing water penetration, or by interaction with dendritic cells, or a decreased mast cell response [16, 24].

13.2 Cold Urticaria

This consists of the appearance of pomphoid lesions on skin or mucosal sites after contact with cold objects, water, or air, or after the ingestion of cold drinks or foods. Among the forms of physical urticaria, cold urticaria can present in various guises: familial or acquired, immediate or delayed, localized or systemic, primitive or

Table 13.4 The various forms of cold urticaria

1. Familial
Localized (delayed, after 9–18 h)
Systemic (immediate)
2. Acquired
Localized
Immediate
Delayed
Cholinergic cold dermographism
Due to localized reflex
Systemic
Due to cold
Due to generalized reflex
Cholinergic cold urticaria
Idiopathic
Secondary
Viral infections (respiratory virosis, HIV, infectious mononucleosis)
Bacterial infections (borreliosis, hepatitis, *Helicobacter pylori* colonization, acute toxoplasmosis)
Insect stings
Drug intolerance or allergy (penicillin, griseofulvin, oral anticoagulants, diazepam, alprazolam)
Atopy
Coeliac disease
Diseases featuring cryoglobulins, cryofibrinogen or haemolysins due to the cold
Autoimmune diseases (connectivitis, thyroiditis, erythema nodosum)
Cold paroxystic haemoglobinuria
Myeloproliferative diseases (myeloma)

secondary (Table 13.4). The incidence ranges from 1 to 7 % of all physical forms, depending on the various case series [8–10].

The acquired idiopathic form is the most common and the familial form the rarest. Rare forms of atypical contact urticaria also include delayed cold urticaria, where localized whealing appears 12–48 h after the cold exposure, and cold cholinergic forms (in which punctiform pomphoid lesions, 1–2 mm wide, develop after physical exercise in a cold environment, whereas no clinical lesions appear after physical exercise in a warm environment or after exposure to a cold environment but no physical exercise). Another rare form is cholinergic cold dermographism (linear pomphoid lesions appear if the patient is exposed to the cold during or immediately after applying appropriate stimulation; exposure to the cold without such stimulation, or alternatively the application of stimulation in a warm environment, do not elicit any response) (Table 13.5).

Acquired cold urticaria may be secondary to various conditions: viral infections (mononucleosis), infections such as HIV, syphilis, hepatitis, parasites and bacterial infections. In addition, cryoglobulinemia with or without malignancies, reactions to insects, intolerance or allergy to drugs (penicillin, griseofulvin, diazepam, alprazolam),

Table 13.5 Differential diagnosis of the various types of cold urticaria

Clinical forms	Diagnostic
Acquired cold urticarial	A melting ice cube in a thin plastic bag
Atypical acquired cold urticaria	Negative immediate contact stimulation test
Delayed cold urticaria	Delayed urticarial lesions up to 24 h after testing
Cold-dependent dermographism	Urticarial lesions after stroking pre-cooled skin
Cold-induced cholinergic urticaria	Urticarial symptoms by exercise in cold environments
Hereditary subtipes of cold urticaria	
Delayed cold urticaria	Negative immediate contact stimulation test; delayed urticarial lesions after 9–18 h; the lesions typically resolve into hyperpigmentation
Familial cold auto-inflammatory syndrome	Episodic urticarial-like lesions associated with conjunctival injection, fever and other systemic inflammatory symptoms; often delayed lesions (1–2 h)

Modified by Magerl and Coll. [25]

coeliac disease, hypothyroidism, and leukocytoclasic vasculitis may contribute to a similar clinical presentation [26–29].

The onset of acquired idiopathic cold urticaria can occur at any age but it particularly affects young adults, especially the female sex. The classic picture is the development of pomphoid lesions in sites exposed to contact with cold objects, foods, air conditioning or to sudden changes of temperature. Uncovered skin zones seem to be much more sensitive to stimuli. The skin wheals usually develop within a few minutes and persist for 1–2 h. The oral mucosa and tongue may also be affected. In more severe cases with diffuse manifestations, systemic symptoms such as weakness, breathlessness, headache, tachycardia and vertigo can develop. Sometimes even shock symptoms can develop immediately after swimming and it is very important to warn patients suffering from cold urticaria of the dangers of swimming [28, 30–34].

Pathogenic considerations should be made bearing in mind that cold urticaria can also be passively transferred to healthy subjects by means of the Prausnitz-Küstner test; this passive sensitisation has to do with serum IgE, and sometimes IgM, IgG or IgA [35]. It has been suggested that subjects with cold urticaria develop autoantibodies of IgE type, but also IgG, against skin antigens prevalently associated with the skin mast-cells. Anti-nuclear serum autoantibodies (acting against the B laminar fraction) have occasionally been demonstrated [36]. The efficacy of antibiotic treatment, demonstrated in a high percentage of patients, has recently given rise to the suggestion that acquired forms may have a microbial origin, possibly of a subclinical nature [37].

Histamine, a chemotactic neutrophilic factor, and some chemotactic eosinophilic factors, are among the main mediators of cold urticaria. In the acquired idiopathic form, tests of immersion in cold water have, instead, elicited a decreased chemotactic neutrophilic index; this event, described as "the granulocytic inactivation phenomenon" seems to be highly specific and is not present either in chronic urticaria or in other forms of cold urticaria [9]. Quinines and some derivatives of arachidonic acid (PGD2, LTE4) sometimes appear to be increased; they may amplify the biological effect of other mediators [38–41].

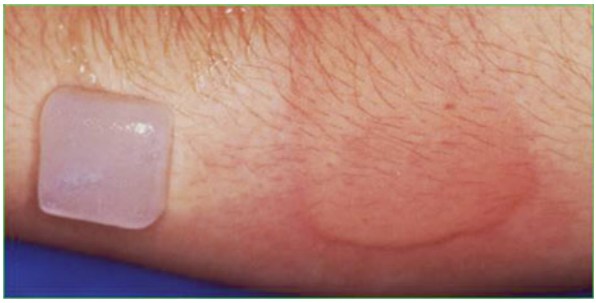

Fig. 13.2 Itchy skin wheal on the site of ice cube test

The observation that topical capsaicin, an antagonist of substance P released at the level of the nerve terminals, can inhibit local reactions to contact with the cold implies that this neuropeptide may play an important role in triggering the complaint. On the basis of these data, a defective thermal and/or vasomotor regulation of central origin may be postulated [9]. During severe episodes of cold urticaria, associated with systemic symptoms, high serum levels of TNF-α, a powerful pro-inflammatory cytokine, have been demonstrated [42].

