Bites of Venomous Serpents and Their Treatment

Wherever Serum is Employed the Mortality Has Become Almost Zero

Dr. R. Burnier

THE principal venomous serpents of France are two vipers (*Vipera herus* and *V. aspis*), which, though less formidable than their tropical congeners, annually kill a few persons and wound many others. Only a few years ago, from 30 to 40 per cent of viper bites proved mortal, but now Dr. Calmette's researches have furnished a cure which is absolutely certain, if it is promptly applied.

The treatment is an outgrowth of Calmette's study of the toxic properties of serpent venom, which vary in different serpents. There are two great families of venomous serpents: the *Colubridae*, with fluted poison fangs, represented by the East Indian cobra; and the *Viperidae*, with perforated fangs, represented by the European viper and the American rattlesnake. All serpent venoms, but especially those of *Viperidae*, contain a proteolytic ferment which liquefies gelatin, albumen and fibrin, and which is destroyed by heating to 158 deg. Fahr. All venoms also possess power to dissolve the red and white corpuscles of the blood, and this hemolytic property requires for its destruction heating to 212 deg. Fahr. for half an hour. Serpent venoms contain, in addition, numerous toxins, called cytotoxins and bacteriotoxins, which destroy microbes, protozoa, and the cells of the liver, kidneys and other organs, more or less rapidly.

But the most important poisons in serpent venom, those which cause death, are two in number. One is a poison to the nervous system, called neurotoxin, which, according to Calmette, inhibits the respiratory centers and causes death by suffocation. The other poison, hemorrhagin, first coagulates, then redissolves the blood and destroys the walls of the blood-vessels, besides producing severe local inflammation. All serpent venoms contain both neurotoxin and hemorrhagin, but in varying proportions, neurotoxin predominating in *Colubridae*, and hemorrhagin in *Viperidae*.

These facts explain the differences in the effects produced by the bites of serpents of different species. In a person who has been bitten by a cobra, the most conspicuous symptoms are of nervous character. There is very little local pain, little or no swelling, but the patient soon experiences a sort of lassitude and an irresistible desire to sleep. His respiration becomes labored, his pulse slow and weak, until he falls into coma and dies. In some cases, the heart continues to beat two hours after respiration has ceased. The whole tragedy occupies only a short time, rarely exceeding six hours.

The bite of a viper or a rattlesnake, on the contrary, instantly produces intense pain, the bitten part quickly swells and becomes filled with bloody serum, and the whole limb is attacked by severe cramps. The patient suffers with burning thirst and dryness of the mouth, sometimes with hemorrhages of the eyes, stomach and bowels. The consequences vary with the circumstances of the bite. If the venom is introduced into a vein or a very vascular part, it almost always causes death by coagulation of the blood and embolism. If the bite is inflicted through the garments very little poison is absorbed, but even in this case the wound swells, some-

times enormously, and it may develop gangrene or phlegmons, the cure of which requires prolonged treatment. Convalescence is often very slow, the intellectual faculties may be impaired and, in children, an arrest of development has been observed. Temporary blindness has been noted in human beings, and it is frequently observed in

The fer-de-lance (*Lachesis lanceolatus*) of Martinique.

Imprints made on the skin by the bites of various serpents. At the left, non-venomous *Colubridae*; in the middle, venomous *Colubridae*; at the right, *Viperidae*.

domestic animals that have been bitten on the head. Bites on the head and neck are more dangerous than bites on the limbs, as fatal asphyxia may be produced mechanically by swelling of the throat.

The symptoms presented by the patient, therefore, show whether the serpent that has bitten him belongs

several persons in succession, it loses some of its venom with each bite, and the bites last inflicted are not very dangerous. A bite inflicted through leather or cloth leggings is less dangerous than a bite on the bare skin. The size of the victim should also be taken into consideration. The relative mortality is much higher in children than in adults.

Venomous serpents enjoy a considerable degree of immunity, especially against their own venom. Even non-venomous serpents show great resistance to serpent venom, and so do some mammals, including the hedge hog, the mongoose and the hog, all of which are great snake-hunters. The hedge hog, of course, is protected by its spines, and the domestic hog, which suffers little when bitten by serpents, is protected by its tough hide and its thick layer of fat.

