Delphinium or *Larkspur* (fam. *Ranunculaceæ*).—The general subject of larkspur, as to constituents and activity, has been considered under the title of Stavesacre Seed. So well known a garden flower scarcely requires description. The accompanying illustration of *D. glaucum*, the tall larkspur, often miscalled aconite, gives a sufficiently good idea of the genus in general (see Fig. 3860). Some of the species are larger, many much smaller. The flowers are usually of some shade of blue, sometimes purplish. Many species abound in the grazing regions of Western North America, and they are much dreaded as stock poisons by herders, though the poisoning of human beings is not recorded, and is not likely to occur. These poisons are to be classed partly with aconite, to a lesser extent with stavesacre, as to the nature of their effects. The symptoms are muscular incoördination, motor paralysis, beginning at the posterior extremities, great cardiac and arterial weakness, and hypersensitive skin, with the special senses not affected. Convulsive tremors, especially of the posterior limbs, come on early and are followed by convulsions which increase in violence, and in one of which the animal usually dies. Death appears to be due chiefly to failure of the circulation. Atropine has been found a fairly good antidote, and potassium permanganate has also been found useful.

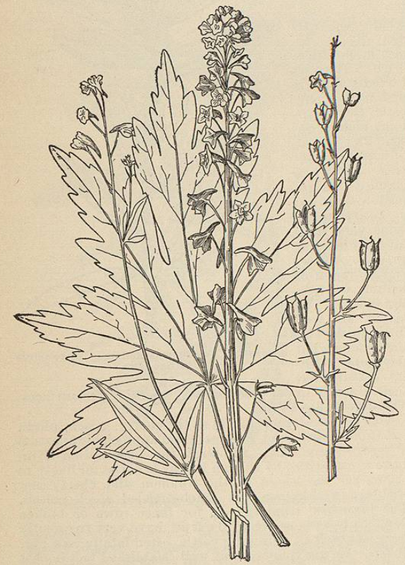

Fig. 3860.—Delphinium glaucum. (One-third natural size.) (After United States Department of Agriculture.)

Loco Weeds (fam. *Leguminosæ*).—Although poisoning by this famous group is confined practically to stock, especially horses and sheep, yet no article on poisonous plants could be considered complete without reference to it, particularly as it represents a very large and varied class of leguminous poisons which more or less affect the human system as well. The loco weeds pertain to the two genera *Astragalus* and *Aragalus* (*Oxytropis*), and knowledge as to their specific identity is in a number of cases indefinite and uncertain. They are perennial herbs, growing mostly in tufts or hummocks, with a dense rosette of radical leaves and papilionaceous, mostly purple or purplish flowers in spikes or racemes. The leaves are elongated and pinnate, the leaflets mostly numerous and more or less oblong or varying from ovate to obovate. The fruits are constructed like small pea pods, the seeds mostly resembling small peas and often rattling loosely in the dry pod. The herbage is without disagreeable taste. Animals are not naturally disposed to eat it; but having once done so, in case of scarcity of other food, they become ravenously fond of it and forsake all else in order to eat it. The poisonous constituents are not known, though great efforts have been made to isolate them. All indications point to their being of the nature of toxalbumins. Whatever they are they are excreted in the milk of the mother, since suckling lambs are frequently fatally poisoned together with the mother. Poisoning may be either acute or chronic, the latter being much more common. The symptoms are chiefly cerebral. There are incoördination and remarkable disorders of vision, though rarely blindness, and this usually in acute poisoning. The effect upon the vision seems to be that of causing objects to appear distorted. A similar effect upon hearing is observed. There are great and progressive disorders of nutrition, and these are especially referable to the skin and its appendages, sheep frequently losing the whole or part of their fleece and the teeth becoming loosened. Death, in cases of long duration, is usually from malnutrition. Very often the animal dies as a result of accidents, incurred either through frenzy or through weakness incident to the poisoning, such as falling into the water while drinking, and being unable to rise again. There is no known treatment for this form of poisoning other than to remove the cause and apply general restorative treatment.

Henry H. Rusby.