Histologically, the inflammatory dermal infiltrate features two different cellular patterns, one with a predominance of neutrophils and the other of lymphocytes. This is likely the result of two different stages of the same process: the neutrophils may prevail at first, and then the lymphocytes take over [43].

Cold urticaria can be associated with chronic urticaria or other urticarial forms with physical causes, especially dermographism and cholinergic urticaria. The diagnosis is often confirmed by the ice-cube test: a melting ice cube in a thin plastic bag (to avoid cold damage to the skin). When applied to the flexural surface of the forearm for 5–10 min, an itchy skin wheal will develop on the site of the test, that should be assessed 10 min after removing the ice cube (Fig. 13.2).

A positive ice cube test confirms the presence of cold urticaria and should prompt further tests to determine individual temperature and/or stimulation time thresholds [25, 28, 29, 44]. For this purpose, a Peltier element-based electronic provocation device (TemptTest®, Emo Systems GmbH, Berlin, Germany) has been designed, that allows simultaneous skin exposure to 12 different temperatures ranging from 4 to 42 °C, in a standardized and reproducible manner [45]. Critical temperature threshold tests enable patients to be better instructed on how to avoid situations that will cause them urticaria. They also gauge how effectively patients are protected by therapy, and allow individualized treatment optimization [46]. Laboratory tests are of limited value in most cases of cold urticaria [47]: therefore additional tests should be limited to those required to exclude underlying diseases and identify associated diseases suggested by the clinical history. The ice cube test is negative in familial and cholinergic cold urticaria forms (Table 13.4).

The clinical course of acquired idiopathic cold urticaria is long, ranging from 2 to 10 years.

As regards treatment approaches, the patient must first of all be carefully informed about all the possible triggering factors and especially the danger of

swimming in cold water (in any case, such patients must never swim unaccompanied). Threshold testing (e.g. using TempTest ®) can help patients to recognize and control cold exposure in their daily life [20]. Treatment with antihistamines is the most common and most efficacious symptomatic therapy [48, 49]. In many patients, however, very high dosage antihistamines, up to four times the daily recommended dose, are needed to obtain a satisfactory response [49, 50]. In such cases unsuccessful treatment can severely harm the patient's quality of life, and indeed these patients are also at risk of developing life-threatening complications, including suffocation from pharyngeal angioedema induced by cold foods or beverages, and drowning after experiencing shock-like symptoms during aquatic activities. For these reasons it is essential to establish an optimal antihistamine treatment regimen for each patient. Other therapeutic options in severe cases or those with a poor response to antihistamines include leukotriene antagonists [51], cyclosporin [52], anti-IgE [53], and corticosteroids [54]. Successful treatment has recently been reported with some TNF-alpha inhibitors, such as etanercept [55] and omalizumab [56]. Other drugs, such as cyproheptadine, ketotifen, oral cromoglycate and H2-blockers, are not effective [57].

Patients suffering from severe forms of cold urticaria (at risk of oropharyngeal edema or shock-like reactions) must carry an emergency medication kit containing corticosteroids, antihistamines and epinephrine (adrenaline) injector, and be properly instructed as to how to use it.

In some cases antibiotic treatment may have to be considered, as this has sometimes proven useful even in the absence of a manifest infection. This will consist of high doses of penicillin (e.g. oral phenoxymethylpenicillin 1 MU/day for 2–4 weeks, or intramuscular benzylpenicillin 1 MU/day for 20 days) and tetracyclines over 2–4 weeks (e.g. doxycycline 200 mg/day for 3 weeks) [44, 58].

Patients must also protect themselves against cold air by wearing appropriate clothing, including gloves and woolen socks. It may be possible to induce tolerance (hardening) to the cold [59]. Clearly, the induction of tolerance must be done very cautiously at the beginning, under supervision, because of the risk of systemic reactions, and the patient should be hospitalized. A very good patient compliance is needed (involving as it does cold showers several times daily on an increasing body surface and at decreasing temperatures; the initial temperature of the cold water must be 5 °C above provocation), and the patient should know that discontinuation will cause the re-presentation of the symptoms [59]. Treatment with topical capsaicin, the principle ingredient of chili peppers, has been shown to prevent symptoms [59]. Capsaicin induces a depletion of neuropeptides from sensory nerve fibers, that might contribute to the onset of the symptoms, although a pathogenic role in cold urticaria has still to clarified [60].

Familial cold urticaria has a dominant autosomal transmission. Pomphoid lesions appear, associated with burning rather than itching, between 30 min and 3 h after exposure to cold winds. Atmospheric cold is a typical trigger, but handling cold objects or ingesting cold food or beverages can also bring on symptoms. The ice-cube test is negative. General symptoms often develop: shivering, fever, muscle and joint pain, headache. The symptoms are present

from birth and persist throughout life. The pathogenic mechanism [61–64] is not clear, and the passive transmission test is negative. Leukocytosis is generally present and skin biopsy reveals a polymorphonuclear infiltrate. Diagnosis is on the basis of a positive family history, onset at birth, a negative ice-cube test and the presence of systemic signs. Daily antihistamines have been reported to decrease symptom severity. In some cases, stanozolol, an attenuated androgen, can help [65].

13.3 Aquagenic Pruritus

Showering or bathing are very enjoyable daily interludes, essential for hygiene and sometimes as a form of treatment. However, some subjects suffer acute pruritus as a direct consequence of bathing. In some of them, contact with water is an indirect stimulus (acute pseudo-aquagenic reactions) (Table 13.3), while in others the pruritus is a direct local effect of skin contact with water, as in aquagenic urticaria (featuring objective signs), and aquagenic pruritus (no objective signs).

The latter, in turn, may be classified as:

1. true aquagenic pruritus (Table 13.6);
2. senile aquagenic pruritus (Table 13.7);
3. aquagenic pruritus, observed in 40–50 % of patients with polycythaemia rubra vera (Table 13.8).

