G. G. Habermehl

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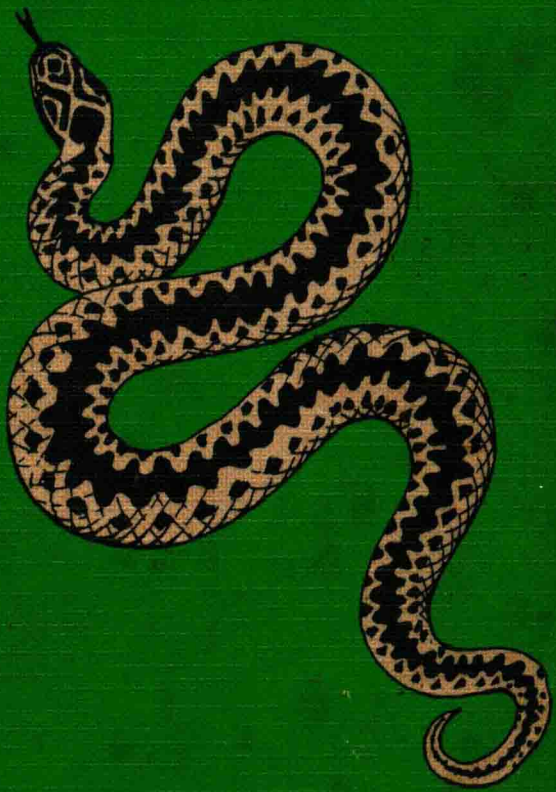

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With 44 Figures and 44 Tables

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# Preface

Venomous Animals have been a threat to man at all times, in the warm and wilder regions more than in the temperate areas. People in especially dangerous regions know about these risks and live accordingly. However, with modern tourism and nearly unlimited travel opportunities more and more people without experience and knowledge about venomous animals come into contact with them; this book is intended to provide these people with an introduction to the subject.

Venomous animals, their habits, their whole ecology and their venoms have been the object or research since the beginning of this century; truly intensive work, however, first started about thirty years ago. Medical treatment therefore has been changed by new insights in the mechanism of action and the constituents of the various venoms. In this regard this book is also directed to physicians, biologists and chemists to give them an introduction in this important and interesting field. New aspects of treatment of envenomations are reported. This book cannot replace bigger textbooks and monographs – they are cited in the references – but it gives an overview and an entry into this field. The original German edition was written at the request of colleagues and students of medicine, biology and chemistry as well as frequent travellers in tropical countries. It was sold out within eight months, thus showing that it really filled a gap. Many colleagues and friends outside Europe asked for an English version, thus encouraging Springer-Verlag to publish it.

I have to thank quite a number of colleagues for discussions, suggestions and reading the manuscript. They are Professor Dr. D. Magnus, Darmstadt and Professor F. Kornalik M. D. Prague, Professor Dr. T. Freyvogel, Basle, Professor Dr. H. Alistair Reid OBE, Liverpool, Dr. J. W. Daly, N. I. H., Bethesda, Md., USA, Dr. Margaret Weiss, Bethesda and Dr. D. Mebs, Frankfurt University Hospital.

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Hannover, May 1981 G. G. Habermehl

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# Introduction

Since antiquity, venoms from plants and animals have not only posed a danger to humans but also a challenge to our ingenuity. There are numerous, striking, often bizarre examples of this from diverse eras and geographic areas. Indians in Central America and in the Northwestern parts of South America today still use the skin secretions of dendrobatid frogs for hunting as arrow poison. In medieval times dried and powdered Spanish flies were (mistakenly) used as a sexual stimulant; and in China and Japan for 4000 years dried and powdered skins of toads have been used as heart medicines (Ch' an-su and Sen-so). And in the Old World, parallel to that, extracts of *Scilla maritima* (sea-onion) or *Digitalis* (foxglove) were used for the same purpose. Modern science was able to show the chemical similarity of both substances.

