THE EVOLUTION OF THE VENOM APPARATUS IN SNAKES FROM COLUBRIDS TO VIPERIDS & ELAPIDS

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ABSTRACT: The venom apparatus of poisonous snakes consists of a fang and associated venom gland (or glands). Venomous snakes evolved from nonvenomous ancestors. The course of this evolution, the adaptive advantages of the changes at each stage, and the implications of the findings to snake phylogeny, pharmacology, and clinical strategies of treatment of envenomations are the subject of this paper.

In particular, it is argued in this paper that: (1) both viperid and elapid snakes evolved from opisthodont ancestors; (2) the Duvernoy's gland in most colubrid snakes should not be seen as a gland "on its way" to becoming a venom gland, but should be examined for the immediate biological role it plays in the life of those snakes possessing such a gland; (3) it would be useful to distinguish between a property of an oral secretion (e.g. toxin) and its biological role (e.g. venom); (4) strategies of treatment of envenomation would profit if it were more fully appreciated why venom is composed of more than just a suite of toxins.

INTRODUCTION

The venom apparatus of poisonous snakes consists primarily of two components: a modified tooth, the fang by which venom is delivered into prey, and the venom gland (or glands) where toxin is produced and stored. Venomous snakes use the venom apparatus to rapidly kill prey and secondarily in defense from their own enemies.

The structure of fangs and venom glands are the subject of many revealing descriptive papers (e.g. Kochva and Gans, **1966;** Rosenberg, **1967;** Nickerson, **1969;** Gabe and Saint Girons, **1971;** Halstead et al., **1978).** However, clarifying the evolution of the venom apparatus has proved to be a more contentious and elusive task (Smith and Bellairs, 1947; Kroll, **1976).** In part, this arises from phylogenies of snakes constructed upon only a general or anecdotal knowledge of the functional morphology of the jaw apparatus. Thus, the first purpose of this paper is to review the functional role of both the apparatus and the evolutionary antecedents of the venom apparatus. This will lead to the formulation of focused hypotheses that yield testable predictions.

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The conclusions reached herein about the evolution of the snake venom apparatus shed a different light upon ophidian taxonomy and phylogeny, venom pharmacology, and even upon clinical treatment of snakebite. Thus, the second purpose of this paper is to discuss the implications of these conclusions for these related areas.

RESULTS

A) *Evolution of the Fang*

1. *Morphological Series*

Venomous snakes evolved from nonvenomous ancestors. Three families of snakes are immediately involved: Colubridae, Viperidae, and Elapidae (including sea snakes). Viperids and elapids are poisonous snakes with sophisticated venom apparatuses used to quickly kill prey. However, most colubrid snakes are basically nonvenomous. True, some such as Dispholidus seem to parallel viperids and elapids in that they possess a highly toxic venom apparatus and use it to rapidly kill prey. But, the vast majority of colubrids are truely nonvenomous.

The origin of viperid and elapid snakes from colubrids has been a longstanding concern among those interested in advanced snakes (Boulenger, 1893, 1896, 1917; West, 1895; Alcock and Rogers, 1902; Phisalix, 1912, 1922). Several relationships have been proposed. One suggests a single origin of venomous snakes from colubrids (Cope, 1900; Mosauer, 1935); another that elapids arose from opisthoglyphous colubrids, and viperids from proteroglyphous colubrids (Anthony, 1955). The relationship I use here is that both elapids and viperids evolved from opisthoglyphous colubrid ancestors, but independently (Kardong, 1980). This evolution of venomous snakes from opisthoglyphs probably occurred several times (Kochva et al., 1967; Bourgeois, 1968; McDowell, 1968; Savitzky, 1980). However, despite a lively polyphyletic origin of venomous snakes, these fall along but two pathways, one leading to viperids and viper-like snakes, and the other to elapids and elapid-like snakes. It is beyond the scope of this paper to identify how many times each of these paths was traveled by evolving snakes. Instead, the purpose is to analyze the general adaptive advantage of changes on each evolutionary highway.