True aquagenic pruritus, first reported in 1970 by Shelley [66], features intense pricking or burning pruritus, that develops after contact with water,

Table 13.6 Diagnostic criteria for aquagenic pruritus

1. Intense, recurrent itching after contact with water, regardless of temperature
2. Itching onsets within a few minutes after contact with water and may persist for up to 2 h
3. No visible skin signs
4. Cold aquagenic cholinergic heat and cold localized heat urticaria forms and symptomatic dermographism have been excluded
5. Polycythaemia rubra vera has been excluded

Table 13.7 Diagnostic criteria for senile aquagenic pruritus

1. Especially in the female sex (75 %), in subjects over 60 with pale skin
2. Excessively dry skin
3. Intense itching after drying
4. The intensity of the itching sensations is proportional to the duration of exposure to water and the degree of skin dryness
5. Triggering factors: contact with water and consequent dryness of the skin, variations in temperature, friction
6. The itching starts on the legs or forearms, then spreads and persists for 10–60 min
7. The intensity of the itching increases with age and during the winter

Table 13.8 Diagnostic criteria for aquagenic pruritus associated with polycythaemia rubra vera

1. Only subjective signs as in aquagenic pruritus
2. Specific symptoms of the disease
3. More frequent onset of spontaneous itching
4. Itching generally depends on the temperature of the water
5. Hot baths elicit worse itching than cool baths
6. Cooling of the skin provokes itching
7. The intensity of the itching is not correlated with the severity of the disease

Table 13.9 Diseases which may cause aquagenic pruritus

Dermatological diseases	Juvenile xanthogranulomas, urticaria factitia
Infectious diseases	Hepatitis C
Intestinal diseases	Lactose intolerance
Solid neoplasms	Uterine cancer
Haematological and lymphoproliferative diseases	Polycythemia vera, haemochromatosis, acute lymphoblastic leukemia, essential thrombocythemia, myeloblastic syndrome, T-cell non-Hodkin's lymphoma
Drugs	Antimalarials (chloroquine, hydroxychloroquine), bupropion, clomipramine

regardless of temperature, with no apparent objective signs. It lasts between 10 and 120 min. In some subjects it manifests during bathing, while in others the onset occurs immediately after they come out of the water. In almost all cases the legs and thighs are mainly affected, although the trunk and arms may also be involved [8, 67].

There are few studies of the prevalence and incidence of aquagenic pruritus: in small patients cohorts the incidence ranged from 1.4 % [68] to 4.5 % [69], and up to 23.8 % in a cohort of young Nigerians [70]. The affliction is often reported as an accompanying or premonitory symptom in various underlying systemic diseases (Table 13.9) [71–74]. The onset of aquagenic pruritus is observed above all in subjects with no underlying disorder; these forms, of uncertain origin, have been subdivided by some authors into two subgroups depending on the patients age, young or elderly [68, 75].

The most common association is with polycythemia rubra vera (PcV), first reported in 1985 [76, 77]. Pruritis, that may precede the onset of PcV by as many as 13 years [72], is present in 40–50 % of patients with PcV. A mutation of the janus kinase 2 enzyme (JAK2) has been found to be strongly associated with aquagenic pruritus in PcV patients; the mutation affects a valine-phenylalanine exchange at position 617 (JAK2617 V>F) [78]. Subjects with a homozygotic mutation have a significantly higher rate of aquagenic pruritus than those with a heterozygotic mutation [78].

Drug-induced aquagenic pruritus seems to be rare; some antimalarial drugs (chloroquine, hydroxychloroquine) and anti-depressants (bupropion, clomipramine) have been implicated [74, 79, 80].

The mechanism of cutaneous induction of aquagenic pruritus is not well understood. Although both the release of histamine and mast-cell degranulation have been demonstrated, histamine does not seem to be the main mediator. Intradermal injections of acetylcholine do not reproduce the itching symptoms [74, 81, 82]. An increased fibrinolytic cutaneous activity has recently been shown, although the plasma fibrinolytic activity was within normal limits [81]. This increased fibrinolytic cutaneous activity can be blocked by ε-aminocaproic acid, suggesting that the increased activity may be due to an inherently increased plasminogen activity. Intradermal histamine and acetylcholine injections trigger an increased cutaneous fibrinolytic activity, which implies that the phenomenon may be secondary to histamine and acetylcholine release.

Aquagenic pruritus does not respond well to H1 and H2 antihistamines, that only partially relieve the symptoms. The most efficacious treatment, that can reduce symptoms up to 100 % in 50 % of patients, is UV therapy [67, 73, 83, 84], which acts by minimizing the blood levels of eosinophils. Both systemic and bath PUVA (also reducing PUVA to one to two times a week), and the combination of UVA/UVB, as well as a narrow band and broadband UVB therapy, can reduce pruritus. Other drug options include anticonvulsant drugs (pregabalin) [74], propranolol, a beta-receptor antagonist of adrenaline [85], and atenolol, a long acting beta-1 selective adrenergic receptor blocker [82]. Emollients and alkalization of bath water (pH 8), by adding sodium bicarbonate (0.1–0.5 kg/bath), reduce the itching symptoms in some cases.

13.4 Contact Dermatitis

Contact dermatitis caused by the swimming costume is rare but possible, due to sensitisation to the elastic (rubber additives) or dyes.

Contact dermatitis from diving equipment can be observed, due to professional or sports activities, and induced by the mask (Figs. 13.3 and 13.4), goggles, snorkel, fins and rubber wetsuits [86–89]. The sensitising substances responsible are mercaptobenzothiazole, thiourams, dithiocarbamates, paraphenylenediamine, thiourea compounds, formaldehyde, butylphenolformaldehyde resin, isopropyl-phenyl-paraphenylenediamine, and carbamates.

In sensitized subjects, snorkels can also cause inflammation of the mouth, that generally starts with an intermittent, mild burning sensation associated with ingesting hot drinks or spicy foods.