Although humans certainly have been aware of the poisonous nature of some snakes from the beginnings of our history, it took a long time until ideas about their venoms took form. Mithridates, king of Pontus (123–63 B. C.) drank the blood of snakes to become immunized against snake bite. Maimonides in 1198 wrote a treatise on "Poisons and Their Antidotes" in which snake bite envenomation is mentioned, but there is nothing told about the origin of snake venom. The Italian physician Francesco Redi (1626–1697) in 1664 wrote a book "De Venenis Animalibus" and was the first to describe the venom apparatus of snakes. He showed that venom could be obtained only from the venom glands and teeth and not the whole animal which until then was supposed to be toxic. A similar story may be told about the salamander. In ancient times the most unusual ideas were reported. Plinius Secundus, the famous Roman author of a multivolume book "Historia Naturalis", Natural History, wrote among others: "Inter omnis venenata, salamandra scelus maximum est" – "Among all venomous animals, the sala-

mander is the most wicked one! Other animals harm individuals only and do not kill several at the same time. The Salamander, however, is able to kill whole peoples." In other books one may read that the salamander is able to extinguish fire.

In Germany in the 17th century a wife tried to kill her husband by cooking a salamander in his soup. She was caught, seized and condemned to death, not for the attempted murder, but for using witchcraft.

It has only been during the past 80 years that animal venoms have been the subject of intense scientific investigation, at first from the clinical and pharmacological point of view, then from the chemical. Snake venoms first stood in the foreground of research, and the names of Vital Brazil and the "Instituto Butantan" in Sao Paulo as well as of Albert L. Calmette and the "Institut Pasteur" in Saigon are due special mention. Since the mid-twenties of this century, the chemistry of animal venoms has been studied intensively. The pioneering work in this area were investigations on toad venoms by Heinrich Wieland and his group in Munich and Freiburg. The book "Die Biochemie der tierischen Gifte" by E. Kaiser and H. Michel, which appeared in Vienna in 1958, greatly stimulated the field. A few years later, so many laboratories all over the world were investigating medical, biological and chemical aspects of these venoms that an international symposium on animal toxins and toxic animals was held in Sao Paulo (1966) and the International Society on Toxinology was founded (1964).

In the meantime it turned out that many more animals are venomous or poisonous than originally thought. Our conception of "toxins" had to be revised, too: we must not only consider their pharmacological activity, but also a defined and ecologically relevant function in biology, be it for catching prey or protecting against enemies. Consequently one must distinguish between "actively" and "passively" venomous animals. The latter may be divided into "primary venomous" animals that possess organs especially developed for defense (e. g. amphibia, beetles) and "secondary venomous" or "poisonous" animals that happen to be toxic during certain seasons of the year and usually become toxic by chance via the food-chain (e. g. shell-fish or certain fishes).

In this connection the question of "toxicity" arises. A measure for it is the $LD_{50}$; that is the lethal dose for 50% of test animals.

Mice are generally used for these tests, but the values found by this way must not be transferred to other animals or men. But at least they give an idea of the order of magnitude.

In this book medical considerations will receive extensive coverage first because the number of incidents involving poisonous animals is increasing (for various reasons), and second because modern clinical methods for treating attacks by venomous animals need to be reviewed. This is particularly important because many books deal with treatments that are more akin to mythology or folk medicine than modern science. The number of such has decreased in recent years, but even in recognized journals from time to time treatments are dealt with that are useless or even dangerous, especially if they delay effective therapy. How often do significant cases of poisoning occur from bites or stings?

It is frequently accepted that every sting or bite necessarily leads to a toxic reaction and that such a reaction is usually fatal. Fortunately this is wrong. According to reliable statistics and calculations, the average rate of mortality is around 2.5%. But even without fatal consequences, a bite or sting may cause permanent damage to the afflicted body part. Animal venoms exhibit a fascinating variety of pharmacological actions and chemical structures. In addition to the widespread peptides and proteins biogenic amines, alkaloids, heterocyclics, terpenes, steroids and glycosides – a broad spectrum of substance classes may be found. A corresponding breadth of pharmacological activity is seen: Besides numerous enzymatic activities, true toxic effects can be observed that are caused by cardiotoxins, neurotoxins, hemotoxins or cytotoxins. The study of the biosynthesis of such compounds puts evolutionary relationships in a new light and serves as an additional criterium for the systematic biologist. As interesting as these animals are for the scientist, they are potentially very dangerous for the inexperienced and careless laymen, especially travellers and vacationers. Among the species that are known to provide the unwary with a nasty experience are the venomous marine animals. Sea urchins are at least visible, and one may avoid them; more insidious are the sting rays, or stone fishes, which are quite often hidden in the sand; or doctor fishes or scorpion fishes, which defend their hunting ground and may attack divers. Quite malicious are the nettle cells of coelenterates i. e., jelly fish, sea wasps, sea anemones, sea nettles and corals,