POISONOUS REPTILES.—All poisonous reptiles, with the single exception of the lizard Heloderma, belong to the order Ophidia—snakes. It is a popular error that snakes are easily divided into harmless and poisonous ones by readily recognized characteristics. Such division, however, is by no means a simple affair. The usual classification into Colubridæ—comprising all harmless snakes,—Colubridæ venenosæ, and Viperidæ indicates the close anatomical relationship between harmless and venomous snakes, and in external appearance mimicry is so frequently displayed that no one at a hasty glance is able to distinguish a harmless snake from its venomous relation. Thus, even experts have been subject to fatal mistakes. Indeed, nothing but a close inspection of the dentition can determine the nature of a specimen in question.

Distribution of Snakes.—It is but natural that the popular mind and imagination should have been occupied since time immemorial with poisonous snakes. The frequent and almost mysterious deaths after snake-bite have surrounded the whole class with a halo of fear and reverence which has not been confined to a few localities, but, in fact, has spread throughout the whole inhabited world, for poisonous snakes are found in all countries of the temperate, and more so, of the tropical zone. Numerous genera of the Hydrophids, elegant swimmers with a laterally compressed tail, swarm throughout the whole intertropical part of the Pacific Ocean. Their bite is justly dreaded. The tropical islands, however, and the tropical countries of the old continent are haunted by the worst kind of snakes, the Elapidæ. A large number of genera and innumerable types of every genus render parts of those countries, and especially of the islands, almost uninhabitable. The chief representatives of this genus are the Cobra di capello (Naja tripudians) and the somewhat smaller, though not less dangerous Krait (Bungarus fasciatus), both living throughout the whole of East India. The most formidable is the King-Cobra or Hamadryas (Ophiophagus elaps), the largest of all poisonous snakes; it attains the length of fourteen feet and it alone enjoys the reputation of attacking and even pursuing man. Its nearest relative, the Aspis of Cleopatra (Naja haje), the symbol of the Egyptian kings, lives throughout almost the whole of Africa. In the Western world this genus is represented by the beautiful coral snakes alone; one of them, Elaps fulvius, lives in our Southern States, where it is little feared on account of its alleged good nature, or rather its lack of irritability; its poison is, however, as active as that of its East Indian congener. Snakes are very numerous in Australia. Two-thirds of these are poisonous, and they belong exclusively to the family Elapidæ; the Tiger snake (Hoplocephalus curtus) and the black snake (Pseudechis porphyriacus) have a fearful reputation. Europe has none but various species of vipers; the well-known common viper (Pelias berus) lives in England, Germany, and chiefly in France. In the departments of Vendée and Loire Inférieure alone were reported 321 cases of bites with 62 deaths in six years, in Auvergne 14 cases with 6 deaths; in the South around the Mediterranean the more dreaded sand viper (Vipera ammodytes) is found. East India again has one of the most formidable vipers, the chain viper (Daboia Russelii), and in Africa there is the sluggish but very poisonous puff-adder (Clotho arietans). The greatest number of species of vipers are found in America, all of them belonging to the sub-family of the Crotalidæ or pit-vipers, so called from a deep pit lying between the nostril and the eye.*

The chief representatives of the pit vipers in the United States are the rattlesnakes. The banded rattlesnake (Crotalus horridus) is present throughout the whole territory from the Atlantic to the Rocky Mountains and far into Canada. Of the remaining six species of rattlesnakes we have to note the largest of all North American snakes—the diamond back (Crotalus adamanteus) of Florida and the South, and the swift prairie rattler (Crotalus confluentus) in the Mississippi Valley, and in the great Western basin; finally the smallest of all, the massasauga or ground-rattler. To the same sub-family belong the Southern water-snakes, the moccasin (Ankistrodon piscivorus)—animals so sluggish that they do not try to escape from an approaching man, and hence are not a little dreaded by the negroes working in the rice-fields; and finally, the beautiful copper head (Ankistrodon contortrix), which is not at all rare in the whole East—in fact, lives almost in the same expanse as the banded rattlesnake. In the Tropics almost all species grow to a larger size; thus the copper head is repeated in the larger *fer de lance* (Bothrops lanceolatus) of the West Indies; the rattlesnakes of Central America grow larger, as does

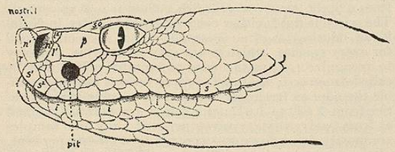

Fig. 3861.—Head of Rattlesnake.

the Crotalus durissus; and in the Orinoco Valley there lives the bushmaster of the Dutch settlers (Lachesis mutus), about as large as the Hamadryas of India.