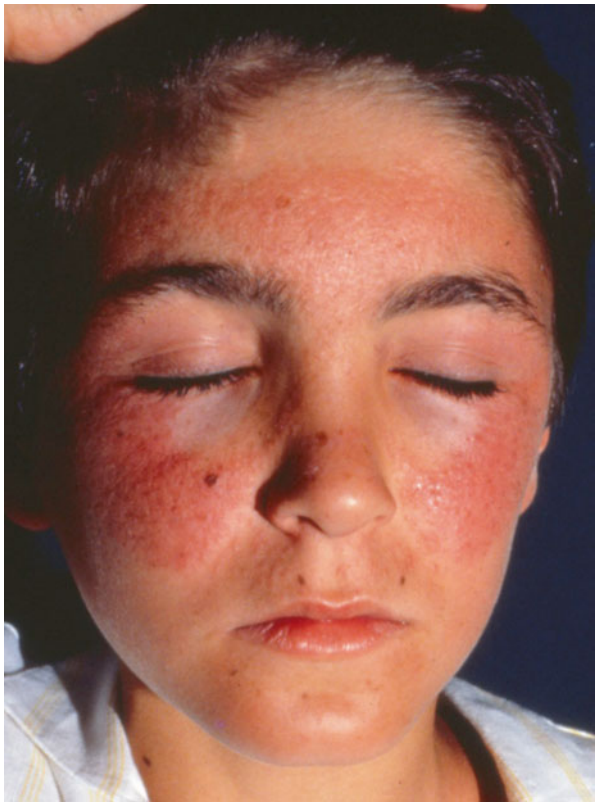

Fig. 13.3 Allergic contact dermatitis to rubber mask

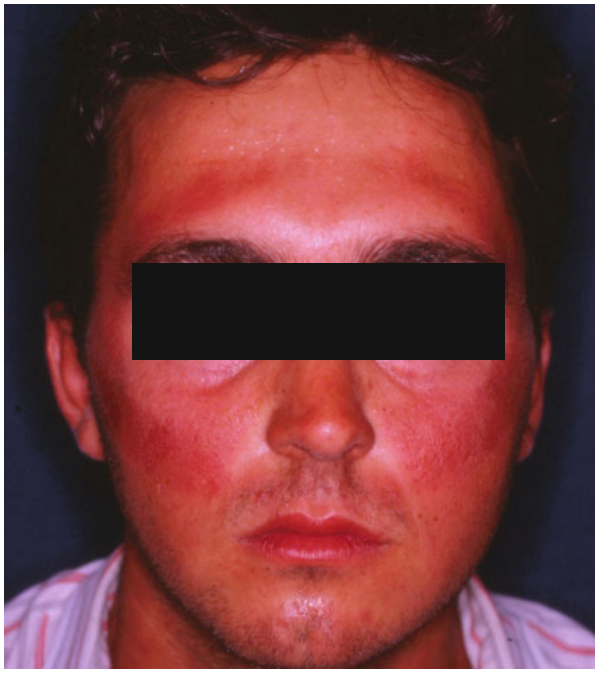

Fig. 13.4 Allergic contact dermatitis to rubber mask

13.5 Saltwater Dermatitis

Prolonged immersion in seawater causes electrolytic alterations due to percutaneous absorption (immersion syndrome). Occasionally, a skin peeling effect may appear where the swimming costume hugs closely, that may even evolve into ulceration due to the combination of friction and the abrasive effect of the salt.

Surfer's nodules are hard and indolent and onset at the level of the anterior tibial region. They are reversible and caused by continual contact with the board. These pretibial fibrotic masses may be dermal or hypodermal, and deformity of the underlying bone and calcifications can also ensue [90].

External otitis is an acute bacterial infection of the external ear fostered by the macerating effect of the water and the persistent humidity of this part. The clinical symptoms are pain, exudation, pruritus and sometimes fever and impaired hearing. The most common bacterial cause is *Pseudomonas aeruginosa*.

13.6 Freshwater Dermatitis

Swimming in chlorinated pools has a dehydrating effect on the skin and hair (anti-oil action) that is more evident in atopic subjects. Depending on the concentration, chlorine has a bleaching effect on the hair, which is most apparent in blonde subjects and in the summer months in combination with the sunrays. A greenish tinge may develop in blonde subjects who often swim in strongly chlorinated pools; shampooing the hair immediately after swimming is the best prophylaxis. Temporary chemical conjunctivitis (so-called "red eyes") is observed in subjects who swim with their eyes open.

Various dermatological diseases (Table 13.10) can be caused, via different pathogenic mechanisms, by chemical irritants [91, 92], allergens [92–96] and infectious agents present in swimming pool water [97–102], as well as by the irritant effect of water itself [103]. In particular, these diseases can be of occupational type (in professional swimmers, hydrotherapists, physiotherapists, and swimming pool workers such as cleaners and attendants) [104, 105].

Chlorine and bromine-based compounds are widely used to disinfect swimming pool water, destroy microorganisms and oxidate organic waste originating in the bather's body. The weak hypochlorous acid formed in the reaction between chlorine-based compounds and water is the main active compound in such disinfection processes. The undissociated form of this acid reacts with the cellular component of the microorganism and destroys it, while the hypochlorite anion assists in the oxidation of organic waste followed by formation of chloramines [104]. Both irritant and allergic contact dermatitis, induced by the chemical disinfectants, has been observed among pool users [96, 104–108]. Since the 1980s, owing to their potent action against waterborne pseudomonas, bromine derivatives have largely replaced chlorine derivatives as disinfectants in many swimming pools, resulting in a higher incidence of skin irritations [105]. Other symptoms include hair discoloration, reported in 30 % of swimmers [101], changes in the fingernails and toenails, and irritation and drying of the oral and genital mucosa.

Table 13.10 Dermatological diseases from swimming pools

Irritant contact dermatitis
Allergic contact dermatitis
Folliculitis
Hot foot syndrome
Swimming pool granuloma
Warts
Molluscum contagiosum
Xerotic skin
Hair discoloration
Fingernails changes
Aquagenic wrinkling
Chemical conjunctivitis
Otitis externa

Aquagenic skin wrinkling, a classic manifestation in patients with cystic fibrosis, presents in the form of white, oedematous, poorly delineated papules and plaques of the palms of the hands and soles of the feet, following water exposure [109, 110]. The lesions appear within 2 min of exposure, are transient and resolve within a few hours after the end of exposure. Other signs include discomfort, pruritus, tingling and hyperhydrosis. Histologically, there is hyperkeratosis and dilation of the eccrine ostia [111, 112]. This phenomenon has been given various names, when observed in absence of cystic fibrosis, such as aquagenic keratoderma, aquagenic syringeal acrokeratoderma, aquagenic palmoplantar keratoderma, and transient reactive papulotranslucent acrokeratoderma.