especially the tentacles of jelly fish, which may cause severe burns even after separation from the animal. About 50,000 incidents involving marine animals are estimated to occur worldwide each year. This figure does not cover the 20,000 cases of intoxication by consumption of poisonous fish or shellfish. Fortunately nearly all of these accidents are not severe; the number of fatal cases probably does not exceed 300. In many parts of the world snake bites are not uncommon occurrences. 1.7 million snake bites may occur per year, 40,000 resulting in fatality. About half of these cases (in which the circumstances were known) were caused by carelessness, and the saying "an ounce of prevention is worth a pound of cure" certainly rings true here, too. Such preventive measures merely apply common sense. Snakes should never be frightened; they are usually more afraid of humans than vice versa, and they most often bite in selfdefense. In case of any doubt go out of their way and restrict your contacts to reading about them in books such as these!

**Protection from Snake Bites**

An active immunization against snake toxins is practically impossible. Hence precaution is the best protection. Most snake bites occur on the feet (60%) as a result of walking barefoot. 77% of bites are on the shank (including the foot) and could have been avoided by wearing boots. Considering that more than 96% of all snake bites occur on feet, legs and hands, one may see what an important role carelessness plays or how important precaution is. Good precautionary measures are:

1. Not walking barefooted.
2. Stepping hard when walking.
3. Not turning or lifting stones with your hands, unless you are sure that no snake is hidden under them. Use a stick instead.
4. Not reaching into holes without previous inspection.
5. Being especially careful about snakes after sunset.
6. Not attempting to needlessly kill a snake; many snakes bite in self-defense.
7. Not swimming in waters where snakes abound. Many land species of snakes swim well and may bite while in water.

The number of fatal snake bites may seem high; however, the number of fatal bee and wasp stings is about the same. On the

American continents "snake bite kits" are available for first aid; they contain serum and syringes. Their manufacturers are listed on page 194, and they may be obtained at drugstores, from physicians or from the producer directly. It is usually necessary to indicate the geographic area of travel when ordering such a kit in order to get the special sera. A layman without experience in injecting sera should never try to utilize these kits.

Stings and bites from scorpions and spiders are so frequent that one can hardly obtain reliable figures on incidence. In Mexico, about 70,000 scorpion stings per year are estimated, 1200 of them fatal. Except for the *Uloboridae,* all spiders are venomous; few species, however, really pose a danger to humans. The fangs are generally not strong enough to penetrate human skin, but in any case one should avoid touching them with unprotected hands. Scorpions and spiders usually are hidden during daytime, sometimes under a thin layer of sand. Again, it is advisable not to walk

**Table 1.** Lethal bites and stings by venomous animals in the USA from 1950 until 1954

| Animals | Number | Percent |
|---|---|---|
| *Insects* | 86 | 40.0 |
| Bees | 52 | 24.2 |
| Wasps | 21 | 9.8 |
| Yellow jackets | 7 | 3.2 |
| Hornets | 5 | 2.3 |
| Ants | 1 | 0.5 |
| *Poisonous snakes* | 71 | 33.0 |
| Rattle snakes | 55 | 25.6 |
| Mocassins (Cottonmouth) | 2 | 0.9 |
| Coral snakes | 1 | 0.5 |
| Unidentified | 13 | 6.0 |
| Spiders | 39 | 18.1 |
| Scorpions | 5 | 2.3 |
| Nettle animals | 1 | 0.5 |
| Sting rays | 1 | 0.5 |
| Yet undefined animals (insects, spiders, scorpions) | 12 | 5.6 |
| Total | 215 | 100.0 |

barefoot. They come out to hunt in the evening, a time of many accidents, requiring extra precaution. Clothes, shoes or food placed on the floor are a special invitation to these animals. In dangerous areas such items should be carefully sealed in a plastic bag. A rather reliable and representative review of incidents involving venomous animals in the USA (1950–1954) is given in table 1.