More important than this natural immunity is acquired immunity. In every country infested with venomous serpents, there are persons who claim to be immune to the bites of serpents, either because they are insensible to the effect of the venom, or because they possess secret methods of treatment. Some East Indian snake charmers extract the fangs of the serpents which they exhibit, but there is no doubt that many perform with serpents that have not been thus treated, yet fatal accidents are rare among these people, who claim, perhaps with truth, to possess a secret process of immunization, which is handed down from father to son.

Fraser has proved that repeated ingestion, by the mouth, of small doses of venom gives white rats and young cats power to resist several times the normally fatal subcutaneous dose. Possibly the serpent charmers immunize their young sons by a similar method. It has been asserted that some serpent charmers cause themselves to be bitten occasionally by young cobras, and that others practise graduated inoculation. A similar method is employed by French viper hunters. Calmette knew one of them who took care to be bitten, at least once each year, by a young viper. If he neglected this precaution and then happened to be bitten, the effects of the bite were far more severe than usual.

The researches of Calmette on cobra venom, and those of Phisalix and Bertrand on viper venom, proved that

Head of the red viper or asp (*Vipera aspis*).

to the viper or the cobra family. In some cases, an examination of the impression made on the flesh by the fangs and teeth will show whether the serpent was one or the other of these venomous reptiles, or a non-venomous member of the cobra family.

The gravity of the bite, of course, is proportional to the quantity of venom injected. When a serpent bites

animals can be made immune to several times the normally fatal dose of venom, by repeated hypodermic injections of very small doses, and that the blood serum of animals thus immunized possesses both immunizing and curative properties for that particular venom.

This is the principle of Calmette's serum treatment, which is now employed wherever venomous serpents constitute a public manace, and which has saved the lives of thousands of human beings and domestic animals. The serum possesses antitoxic, prophylactic and curative properties. That is to say, a mixture of venom and serum in proper proportions produces no effect when injected; an animal which has received a sufficient dose of serum is able to resist the action of normally mortal doses of venom, injected subsequently; and an animal which has received a normally mortal dose of venom can be saved by injecting serum without delay. The serum is most efficacious against venoms of the class from which it has been derived, but, in Calmette's opinion, the serum obtained from cobra venom is an effective antidote to the bites of certain *Viperidae*, including the vipers of France, the horned vipers of Africa, and the rattlesnake of America. This opinion is not shared by most authorities. According to Tidswell, Lamb, Martin and Vital Brazil, each serum is a specific antidote for the venom from which it is derived, so that the serum obtained from cobra venom confers immunity only against the bites of cobras and, theoretically, a special serum is required for each species of serpent. This difficulty is evaded, in practice, by using a polyvalent serum, obtained from animals inoculated with a mixture of venoms.

In most countries infested with venomous serpents, the teachings of Calmette are followed, and specific or polyvalent serums, adapted to local requirements, are prepared. In India, Semple obtains a serum from animals inoculated with the venoms of the two most common venomous serpents, the cobra and the daboia. In Brazil, Vital Brazil makes three serums—for the

The rattlesnake (*Crotalus tinificus*).

rattlesnake and two other species or classes. Rattlesnake serum is prepared in Philadelphia. At the Pasteur Institute of Lille, which supplies all the French colonies, Calmette produces a polyvalent serum from mixed venoms of *Colubridae* and *Viperidae*. The former are obtained in abundance from French Indo-China, but there is often a shortage in viper venom. Hence Calmette's serum is especially anti-neurotoxic, while its anti-hemorrhagic power varies greatly, according to the quantity of viper venom which the inoculated horses have received.

The serum is prepared by the following method: A horse is first injected with a mixture of venom and hypochlorite of lime. The injection is repeated every three or four days, the proportion of hypochlorite being gradually diminished to zero, and the operation being interrupted if the animal loses flesh. After this treatment has been continued about 16 months, the horse can withstand the hypodermic injection of 2 grammes (30 grains troy) of dry cobra venom, which is about 80 times the normally mortal dose, and is in condition to furnish an efficacious serum. The animal is then bled, 8 liters of blood being drawn 12 days after the last injection of

venom, 6 liters after an interval of 5 days, and 6 liters after a second equal interval. These 20 liters of blood yield a little more than 10 liters of serum, which is decanted into bottles, which are sealed and sterilized. The serum retains its activity for several years, but more certain preservation for a much longer period can be assured by desiccating the serum and sealing it in glass capsules, each containing one gramme (15.4 grains troy) of the dried serum, which when required for use, is dissolved in 10 cubic centimeters (one third fluid ounce) of water that has been boiled and cooled.