13.7 Dermatitis Associated with Deep Sea Diving

Notoriously, both occupational and amateur scuba divers are exposed to an enormous variety of risks, including skin problems [113].

Staphylococcal skin infections are relatively frequent and also difficult to treat [114]. The pressurized environment, with a high partial pressure of oxygen, high temperatures and sometimes humidity exceeding 90%, are conditions that favor *Pseudomonas* external otitis. This problem can be preventable by good prophylactic hygiene and by use of aluminum acetate ear drops [115]. Overheating inside the wetsuit can cause local burns. Underwater welding procedures can induce erythema and telangiectasia. The skin folds trapped in the wetsuit can present linear abrasions.

During decompression, divers may notice itching, with or without an urticarial eruption, mainly localized on the back or trunk [116]. If they stay underwater for long they may develop a form of "napkin rash", due to having to attend to physiological needs.

13.8 Occupational Chronic Traumatic Scleroedema

Diffuse delayed reactions of the backs of the hands may manifest as a particular form of chronic scleroedema. This traumatic lymphoedema is an occupational complaint and we have often observed it in fishermen, caused by repeated penetration of

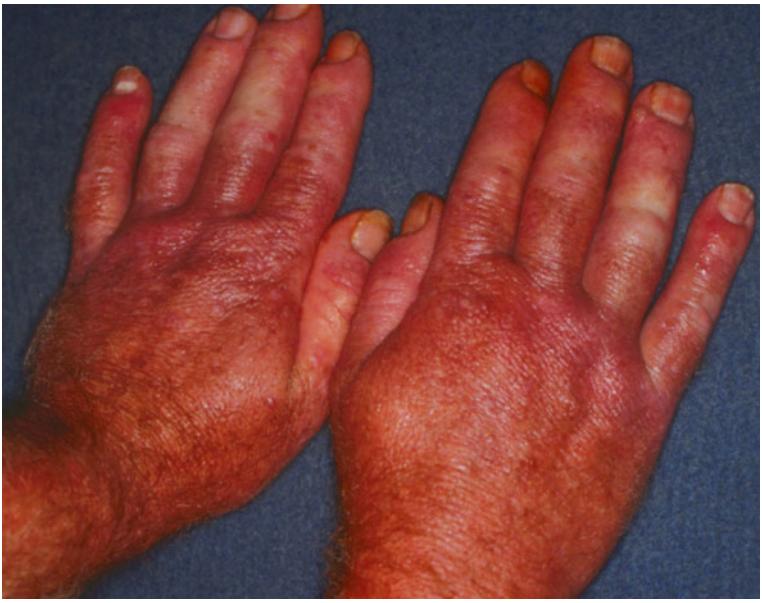

Fig. 13.5 Chronic traumatic scleroedema of the hands in a sea urchin fisherman. Acrocyanosis and skin atrophy are also evident

sea urchin spines, together with the constriction of the wrists caused by the wetsuit and the low temperature of the water. It manifests with hard, persistent oedema of the backs of the hands and sometimes also of the forearms (Figs. 13.5, 13.6, and 13.7) [116, 119].

The oedema is firstly recurrent but within a few years it becomes persistent, very hard and clearly distinct, ending in a sharp line at the wrists. It can persist for many years even after abandonment of the working activity and may be associated with "sea urchin granulomas", functional impairment of the wrists and fingers, dystrophic alterations of the nails and sometimes acrocyanosis, "cigarette-paper" atrophy of the affected skin and morphological alterations of the joint. In one case with intense scleroedema and granulomas, lymphography of the upper limb showed an irregular spread and distribution of the contrast medium on the back of the hand (Figs. 13.8 and 13.9) [117–120].

This picture of hard scleroedema closely resembles Secrétan's syndrome, a cutaneous artefact due to self-infliction of various repeated mechanical stimuli (haemostatic ligatures, occlusive bandaging, traumas) for financial gain (generally to obtain a pension) or psychiatric reasons [121].

Spontaneous, chronic professional scleroedema of the hands must thus be differentiated from self-inflicted complaints (Table 13.11) and other acute or chronic lymphedemas, such as lymphatic aplasia, recurrent erysipelas, deep thrombophlebitis, angioedema, chilblains, urticaria due to the cold, filariasis, venous obstruction, complications of surgical operations and radiotherapy for breast cancer or other tumors.

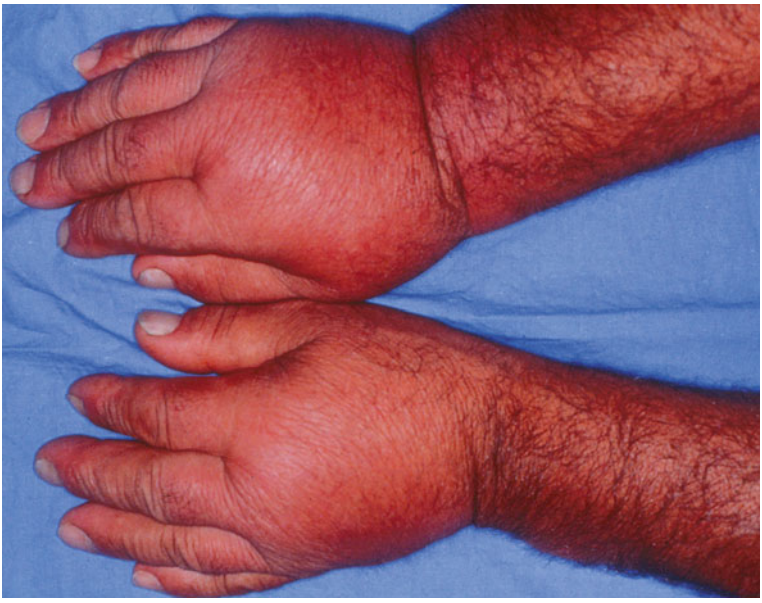

Fig. 13.6 Intense chronic traumatic scleroedema of the hands and forearms. The fisherman had stopped this working activity 15 years before. The joint function is impaired (Reproduced with permission from Bonamonte and Angelini [117])