If we focus our attention on the maxillary bone and the teeth it hears, then one can construct a simple morphological series *(sensu* Maslin, 1952) through which the maxilla and its teeth transform into the shortened maxilla and fang of elapids on the one hand, and viperids on the other (Fig. 1). Notice that within colubrids, there exists a range of morphological conditions. The first state, and presumbly phylogenetically the most primitive, is exhibited here by *Pituophis* wherein the shaft of the maxilla is long, its teeth numerous, and the dentition basically homodont (*sensu* Edmund, 1969). In a more derived condition, as exhibited by *Dispholidus,* the maxilla is shortened, the teeth reduced in number,

and the dentition heterodont. Heterodonty is achieved by the differentiation of the posterior maxillary teeth that lengthen through this series, change shape, and eventually come to bear a groove along their sides.

ELAPIDAE   **VIPERIDAE**
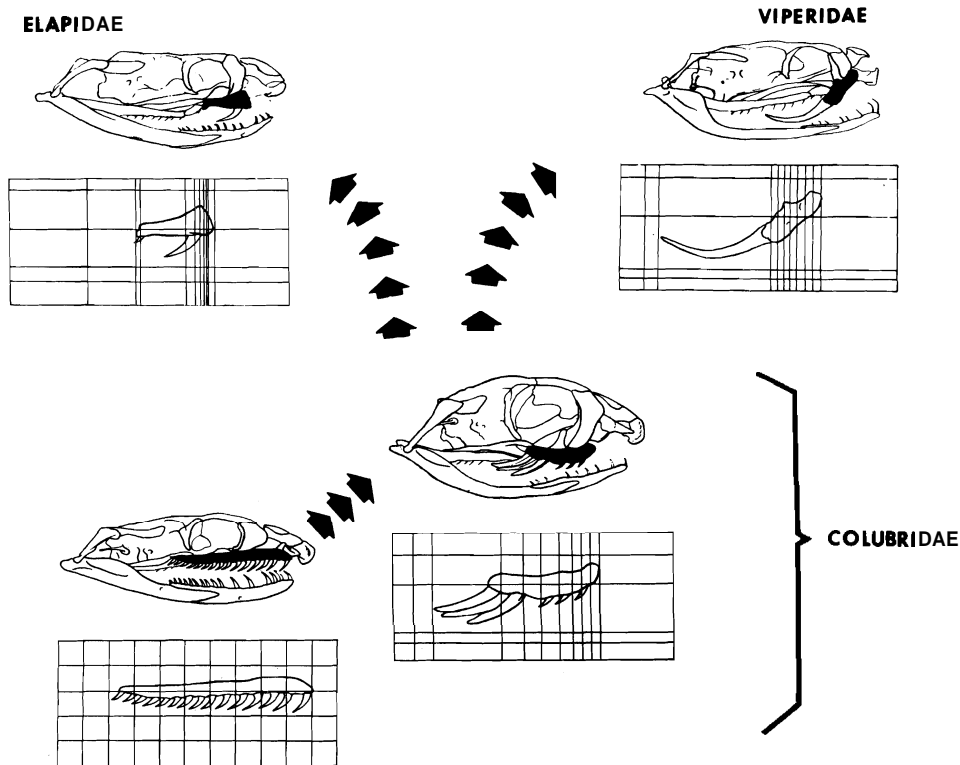
COLUBRIDAE

Fig. 1 — Transformation series of the maxilla and teeth it bears within the family Colubridae and to the families Elapidae and Viperidae. The rectangular co-ordinates laid over the isolated maxilla diagrammatically express changes within this morphocline. Through this series, the maxilla shortens, tooth number is reduced, and the posterior maxillary tooth lengthens. In elapids, this tooth has migrated forward to a more rostral position on the maxilla. In viperids, this tooth resides at the posterior end of the maxilla, but kinetically rotates forward during the strike. Actual skulls depicted among the colubrids are those of *Pituophis* (left) and *Dispholidus* (right). A *Naja* and *Vipera* skull represent Elapidae and Viperidae, respectively.

