snake venom poisoning

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preface

This book was written with the physician in mind. It is not intended to be a compendium on herpetology or on the chemistry, physiopharmacology, pathology, and immunology of snake venoms; nor, I trust, did it turn out that way. However, it is written with the conviction that many of the problems faced by the physician would be solved if we knew more about biology, and it has been put together with this in mind.

Certain data on the general biology of venomous snakes, their distribution, the structure of their venom apparatus, the chemical nature of their toxins and their modes and sites of action, immunological phenomena, and other topics of importance to the physician have been included, for a basic knowledge of these data is essential to better patient care.

In this respect it is comforting to have found that after more than 25 years of exposure to physicians and snakes, the former have a unique interest in the latter and what makes them tick (or rattle). A room full of physicians is more likely to cast the lecturer a greater number of thought-provoking questions on every manner of snakedom than any other pit full of scholars. For that reason, considerable basic biological data on snakes and snake venoms have been included. These bits of information are usually not only of *interest* to most physicians, but at sometime in their lives they will definitely find them of *use*.

There are many others besides physicians who may find this text useful. From our files at the Laboratory of Neurological Research of the University of Southern California, and at the Los Angeles County-University of Southern California Medical Center, we know that in the past 25 years we have received approximately 3,900 letters and have logged almost 10,000 telephone calls from zoos, herpetological societies, associations, and clubs; snake and venom collectors; political officials; poison control centers; Boy Scouts and their leaders; customs' officials; explorers; amateur and professional herpetologists; departments of fish and game; medical information clearing facilities; public health officers, paramedics, firemen, and policemen; museums, humane societies, and serpentariums; insurance companies; trappers; fishermen; lawyers; dune and desert buggy enthusiasts; snake canning factories; land developers; overseas contractors, "desert rats"; school teachers and

students ("Send me everything you know about snakes and please before next Friday. Enclosed is a stamp."); gardeners; anxious parents; veterinarians; summer camp operators; water, light, gas, and telephone companies; fruit and produce companies; libraries; wine and whiskey manufacturers (who use snakes in their brew); and lastly, that large group of well-meaning authors of popular articles, newspaper and magazine, who phone almost weekly, stationed at their typewriters on a 5-minute deadline, and wanting to have (in 3 minutes or less) a condensed version of the "latest" (rarely the "best") method of treating the bites of the 350 different species of venomous snakes.

There are two other groups for whom this book should be of particular importance: those individuals in academic institutions working with venoms and venomous snakes; and organizations producing antivenins or products from snake venoms and, needless to say, their medical emergency rooms.

Although this book has not been particularly oriented for graduate or undergraduate students, I trust some may find it valuable as a reference work on the chemistry, pharmacology, and immunology of snake venoms or for studies on venomous snakes and the nature of their venom apparatus. In this respect, much of the text has been developed from graduate and house staff lectures on snake venom poisoning that have been presented in a formal course, *Physiopharmacology of Toxins,* at the University of Southern California and at the Los Angeles County General Hospital (presently the Los Angeles County–University of Southern California Medical Center) over the past 20 years. Parts of these lectures have also been presented in course work at Loma Linda University and the University of California at Los Angeles, among other universities.

It is difficult, and perhaps a little presumptuous, to prepare a monograph on a subject that invades as many disciplines as does venom poisoning. However, it seems desirable at this time, when there is a certain amount of consistency in our data on the chemical and pharmacological properties of venoms, and adequate clinical experience, to put together a compendium that will serve as a guide and reference work for the physician and, it is hoped, present a critical review of some of the more important problems in toxinology.

I am only too well aware, however, that this effort cannot be fully comprehensive, and any succinct dissertation on a problem so complex as snake venom poisoning is almost certain to be incomplete. In addition, the subject of snake venom poisoning and the treatment of the envenomated victim are still very open topics. Unlike many entities in medicine, there are a variety of factors that can influence the diagnosis and treatment of the poisoned patient, so that the discipline of toxinology proves, perhaps more than most other clinical areas, that the practice of medicine is still an art and not a science. Besides, snakes will be snakes.