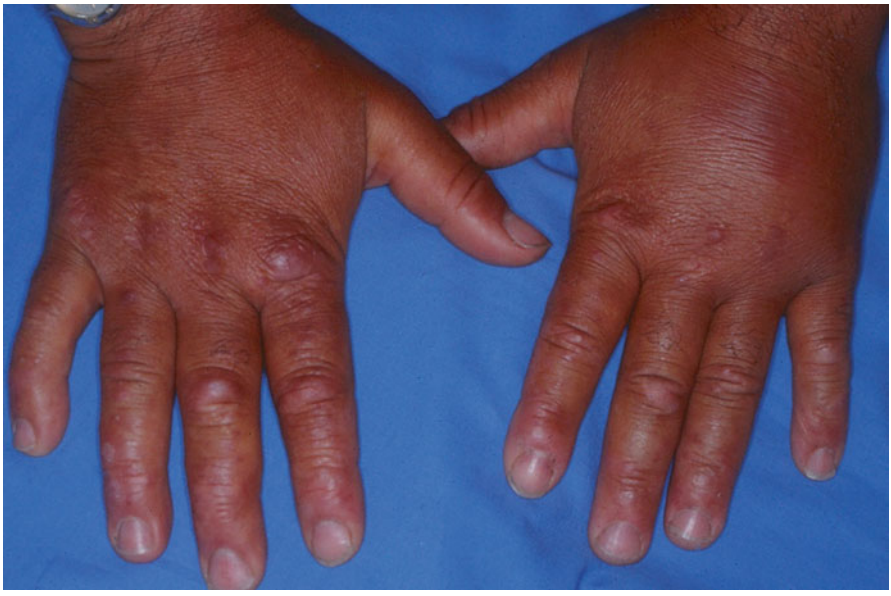

Fig. 13.7 Chronic traumatic scleroedema of the hands and granulomas from sea urchins (Reproduced with permission from Cassano and Coll. [118])

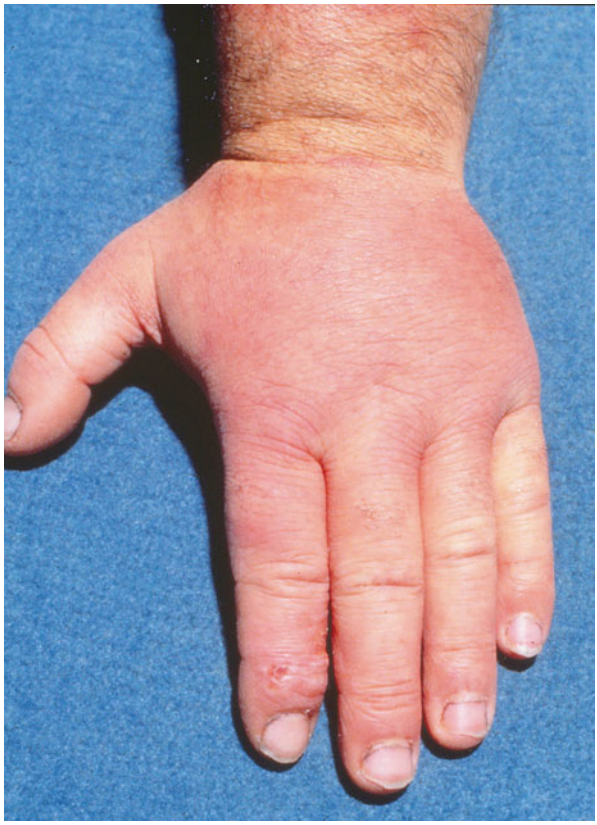

Fig. 13.8 Irreversible chronic traumatic scleroedema and granulomas from sea urchins in a subaqua diver

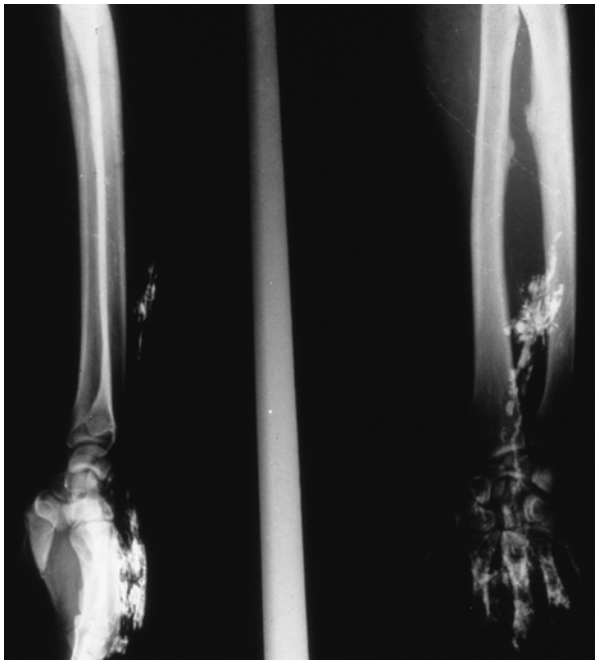

Fig. 13.9 The same case as in Fig. 13.8. Lymphography shows irregular flow and distribution of the contrast medium on the back of the hand

Table 13.11 Differential diagnosis between spontaneous professional scleroedema (SPS) of the hands and non spontaneous Secrétan's syndrome (NSSS)

	SPS	NSSS
Acrocyanosis	++−−	++−−
Lesions		
Monolateral	+−−−	++++
Bilateral	++++	+−−−
In association with		
Artefact dermatosis	−−−−	++−−
Sea urchin granulomas	++−−	−−−−
Age and sex		
Young women	−−−−	++−−
Young or elderly men	++++	++−−
Worse in winter	++++	−−−−
Lesions persist after abandonment of working activity	++−−	−−−−
Psychiatric problems	−−−−	++−−

13.9 Cutaneo-Systemic Complaints in Fishermen

Deep-sea fishermen can be victims of rare, practically unthinkable events nowadays such as a possible encounter with a bomb containing mustard gas. From 1970 till now, we have observed 12 fishermen with dermatitis whose onset occurred 6–10 h after fishing in the open sea outside Molfetta, a city 30 km to the North of Bari [122, 123]. All these patients presented an intensely erythemato-oedematous dermatitis featuring widespread blistering lesions with a clear liquid content (Figs. 13.10, 13.11, and 13.12). The affliction particularly involved the hands, forearms and face (where the erythema and oedema were more marked, being especially severe on the eye-lids), while in three cases the genitals were also affected (Fig. 13.13), with intense erythema in two cases and erythema, oedema and blisters in 1. All the cases were associated with severe conjunctivitis, lachrymation and photophobia. There was intense burning and itching at the affected sites. In six patients the skin symptoms were associated with headache, vomiting and nausea.