Evolution of the maxilla and its teeth within colubrids thus proceeds from an aglyphous to an opisthoglyphous condition. Between these two extremes lie most colubrids showing graded, intermediate states. For instance, next after the initial condition would follow snakes that possessed maxillae with slightly elongated maxillary teeth (e.g. *Thamnophis*). Next would lie snakes possessing long, rear maxillary teeth, but with secretion groves (e.g. *Crotaphopeltis*). A secretion channel too appears

in gradual stages. It would appear first, in this transformation series, as a corner between two adjacent teeth (Taub, 1967) and later as a groove within a tooth (Sarker, 1923).

This trend within colubrids to a shortened maxilla, reduced number of teeth, and elongated posterior tooth continues into the two venomous families. But, the continuation of these trends is established in two different ways. In viperids, the elongate posterior tooth (now a fang) lies at the rear of the shortened maxillary bone. In elapids, the elongated posterior tooth (now also a fang) lies not at the rear of the shortened maxillary bone, but forward on the remaining shaft. Occasionally, small teeth remain at; the posterior end of the elapid maxilla marking the point at which the fang once resided in elapid ancestors.

2. Adaptive Advantages

a) Accretion Hypothesis

A common view holds that these evolutionary changes in the maxilla and its teeth are driven by the increasing and additive advantages long teeth serve in venom injection. Thus, by the accretion of progressive toxic benefits, a venom system develops. This hypothesis predicts that the initial and the subsequent role played by these teeth was in prey capture.

To test this prediction, several living species (Thamnophis, *Crotaphopeltis*) falling within the middle stages of the transformation series among colubrids were examined to see just how they used their maxillae and posterior maxillary teeth. These species possess long posterior maxillary teeth. The results (Kardong, 1979, 1980; Wright, et *al.,* 1979) showed that, in fact, they did not use these teeth extensively during prey capture. Instead, they used these teeth to manipulate prey once already caught (see also Minton, 1944; Platt, 1969; Kroll, 1976). Thus, these teeth, even though slightly elongated, did not serve to inject a venom during prey capture, but instead aided swallowing by acting like small hooks to give better purchase an the slippery or uncertain surface of the prey. Further, comparison of the posterior maxillary teeth and of a venom fang revealed that the two are quite unalike (Schaefer, 1976; Kardong, 1979; Wright et al., 1979).

Thus, no support was found for the predictions of the accretion hypothesis, at least as applied to snakes within the middle of the transformation series.

b) Deglutition Hypothesis

Alternatively, I propose (Kardong, 1979; 1980) that these teeth borne by the maxillary bone initially functioned as hooks or gaffs to improve purchase during swallowing. This role favored, (1) elongation of the teeth, and (2) shortening of the maxillary bone, two changes, in fact, present in the jaws of many colubrid snakes. Once long teeth along the maxillary bone had arisen to serve the requirements of swallowing, then they would be preadapted to subsequent evolution into a new function, that of venom injection. But, the initial adaptive avantage of long maxillary teeth was not related to venom injection, but instead to swallowing.