* The object of this pit, which sinks into a cavity of the maxilla—as it were, a reversed maxillary sinus—is unknown. Leydig calls it the seat of a sixth sense, which means nothing else but that he has no explanation. At closer inspection I found the bottom of the pit not lined, but overspread by a thin membrane, the continuation of the external integument. Under this membrane, showing abundant ramifications of nerves, we find a cavity which opens by a duct at the anterior margin of the orbit. According to the careful investigations of Dr. Pollitzer, who followed it up by serial sections, the nerve connects with the auditory nerve. Pricking or any other irritation did not produce any reaction, nor did the destruction of one or both membranes have any effect upon the movements or the hearing of the snake. The hearing capacity of snakes is still a mooted subject with authorities in natural history.

Poison Apparatus.—Snakes are provided with numerous teeth—solid, pointed, recurved hooks, which serve rather to drag the prey down into the œsophagus than for purposes of attack and defence. While the teeth stand in a single row along either branch of the mandibula, they seem to be almost indiscriminately scatteredall over the maxilla and palate; nevertheless, two rows of larger maxillary with two nearly parallel rows of palatine teeth are readily distinguished. These are the functionary teeth which, after being shed,—a frequent occurrence,—are replaced by the numerous succedaneous teeth scattered throughout the mucous membrane of the palate. A poisonous snake exhibits the same arrangement of palatine teeth. Almost the entire row of maxillary teeth, however, is wanting, and its strength, as it were, is concentrated into one powerful tooth, the poison fang, which projects at the anterior end of the maxilla. It is true, we often find two or three teeth at this point; these are the functional fangs with one or two succedaneous ones which replace the primary functionary whenever lost by accident or shedding. Only the Elapidæ exhibit one or two ordinary conical teeth which are situated directly behind the grooved fang. The fangs are in all cases firmly inserted in the maxilla, immovable, almost erect, in one family, the Colubridæ venenosæ (comprising the cobras and hydrophids); in the Viperidæ, however (including the true vipers and pit-vipers), the movable fangs are only erected for biting, and otherwise in the resting they are folded back toward the palate like the blade of a pocket-knife in a plica of mucous membrane. The maxilla of the Colubridæ venenosæ is rather elongated and horizontal like that of the harmless snakes, but it is considerably shortened and placed almost vertically in the vipers. This short jaw bone, bearing at its lower end the firmly socketed fang, articulates at its upper end with the lachrymal bone, around which it rotates by the action of the pterygoid muscle.

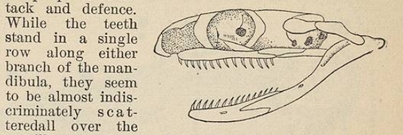

Fig. 3862.—Skull of Harmless Snake.

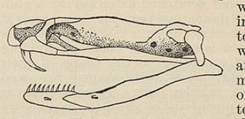

Fig. 3863.—Skull of Cobra (Elaps).

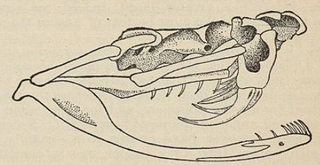

Fig. 3864.—Skull of Rattlesnake.

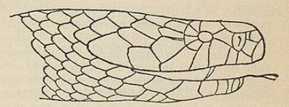

Fig. 3865.—Head of Cobra.

Some writers are of the opinion that, by looking at a wound inflicted by a snake, the species of the animal can be ascertained, and from the foregoing description it can readily be understood how from the

accompanying figures the bite of a harmless or poisonous snake could be determined. We must, however, bear in mind that a snake, while biting, very seldom implants

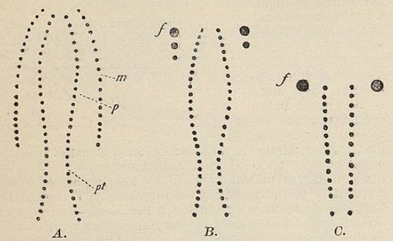

FIG. 3866.—Impression of the Teeth of *A*, harmless snake; *B*, cobra; *C*, viper. *f*, fang; *m*, maxillary; *p*, palatine; *pt*, pterygoid teeth.

all its teeth, and a wound scratched sideways by a gliding fang may be more dangerous than the impression of the whole dentition.