The fishermen referred that when they pulled their nets on board they had found bombs mingled in with the fish (Fig. 13.14). A few hours after handling the nets contaminated with the liquid gas contained in the bombs, they suffered the above symptoms. The dermatitis of the hands and forearms was obviously induced by direct irritant contact with the contaminated bombs and nets, while the other skin and mucosal lesions were caused by evaporation of the gas and hence airborne cutaneo-mucosal dermatitis (irritant airborne contact dermatitis) [123]. In all the cases, the symptoms resolved after 10–15 days, leaving dark skin patches. The conjunctivitis was treated with eye-baths containing 2 % sodium bicarbonate and antibiotic eye-drops. The other symptoms regressed rapidly with symptomatic treatment. Controls after 20–30 days excluded any re-presentation of the dermatitis.

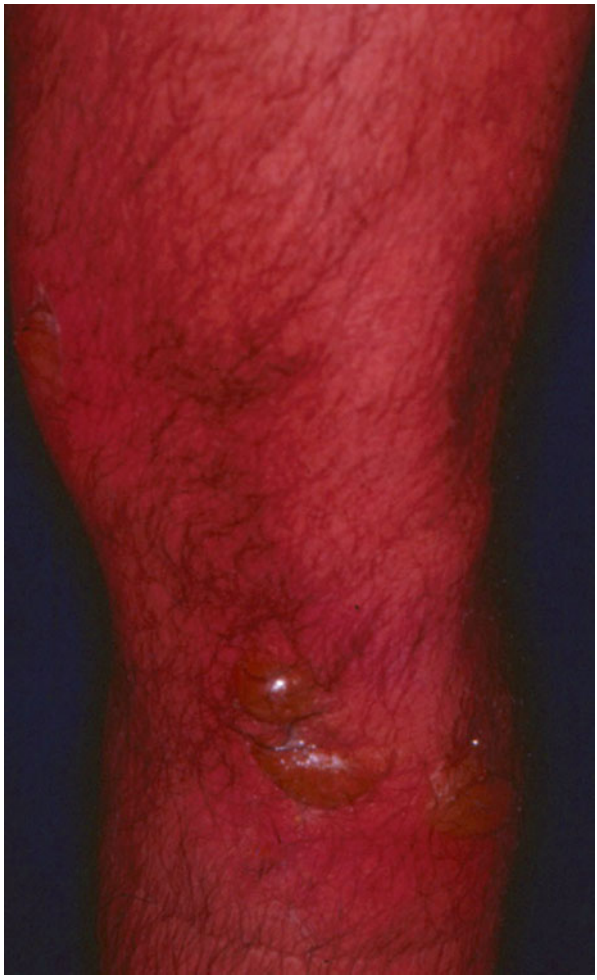

Fig. 13.10 Blistering dermatitis from mustard gas

The risk of fishing bombs is well known to fishermen and the harbor authorities in the area. These authorities report that more than 100 cases of intoxication from mustard gas have been observed over the years. This gas (2,2′-dichlorodiethyl sulfide: $C_4H_8CL_2S$), one of the most aggressive gases used in chemical warfare, is also known as yperite after the city of Ypres (Belgium), where it was first used in July 1917. The English and Americans call it mustard gas because of its characteristic odor. In the pure state it is an odorless, colorless oily liquid, and the characteristic yellowish-brown color and mustard-like smell are due to impurities (ethylsulphides). It is poorly soluble in water but dissolves rapidly in organic solvents or fats; this facilitates penetration of the cells, where it has a toxic effect. It evaporates

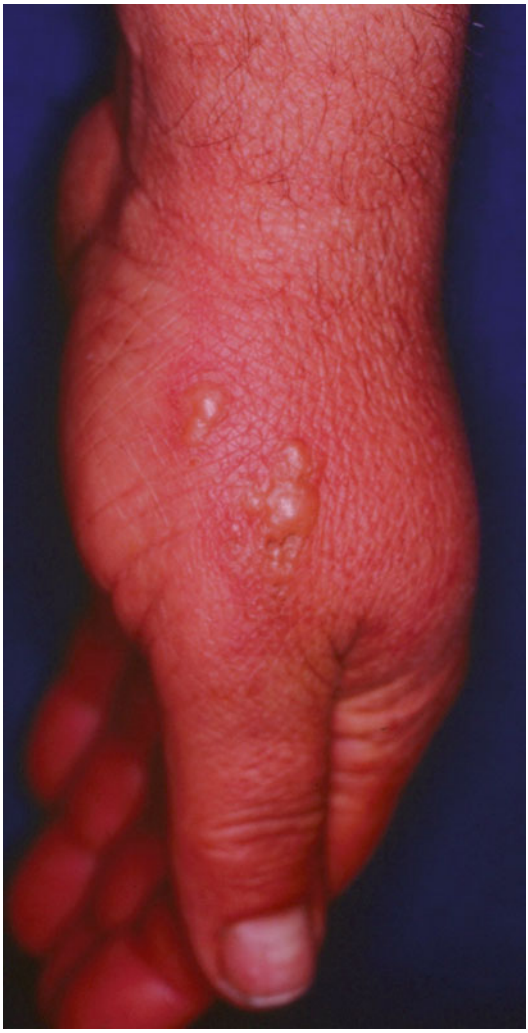

Fig. 13.11 Blistering dermatitis from mustard gas

slowly because of its low vapor pressure, although this increases at higher temperatures. It is toxic in both liquid and vapor form: in the former cases it damages the skin and in the latter, the skin, conjunctiva and respiratory mucosa. Its toxic effects manifest after 4–24 h from exposure [124–126].