B) *Evolution of the Venom Gland*

1 . *Morphological Series*

The evolution of the venom gland, like the previous evolution of the fang, begins within colubrid snakes. Within colubrids, the Duvernoy's gland is the evolutionary predecessor of the venom gland (Gans and Elliott, 1968; Kochva, 1978). A morphological series constructed now for the Duvernoy's gland shows its transformation into the venom gland of viperid and of elapid snakes (Fig. **2).**
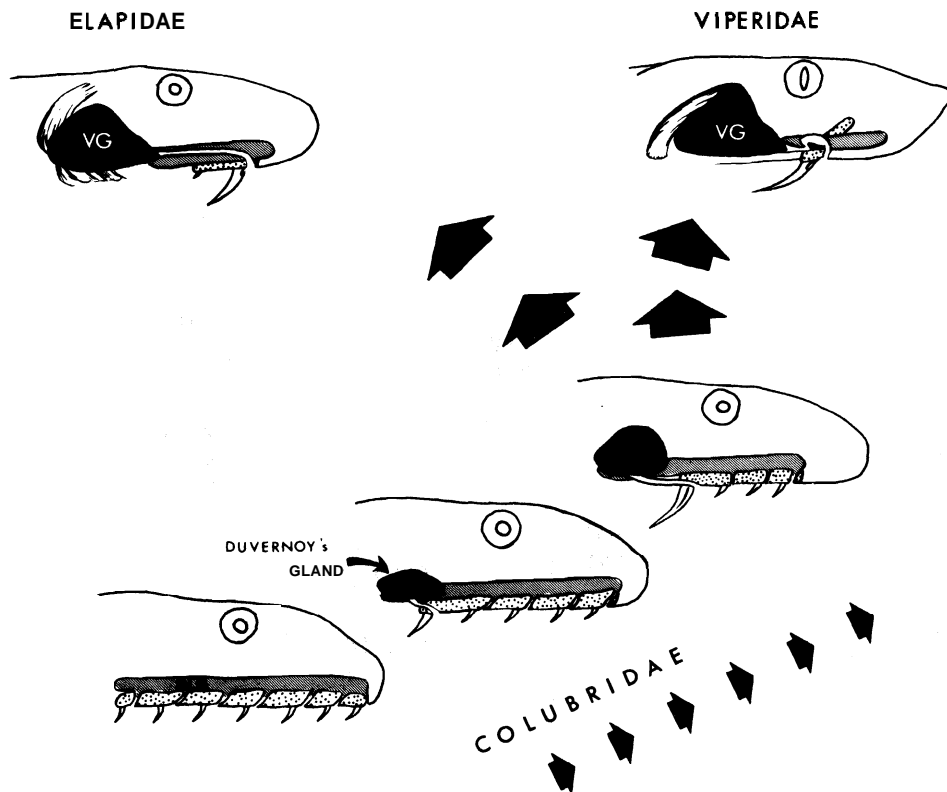

Fig. 2 — Transformation series of **Dúvernoy's** gland. This gland appears first within the middle of the colubrid series. It arises near the posterior end of the **supralabial** gland **(SLG).** Through the **morphocline,** the Duvernoy's gland transforms independently into the venom gland **(VG)** of **elapid** and **viperid** snakes.

2 . *Adaptive Advantages*

a) *Accretion Hypothesis*

Again, the conentional view is that the Duvernoy's gland was always slightly venomous and that the increasing, additive advantages of venom injection drove the changes leading eventually to appearance of a fully venomous gland. But, again there is reason to doubt this hypothesis. First, as just mentioned, eventhough the teeth of colubrids

are long, they are otherwise structurally quite unlike fangs. Second, most colubrid snakes do not have large storage areas to hold venom (Taub, 1967) to inject and rapidly kill prey.

Further, those who subscribe to this accretion hypothesis face a self-imposed paradox, what may be termed the "paradox of imperfection". By the accretion hypothesis, possessors of a Duvernoy's gland are "on their way" to becoming highly venomous, but, as yet, possess only a mild venomous capacity. But, in fact, most living colubrids are so endowed with long, posterior maxillary teeth (Marx and Rabb, 1972) and a Duvernoy's gland (Taub, 1967). In most parts of the world, such colubrids live sympatrically with and outnumber in terms of species, venomous snakes such as viperids and elapids. The paradox lies in the fact that such colubrids with a presumed mildly venomous secretion, but "imperfect" venom apparatus, could be so successful with these two families that possess a highly venomous and efficient venom apparatus. It does seem contradictory that colubrid species could compete and thrive using an "imperfect" venom injection system as successful contemporaries with elapids and viperids.

Perhaps, I have overstated or misstated the paradox. On the other hand, the paradox may arise from a flawed hypothesis, the accretion hypothesis. This, in fact, is my view. Most colubrids simply do not seem to use their oral secretions as venoms. Eventhough the oral secretions of many colubrids are proving to be more toxic than previously suspected (McAlister, 1963; Heatwole and Banuchi, 1966; Vest, 1981), still these same species do not, in fact, use their oral secretions to rapidly kill prey as do truly venomous snakes possessing fangs.