If the patient is treated promptly, before toxic symptoms have appeared, a hypodermic injection of 10 to 20 cubic centimeters (one third to two thirds fluid ounce) of serum usually suffices to prevent poisoning in an adult. While awaiting the injection it is advantageous to ligature the limb, immediately above the bite, and to cauterize the wound with a red hot iron or a solution of potassium permanganate or hypochlorite of lime. If the bite has been inflicted by a large or very venomous serpent, 30 cubic centimeters (1 fluid ounce) of serum should be injected at once. The quantity of serum required varies directly with the time lost and the gravity of the symp-

toms, and inversely with the size of the patient. More is needed for a child than for an adult.

If the case is far advanced and the patient is in a critical state, there should be no hesitation about injecting 30 cubic centimeters into the veins, and repeating the dose if necessary. If the respiratory centers have already been affected, it is advisable to practise artificial respiration, in order to prolong the stage during which the organism can resist the venom until the serum can produce its effect. No matter how desperate the case may appear, there should never be any hesitancy about employing the serum, which has effected cures absolutely unhopd for.

Wherever the serum treatment is employed, the mortality among treated cases has become almost zero. In Sao Paulo, Brazil, of 275 cases treated with appropriate serums only one resulted fatally, and in this case the patient was at the point of death when the serum was applied. In India and some other countries, unfortunately, the natives rebel against the new treatment, and many deaths are still caused by venomous serpents. —Translated for the SCIENTIFIC AMERICAN SUPPLEMENT from *La Nature*.

The Industrial Synthesis of Sodium Cyanide*

Probable That the Supply Will Exceed the Demand Through a New Development

By Charles Gravier

Of the three industrial forms of combined nitrogen—cyanides, ammonia and nitric acid—the cyanides occupy the lowest place in industrial statistics. While Chile annually produces 2,500,000 tons of sodium nitrate, and 1,000,000 tons of ammonium sulphate are furnished by gas works and coke ovens, the annual production of cyanides does not exceed 25,000 tons. The employment of cyanides has greatly increased since the introduction of the MacArthur and Forrest process in the metallurgy of gold, in 1888. Before that date, the annual production of potassium cyanide, the only cyanide then utilized, did not exceed 100 tons.

Four hundred and fifty tons were produced in 1888, 750 tons in 1890, 3,500 tons in 1895, and for several years there was a steady annual increment of about 1,000 tons, consisting partly of sodium cyanide, which had been introduced meanwhile. Almost the entire output of alkaline cyanides is used in the refining of gold, only a very small proportion being consumed in electroplating with gold and silver. But, though the cyanides occupy a comparatively small place in the great industry of nitrogen compounds, nitrogen in the form of cyanogen commands a higher market price than nitrogen in the form of ammonia or nitric acid, which are worth not more than 1.5 francs per kilogramme (13.2 cents per pound) of nitrogen, while the cyanides cost at least 6 francs per kilogramme (52.8 cents per pound) of nitrogen. In these conditions, it would be profitable to convert nitric acid or ammonia into cyanides. The transformation can be effected by various reactions, none of which has been utilized for converting sodium nitrate into sodium cyanide, though cyanides are actually made from ammonia. The inverse transformation is still easier to accomplish, as cyanides evolve ammonia when they are heated in a current of water vapor. Hydrogen cyanide, in presence of water, tends to decompose into ammonia and formic acid, while its salts, in similar conditions, yield ammonia and formates. At red heat, however, the formates split up into carbonates, carbon monoxide

and hydrogen, so that the final result is given by the equation:

Many chemists are now endeavoring to effect the industrial synthesis of ammonia by way of the cyanides. To me this method appears illogical, because hydrocyanic acid, a compound formed from its elements by an endothermic reaction in which 30.5 calories of heat per gramme-molecule are absorbed, will always be more costly than ammonia, which is formed by an exothermic reaction, evolving 12 calories per gramme-molecule.