The purpose of this book is not to convince the reader that danger from venomous animals lurks around every corner. Rather, it is to show how to avoid accidents and behave in case one occurs.

And not everything that looks venomous should be killed. Many of these animals have ecologically important functions and are even protected by law because their importance far outweighs the occasional harm they cause.

# 1 Coelenterates, Cnidaria

## Distribution

*Cnidaria* and *Acnidaria* together form the phylum *Coelenterata.* Here we need to consider the cnidarians or nettles and the venomous polyps, jelly fish, sea wasps, sea nettles, sea anemones and corals. They are found in all seas within a range of about 45° North to 30° South with small geographic exceptions in the North Atlantic due to the Gulf Stream. Table 2 presents summaries on the most important species.

## Poisoning

Poisonings are caused by nettle capsules (nematocysts), which are formed in special cells, the so-called cnidoblasts. The nettle capsules are localized primarily on the tentacles; they are also found, however, in the epidermis of the mouth region as well as in some inner structures. The structure of the nematocysts is remarkably complicated in relation to the size (usually less than 1 mm). When the cnidocils are touched the thread tube is ejected and injected into the skin of the victim; at the same time the venom pours out. It consists of several peptides of relatively low molecular weight that are especially toxic to crustaceans and fishes. Thus, for example, 1 ng/kg of the toxin of the sea anemone *Condylactis gigantea* or 2 ng/kg of the toxin from *Anemonia sulcata* causes paralysis of crabs and shrimps.

The symptoms of coelenterate poisoning vary according to species, site of sting and sensitivity of the victim. As numerous studies have shown, repeated stings result in an increased sensitivity that may finally give rise to an anaphylatic reaction.

Contact with the tentacles leads to symptoms that range from itching to an intense burning; the pain may become so intense that