2. *Deglutition Hypothesis*

Duvernoy's gland secretion (in most colubrids) serves not as a venom. This is to say, it does not serve to help rapidly kill prey during prey capture. Instead, it must serve some other primary biological role or roles for these species. Being associated with the swallowing behavior of snakes, the secretion of Duvernoy's gland may reasonably be expected to play a role in swallowing and/or digestion. However, without further broad study of both the pharmacology of Duvernoy's gland secretions together with studies of the feeding behavior, it is premature to propose any careful alternative hypothesis.

CONCLUSIONS

Early in the evolution of the venom apparatus among snakes, the posterior maxillary teeth were long, but not yet fangs. Instead they served as spikes to help the snake grip slippery, bulky, or difficult prey during swallowing. So too, the Duvernoy's gland was not yet a venom gland, but likely served some other biological role.

Certainly once these teeth were long and the Duvernoy's gland well established, then this system was preadapted for the quite different role

of quickly subduing prey. Later in its evolution, the tooth/gland system then evolved under the increasing advantages derived from the ease and efficiency of rapidly killing prey. But, prehension and envenomation were not the *initial* roles that drove the early evolution of the glandular and dental elements in the jaws of colubrid snakes toward long, posterior teeth on a shortened maxilla.

IMPLICATIONS

A) Snake Evolution

1) *Viperidis and Elapids* - *two venom modes*

Both viperid and elapid snakes evolved independently from opistho-glyph ancestors. At least, this is the view I take based upon the arguments presented herein. The alternative view that elapids (or viperids) arose from proteroglyph ancestors is contradicted by the position of the venom gland (McDowell, 1968), embryonic development (Martin, 1899a,b.c; Kochva 1963; 1965), and rear maxillary tooth structure, position, and function (Kardong, 1980:273-274).

Upper jaw teeth in colubrids serve in two primary capacities-prehension and swallowing. Rut, these two activities are not always shared equally among the teeth. Anterior teeth of the mouth tend more often to be involved in prehension because they are first to come into the vicinity of the prey and because they bear responsibility for snagging elusive prey. Correspondingly, anterior teeth are often long and recurved reflecting their special role in prey capture (Frazzetta, 1966). Posterior teeth, on the other hand, tend to be involved in preingestion/swallowing manipulations. Because of the kinetic motion of the maxilla, rear teeth it bears lie at an especially favorable mechanical position to aid in swallowing (Kardong, 1979). Consequently; posterior maxillary teeth are often long and blade-shaped (Wright *et al.* 1979).

The fang borne by the maxilla in elapids and viperids is, like anterior teeth of colubrids, deployed principally during prey capture. It is thus fashioned similarly. For instance, the fang is conical and often recurved (Klauber, 1956); it is located, during the strike, in the anterior part of the mouth. In this latter feature, however, this forward position in the mouth is accomplished in two different ways. In viperids, the fang rides upon a highly kinetic maxilla that erects during the strike to bring the fang well forward in the mouth (van Riper, 1953; Kardong, 1975). In elapids, the fang rides on a less kinetic maxilla, but has undergone during its evolution a forward migration so that it sits in a more anterior position along the shaft of the maxilla (Fig. 1). Thus, fangs in the two groups enjoy the advantages of an anterior position in the mouth, but this is achieved differently-phylogenetic migration along the maxilla in elapids, kinematic rotation in viperids. Although elapids and viperids are venomous snakes, they seem to be separately derived styles of a venomous mode of life. They differ in the structural features of the

maxilla and fang just mentioned, relative toxicity of tlieir venoms (e.g. Minton and Minton, 1969), and perhaps even in behavioral styles in their strategies of prey capture (Naulleau, 1965; Kardong, 1982).

2) *Duvernoy's gland*

The Duvernoy's gland in most colubrid snakes is unlikely a gland "on its way" to being a venom gland, but shquld be examined for the immediate biological role it plays in the life oȷn those snakes possessing such a gland.