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Occasionally in the text I have mentioned "our group." Such references are made to those individuals who, during the past 25 years, have served as part of a team treating snake-venom poisoned patients at the Medical Center; or who have treated or consulted on such patients elsewhere either as part of the team or as private physicians. Some of these colleagues have been primarily concerned with research relating to snakebite, rather than patient care, but in one way or another all have contributed to the improved management of snake venom poisoning. I thank the following people from the University of Southern California: K.B. Bower and P.R. Saunders, and J.W. Dubnoff (all now deceased); W.A. Wingert, J. Wainschel, R.W. Carlson, R.L. Hoffman, J.W. Parker, D.R. Powars, T.R. Pattabhiraman, E. Steinberg, S.S. Rao, R.G. La Grange, R. Castilonia, D.O. Chinn, P.F. Wehrle, D.C. Redfield, H.M. Weil, J.A. Emery, D.C. Buffkin, F.W. Buess, A.E. Underman, and R.C. Schaeffer, Jr. I am indebted to J.A. Quilligan, R.F. Chinnock, and R. Boche of Loma Linda University; and to M.D. Fairchild, W. Ebeling, and C.E. Juratsch of UCLA. I also appreciate the help of B. Campbell of the University of California, Irvine; T.M. Davidson of the University of California, San Diego; and A.L. Picchioni of the University of Arizona.

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Every writer occasionally gets carried away with his subject and must be brought back to his wiser self by someone with just enough tact, understanding, spirit, and skill to make the process painless. Bernice Kellar provided this element to me and the text, and I am indebted to her, once again, for cleaning up unstructured thoughts and sentences.

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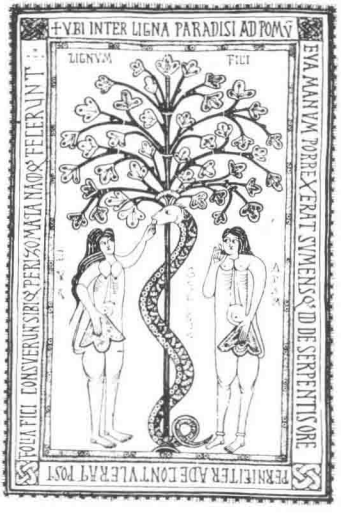
contents

1

introduction



From the very beginnings of human record, few subjects have stimulated the minds and imagination of man more than the study of snakes and snake venoms. No animal has been more worshipped yet more cast out, more loved yet more despised, more envied yet more caged, and more collected yet more trampled upon than the snake. The essence of the fascination with and fear of snakes has lain in their venom. In times past, the consequences of bites by venomous snakes were often attributed to forces beyond nature, sometimes to vengeful deities thought to be embodied in the serpents. To these early peoples, the effects of snakebites were so surprising and varied, and so violent and sometimes incapacitating, that the snakes and their venoms were usually shrouded with myth and superstition.

Snakes have been used in man's worship, magic, entertainment, science, food, sport, medicine, commerce, witchcraft, war and even in tortures on his fellow man. They have been the symbol of love, hate, procreation, health, disease, immortality, sin, death, temptation, riches, poverty, and even wisdom. The Morrises have put it aptly: "It is a paradox. It is both sides of the coin, and mankind has seldom ignored it"[1] (Fig. 1-1).

The venomous and poisonous animals are widely distributed throughout the animal kingdom, from the unicellular protistan *Gonyaulax,* responsible for paralytic shellfish poisoning, to certain of the chordates, the platypus, and the short-tailed shrew. The notable exception appears to be the birds. There are no venomous birds, a fact that one early writer attributed to their proximity to heaven.

Although we do not have an exact figure on the number of such animals, approximately 1,000 species of marine animals are known to be venomous or poisonous,[2] and of the 2500 to 3000 species of snakes, approximately 375 are considered venomous. The number of venomous terrestrial arthropods must number into several tens of thousands. For instance, all spiders, with the exception of two groups are venomous,[3] and there are approximately 20,000 species of spiders. The number of venomous scorpions, bees, wasps, hornets, ants, ticks, and certain bugs, among others, is not known.

Fig. 1-1. Mankind fighting the serpent of Apocalypse.

Definitions and Terminology

BIOLOGY

The words **toxin, venom, poison,** and **venomous** and **poisonous animals** have different meanings to different people. The word **toxin** (Greek = Το-ξικου) was coined to describe the poisonous substances elaborated by growing pathogenic organisms. The term was applied to the products obtained from decaying meat and fish. Subsequently, a toxin was defined as a protein having a poisonous effect, as a substance produced by bacteria, as a substance capable of producing an antitoxin, as a high molecular weight poison, or as a component of a poison. In this book, the word **toxin** is used to define a substance that is derived from the tissues of a plant, animal, or microor-

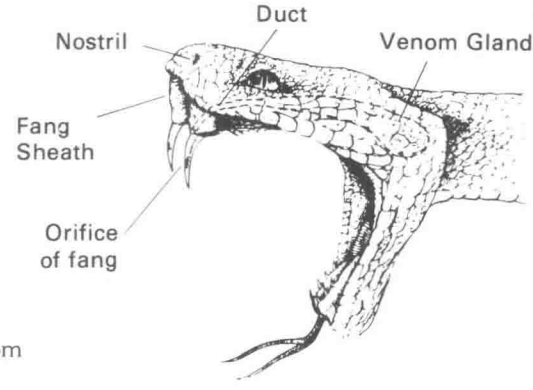


Fig. 1-2. Some relationships of the venom apparatus of a rattlesnake.

ganism which has a deleterious effect on another plant or animal. The word **toxin** can be interchanged with venom and poison, since a toxin can be composed of only one fraction (and not necessarily a protein), several fractions, or even the whole venom.