Fig. 2.—Horizontal section of retort for producing sodium amide.

The cheapness with which metallic sodium can be produced by electrolysis of fused soda, has made possible the development of a process by which a large part of the cyanide required by gold refiners is now produced from sodium, ammonia and carbon.

The English firm of Castner, whose name is intimately associated with the history of sodium, first devised these methods of obtaining the metal and its cyanide, but the industrial production of cyanide was made practicable by improvements introduced by the Deutsche Gold- und Silberscheide Anstalt, of Frankfurt.

The chemical formula of sodium cyanide, NaCN, in which Na=23 and N=14, shows that nearly 2 kilogrammes of sodium are required in order to convert 1 kilogramme of nitrogen from the ammonia form to the cyanide form, and thus to raise its market value from 1.5 francs to 6 francs. The Castner electrolytic process, using a cheap source of electricity, furnishes the 2 kilogrammes of sodium for 2 francs, leaving a margin of 2.5 francs to cover other expenses and profits.

THE ORIGINAL CASTNER PROCESS FOR THE SYNTHESIS OF CYANIDES.

1. *Theory of the Process.*—It is well known that metallic sodium, at a temperature of about 400 deg. Cent. (752 deg. Fahr.) absorbs ammonia gas, forming an amide and liberating hydrogen.

One molecule of this amide and one molecule of sodium cyanide, fused together, combine at 550 to 600 deg. Cent. (1,022 to 1,112 deg. Fahr.), yielding 1 molecule of sodium cyanide and free hydrogen.

Finally, this molecule of cyanamide, mixed intimately with carbon, combines with it at 750 to 800 deg. Cent. (1,382 to 1,472 deg. Fahr.), forming 2 molecules of sodium cyanide.

Thus the molecule of cyanide used in the process is recovered and a second molecule is gained.

By a modified process, in which the employment of cyanide as a reagent is avoided, the sodium amide is converted first into sodium cyanamide, and then, at 800 deg. Cent. (1,472 deg. Fahr.), into sodium cyanide, by direct combination with carbon.

Castner's first idea was to produce sodium cyanide directly from its elements. As the combination is exothermic, evolving 50 calories per gramme-molecule, there can be no doubt of its possibility. I verified this theoretical deduction before I knew of Castner's researches. I obtained sodium cyanide by passing a current of pure nitrogen over a mixture of charcoal and sodium, but the yield of cyanide was small. Castner had previously, in 1894, made similar experiments. He poured fused sodium slowly on charcoal, heated in a vertical cylinder, to which a current of nitrogen was admitted by a lateral orifice. Sodium cyanide accumulated at the bottom of the cylinder. The quantity produced was greater than was obtained by passing nitrogen over a mixture of charcoal and sodium carbonate, but Castner soon recognized the advantage of substituting ammonia for nitrogen.

The original Castner process for the synthesis of sodium cyanide was conducted in two successive stages, sodium amide being produced in one apparatus at 300 to 400 deg. Cent. (572 to 752 deg. Fahr.) and converted into sodium cyanide in a second apparatus at 700 to 800 deg. Cent. (1,292 to 1,472 deg. Fahr.).

2. *Preparation of Sodium Amide.*—The reaction between ammonia and sodium takes place in a horizontal rectangular retort with a sloping bottom (A, Fig. 1). The upper part of the retort is divided into compartments by vertical partitions C which dip slightly into the liquid sodium M. These partitions, which do not extend entirely across the retort and are attached alternately to its two sides, compel the current of ammonia to pass

Fig. 1.—Castner apparatus for producing sodium amide.

A, horizontal retort; B, hearth; C, partitions; M, fused sodium; D, sodium inlet; N, ammonia inlet; F, hydrogen outlet; J, siphon; E, K, N, cocks.

Fig. 3.—Castner apparatus for converting sodium amide into sodium cyanide.

A, retort; B, hearth; C, funnel for introduction of charcoal; D, inlet for fused sodium amide; E, siphon for drawing off sodium cyanide.