B) *Pharmacology*

1) *Toxin and Venom*

A distinction should be made between a secretion that is a "toxin" and one that is a "venom", at least as applied to snake secretions in a biological context. These two terms have grown up in the medical lite- rature with closely related meanings (e.g. Russell, 1980). I don't intend to propose redefinition in a medical or clinical context. However, the transference of these terms into a biological context has led to confusion. As a result, some animals live with an undeserved reputation for danger and even some medical strategies of treatment of suspected envenoma- tions suffer from the confusion.

In a biological context, by "toxic" I mean the lethal *property* of a chemical expressed as an LD_{50} or LD_{100}, for example; it is usually identified and characterized under defined laboratory conditions. However, by the term "venomous" I mean the *function* of the secretion, specifically the biological role (Bock, 1980) of the substance in the life of the animal producing it. Observation of the free ranging animal in its natural habitat is usually or ideally the basis for concluding (or not) that a secretion is used as a venom. The two terms rest on different concepts so more is at issue than mere semantics.

If Duvernoy's gland secretion is shown to be toxic, some suggest from this alone that the snake is likely venomous. However, there are two reasons for resisting such a hasty conclusion.

2) *Incidental Byproduct*

First, to prove a substance toxic in character is insufficient to prove it venomous in practice. Toxicity can occasionally be an incidental byproduct. For example, some components of human saliva are toxic and possess anȁ LD_{50} (Bonilla *et al,* 1971). Yet, no food humans consume require envenomation to make it safe to eat, nor are there enemies thwarted by threat of saliva injection. Toxicity is incidental and those seeking the biological role of saliva look, quite rightly, beyond this property to its digestive roles to understand its chemical character. How- ever, analysis of oral secretions from "nonvenomous" snakes has not always been so sensible. Too often, only the property of toxicity of these secretions seems to have been seriously considered. Certainly, this

is understandable. Lethal dose, if any, can be relatively easily demonstrated, and hence toxicity discovered; also, the toxicity alone makes the substance medically important regardless of its actual biological function. Yet, in many colubrid secretions, toxicity might be, as with human saliva, incidental, a property with no or only secondary biological significance. It would be misleading to call humans "venomous" simply because they possessed a "toxic" saliva. Similarly with snakes. In a biological context, distinguishing conceptually between a toxin and a venom should help avoid such confusion.

3) Other Functions

There is a second reason for resisting the temptation to conclude that a toxic secretion is also automatically a venom. In most colubrids, Duvernoy's gland secretion functions in capacities other than as a venom. Many colubrids possess well developed Duvernoy's glands, yet do not use its secretion to rapidly kill prey. To take an example, the wandering garter snake (Thamnophis elegans) possesses a Duvernoy's gland secretion of alarming toxicity approaching that of some viperid snakes (Vest, 1981; 1982), yet lacks the teeth to inject much secretion (Wright et al., 1979), and does not feed by bringing rapid death to the prey (Peterson, 1978). It possesses the toxicity, but lacks the equipment and behavior to use the secretion as a venom. The secretion from Duvernoy's gland or, for that matter, any secretion released from a specialized organ or group of cells may serve several functions. It may function as a venom, it may paralyze prey, it may tranquilize, it may aid digestion, and so on. In Thamnophis and similar colubrids, what then could be this secretion's function?

4) Alternative or *Additional* Functions

To date pharmacological and biological analysis of Duvernoy's gland secretion has been preoccupied with toxicity (e.g. Philpot et *al.,* 1977), so one is left to speculation about alternative functions. However, several seem likely.

a) Lubrication

Besides Duvernoy's and venom glands, snakes possess additional strips of glandular tissue along upper and lower lips (Taub, 1966) that release their products over the prey to lubricate its passage into the esophagus. Duvernoy's gland secretion, released at the base of rear maxillary teeth, trickles down the sides of these teeth to likely finds its way to the surface of the prey. Thus it could be an additional source of lubricant to facilitate swallowing.

b) Digestion

In viperid and elapid snakes, venom certainly contributes to rapid prey death, but has also been suspected of promoting digestion (Reichert, 1936; Zeller, 1948). Experimental work — injecting venom into mice and then comparing rates of their digestion to controls — indicates that rattlesnake venom actually speeds digestion (Thomas and Pough, 1979).