The word **venom** is usually applied to the toxic substance produced by a plant or animal in a highly developed secretory organ or group of cells, and which is delivered during the act of biting or stinging. **Venomous animals** have a venom gland or highly specialized group of cells, a venom duct (although this is not a consistent finding), and a structure for delivering the venom. While there has been a tendency to employ the term **venom apparatus** to denote only the sting, spine, jaw, tooth, or fang used by the animal to inject or deliver its venom, most biologists now use the term in a broader context; that is, to denote the gland and duct in addition to the fang or sting (Fig. 1-2). The rattlesnake, stingray, and black widow spider are examples of venomous or **phanerotoxic** animals.

A **poison** is a substance that, in relatively small amounts, produces death or impairs seriously the functions of organs or tissues. **Poisonous animals** are generally regarded to be those creatures whose tissues, either in part or in their entirety, are toxic. Poisoning by these forms usually takes place through ingestion of their flesh. Certain pufferfishes, toads, and newts are examples of the poisonous or **cryptotoxic** animals. In reality, all venomous animals are poisonous, but not all poisonous animals can be considered venomous. In this book, when they relate to snakes, the terms venomous and poisonous are sometimes used synonymously.

The study of toxins is known as **toxinology.** The words biotoxin and biotoxinology have found their way into the literature but they appear to be redundant by definition. In general, toxinologists are biologists and physicians who specialize in the study of the properties of the natural-occurring poisons. Toxinologists interested in the venomous snakes and snake venoms are primarily concerned with the structure of the snake's venom apparatus, includ-

ing the ultrastructure, the chemistry, physiopharmacology, and pathophysiology of the venom, and various immunological phenomena related to antivenin production (Fig. 1-3).

However, many toxinologists are primarily concerned with the clinical problem of venom poisoning and its treatment. Others have pursued their interest in the use of venoms as therapeutic drugs or as tools in the study of biological phenomena. A few toxinologists study very definitive mechanisms of poisoning, such as the biophysics of venom ejection. A large following of the science is composed of herpetologists, arachnologists, and marine scientists (particularly ichthyologists) whose primary interest is in the biology of the animal itself, and the biology as it relates to the property of being venomous or poisonous.

Herpetologists are persons who study the structure, habits, and classification of reptiles and amphibians. **Arachnologists** study Arachnida: spiders, scorpions, mites, ticks, and certain other arthropods. **Ichthyologists** usually confine their interests to the study of fishes. A **type specimen**, be it snake,

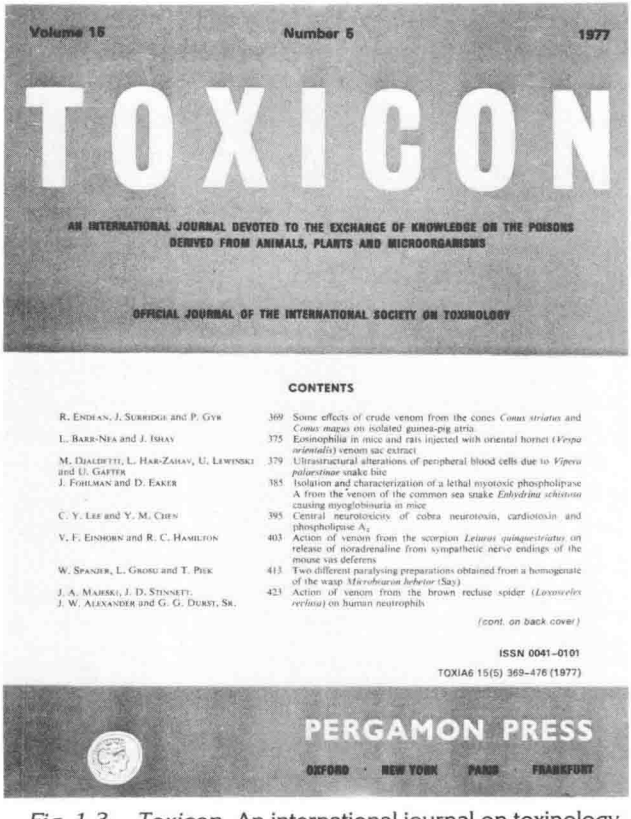


Fig. 1-3. Toxicon. An international journal on toxinology.