Since the First World War, intoxication from mustard gas has been caused only by occupational contact, except for cases arising due to its widespread use during the Iran-Iraq war (1980–1988) [127]. The cases we observed were attributable to the previous presence of factories loading and unloading mustard gas bombs in Molfetta. After the Second World War, the bombs were thrown into the sea about three miles from the coast. The bombs are therefore still fished up sometimes, especially in the summer season when drag-nets are used.

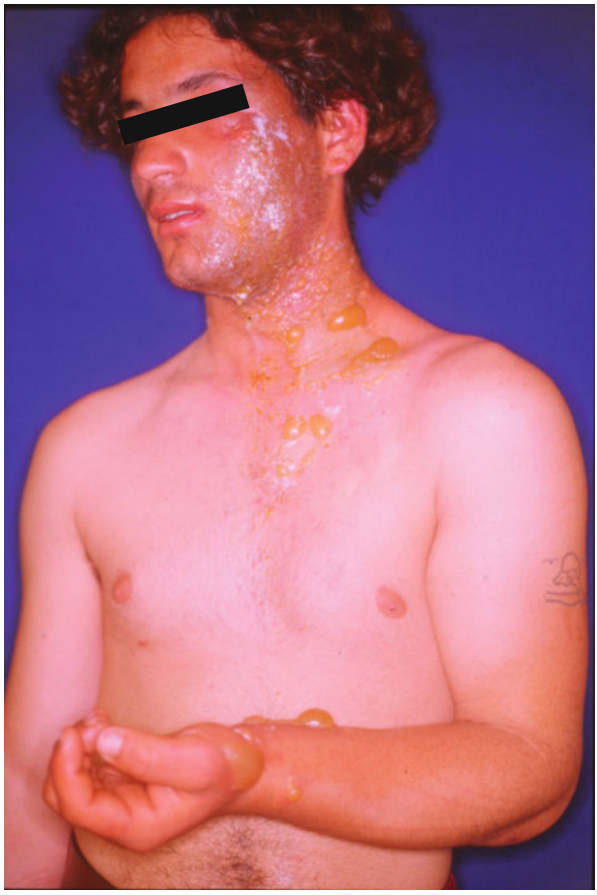

Fig. 13.12 Blistering dermatitis from mustard gas

Although chemical bombs are present in all European seas, similar cases of dermatitis from mustard gas have only occasionally been reported [128–130], probably because it is practically impossible to connect the disease with contamination by fishing nets unless the bombs are actually seen in them. Otherwise, the skin symptoms may be attributed to the harmful action of some marine flora and fauna.

Fishermen should be informed of the risks of fishing bombs in particular areas, and must be instructed to throw them straight back into the water without opening them and in cases of inadvertent contamination, to go straight to hospital. All the contaminated areas of the boat must be thoroughly cleaned and the fishermen's clothes and personal effects must be destroyed. Mustard gas can impregnate clothes and leather objects and persist for a long time. In fact, we have also observed cases of contamination of members of the family due to contact with the fisherman's clothing.

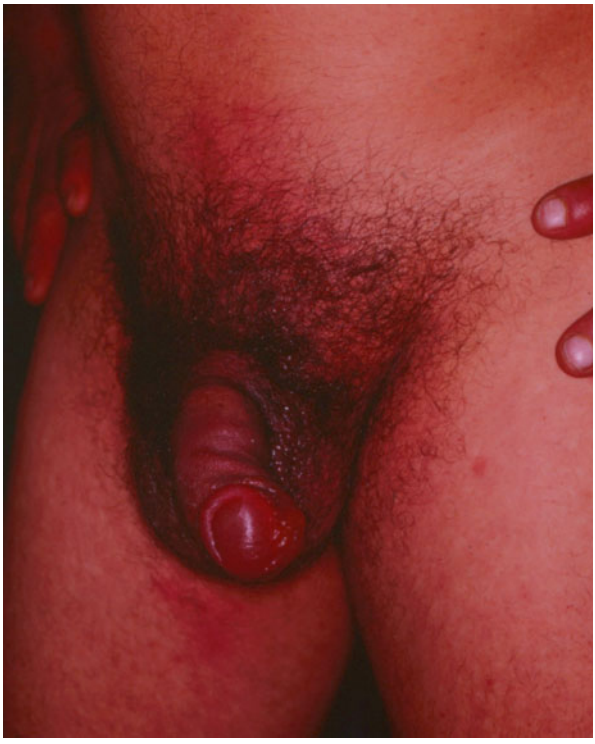

Fig. 13.13 Intensely erythemato-oedemato-exudative dermatitis from mustard gas

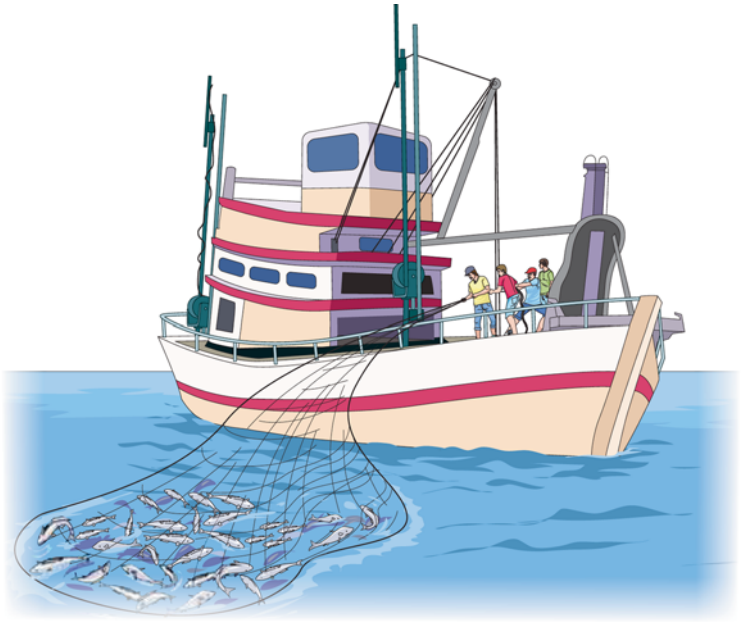

Fig. 13.14 Bombs containing mustard gas can be pulled in together with the fish in dragnet fishing

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