Such venom attributes may be of adaptive value for snakes feeding on large numbers of prey in short periods of time or to enhance digestion in snakes from cold or temperate climates. Similar tests have not been done for the secretion from Duvernoy's gland, but the possibility it serves a similar function seems worth investigating.

c) *Anti-putrefaction*

Snakes swallow their food without tearing or chewing. Digestive enzymes released from the wall of the gut may not always complete the inward spread of digestion before tissues within the center of the bolus putrefy. Venom injected deep (Thomas and Pough, 1979) or Duvernoy's gland secretion inoculated subcutaneously within the prey before swallowing may retard this putrefaction.

d) Detoxify Prey *Secretions*

Many snakes, especially colubrids, feed on amphibians possessing skin glands which contain, depending upon the amphibian species, irritating to actually poisonous secretions (Habermeihl, 1971; Lutz, 1971; Brodie and Tumbarello, 1978). Duvernoy's gland secretion in those colubrids regularly feeding on amphibians may help neutralize these skin secretions released by the amphibian prey.

Further, these oral secretions could contribute to improved oral hygiene or prevent sticky material elaborated by prey from fouling the jaws during swallowing (Gans, 1978; Jansen, 1982). My intent is not to settle the questions of what functions snake oral secretions serve. Instead, I wish to emphasize that snakes, faced with a variety of problems while catching and swallowing prey, might possess various components in the Duvernoy's gland or venom gland secretions that serve a variety of biological roles besides or in addition to envenomation.

Even though introduced into the prey in small quantities compared to a true venom, some propose that the Duvernoy's gland secretion may slow or tranquilize the prey, thus making prey capture less risky and swallowing easier. Perhaps it does. But, tranquilizing prey differs from envenomation. Tooth form (Kardong, 1979; Wright et ag., 1979), maxillary bone structure (e. g. Bogert, 1943; Brattstrom, 1964), and behavior (e.g. van Riper, 1953; Klauber, 1956; Dullemeijer, 1961; Greene and Burghardt, 1978) differ from species that use venom predominantly to capture and dispatch rather than just quiet prey. Consequently, tranquilization seems distinct from true envenomation as a prey handling technique.

C) Clinical Significance

Venoms are complex. Laboratory analysis proceeds by fractionation into molecular components then to separate analysis of each fraction. Some components exhibit toxicity while other components seem to be without toxic effect (e.g. van Mierop, 1976; Russell, 1980). These nontoxic fractions are usually classified as potentiators, activators, or amplifiers (e.g. spreading factors) of the toxic components. Generally this conclusion sems on mark. However, some of these components of venom may lack toxicity, because they are present for biological reasons other than to

promote rapid prey death (e.g. Thomas & Pough, 1979). In fact, even demonstrating toxicity in a particular component does not or ought not to end the search for its possible function. Other attributes, besides toxicity, should be considered if one is to eventually understand the biochemical action and interaction of all venom components.

One fruitful place to begin such an analysis may be with the secretion from Duvernoy's gland. The venom gland of viperids and elapid snakes evolved from the Duvernoy's gland; these venomous snakes feed upon similar foods and thus face generally similar problems with prey as many "nonvenomous" colubrids. Certainly the venom of viperids and elapids functions primarily to rapidly kill prey, but components serving secondary functions are most likely present as well. Venom is a suite of chemicals, all of which go into a victim — toxins and nontoxins alike. Consequently, it seems advisable for strategies of treatment of envenomations to be founded upon a knowledge of all components and their biological roles, not just upon the action of the toxins. Perhaps, somewhat ironically, one place to focus such an analysis of snake venoms, is on "nonvenomous" colubrid snakes.

ACKNOWLEDGMENTS

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