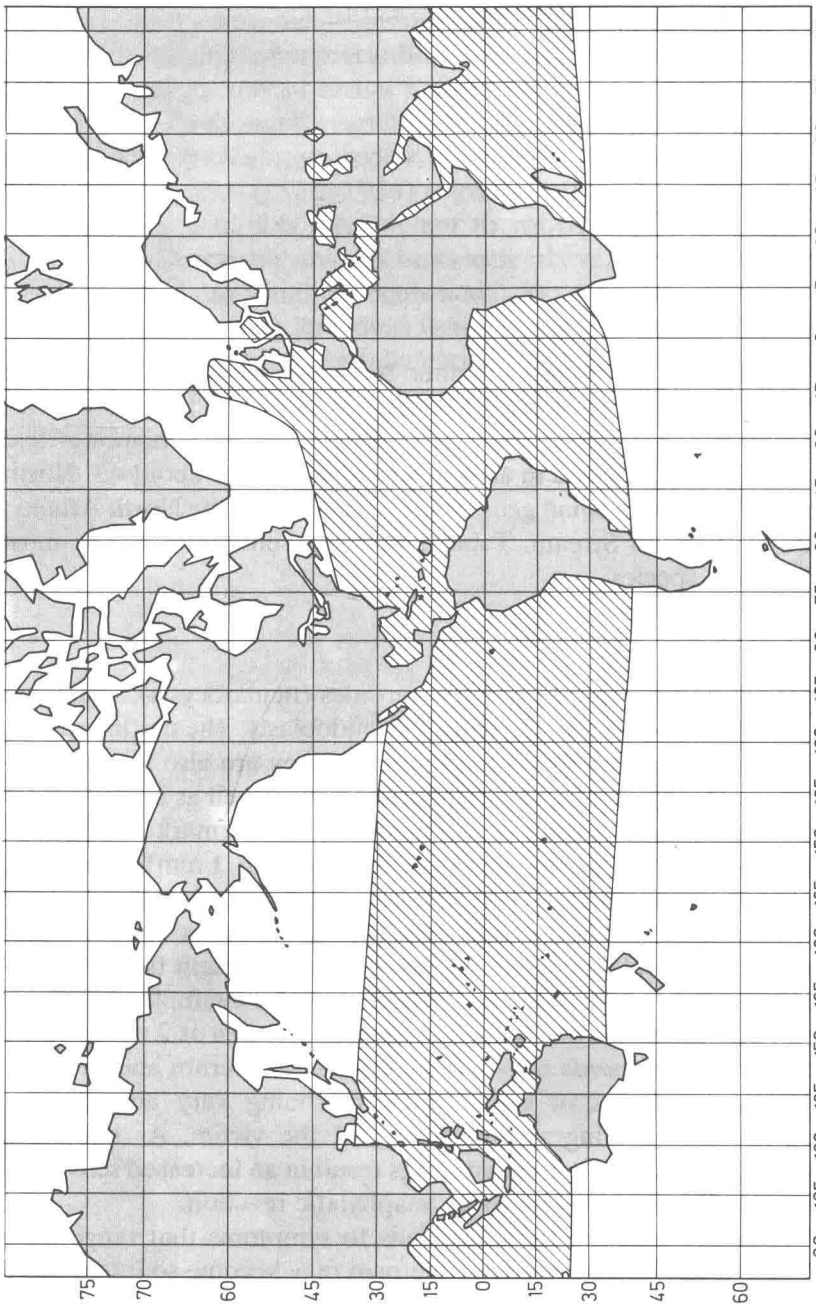


**Fig. 1.** Distribution of coelenterates

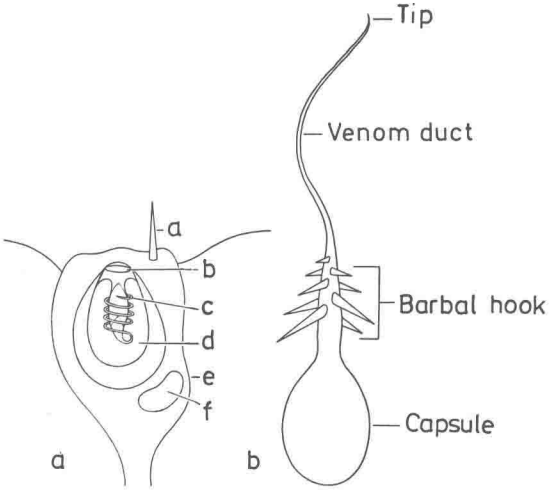


**Fig. 2a, b.** Nematocyst. **a** in rest, *a* cnidocil, *b* operculum, *c* venom duct, *d* venom capsule, *e* cnidoblast, *f* nucleus; **b** in the ejected state

victims fall unconscious. The initially local pains change later on to numbness or into hypersensitivity.

*Sagartia* stings at first cause nettle-like eruptions and later on necrotic ulcers. Stings of *Scyphozoa* may be harmless, as in the case of *Cyanea* species native to the North Sea and Baltic Sea, or painful, as in the case of other *Cyanea, Catostylus* and *Chrysaora* species. Here generalized symptoms are also observed: primary shock, collapse, headache, shivers and fever. In serious cases muscle seizures, paralysis and finally death from heart failure may occur. The same symptoms may be observed after *Physalia* stings.

Fatal stings in humans are rather rare, but when they occur death is usually very rapid, mostly within a few minutes. Victims surviving the first 30 minutes usually recover within a few hours to several weeks. Without doubt the most dangerous among those animals is the sea wasp, *Chironex fleckeri;* the venom is cardiotoxic, and the sting causes hypertension, lung edema and acute heart failure. In fact, the sea wasp probably is the most dangerous venomous marine animal of all. As death occurs within seconds or at most minutes after touching the tentacles, treatment is impossible. Divers must be extremely careful, especially since even adult animals are