Another classification is sometimes made by dividing the venomous snakes according to the shape of their fangs, whether they carry short, cone-shaped, furrowed fangs or long, pointed, tubular ones. This condition is brought about developmentally in the first instance by the folding of the dentine which leaves a longitudinal furrow with an indication of a perforation at the upper and lower end along the anterior surface; and in the second by a complete approximation which produces a perfect tube. The pulp cavity is entirely separated from the poison canal. To the first class, the Proteroglypha, belong the Hydrophids and Elapidæ, or cobras; the latter class, the Solenoglypha, comprises the vipers and pitvipers. The intensity of a poisonous bite is not dependent upon the shape of the fangs, except that a longer tooth, such as that of the viperine snakes, is capable of injecting the poison to a greater depth; indeed, the viperine poison apparatus is the most perfect of any in the venomous snakes.

There is a third class of poisonous serpents, the so-called Opisthoglypha, the furrowed fangs of which, as the name indicates, are situated toward the rear of the mouth. It has long been doubted whether they should be classed among the poisoners, and for this reason they were grouped under the name of "suspecti." Recent investigations, however, have proven to a certainty that they also poison their prey, which mostly consists of small, cold-blooded animals. Catching them first with the innocuous front teeth, they push them gradually backward into the reach of the poison in the back teeth, to the action of which they soon succumb.

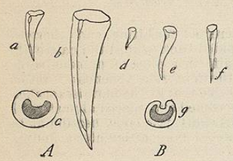

FIG. 3867.—Proteroglypha. *A*, Elapidæ. *a*, Fang of King cobra, eleven feet long (natural size, 8 mm. in length); *b*, the same enlarged (3 diam.); *c*, cross section. *B*, Hydrophidæ. *d*, Fang of pelamys (natural size, 3 mm. in length); *e*, the same enlarged (3 diam.); *f*, front view; *g*, cross section.

The poison gland completes the poison apparatus; the former is closely in contact with either side of the skull, directly below and behind the eye, and is under the influence of the different portions of the temporal muscle. The button-, tube-, or almond-shaped glands taper to a narrow anterior duct, which carries the secretion of the gland to the base of the fang and is provided with a sphincter muscle, so that the snake is able to retain the poison at will, and, indeed, may do so for months. The extraordinary development of the glands, as in the Crotalids, gives to the head that triangular shape which was erroneously considered the characteristic of all poisonous snakes, and which gave to some species the name Trigonocephalus. The elongated glands of the Ethiopian snake Causus rhombeatus extend under the skin on both sides of the spine to the extent of one-sixth of the body's length, while in the East Indian Callophis they reach from the head into the abdominal cavity about one-third of the total length of the body. In spite of these abnormities the poison gland must be considered physiologically as the homologue of the mammalian parotid; the latter is the only one of the salivary glands which produces an albuminous secretion. It is anatomically of great interest that even in harmless snakes the beginning of a poison gland can be traced. It was long known that a part of the supralabial gland—the yellow portion (Duvernoy, Schlegel, Leydig)—is easily separable from the rest; it has not only a duct of its own which in the "suspecti" leads to the posterior grooved tooth, but it also possesses a histological structure differing from that of the supralabial gland. Undoubtedly, this yellow portion of the innocuous snakes is the analogue of the poison gland; even its aqueous extract has been shown to be poisonous to small animals (Blanchard). The structure of the poison gland is that of a compound racemose gland with elongated acini; the glandular substance has columnar, the duct pavement epithelium.

Description of Venom.—The secretion of the other salivary glands and of the mouth is alkaline, while the

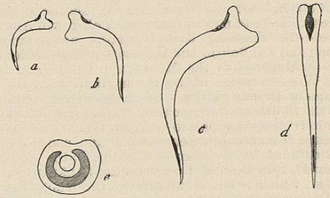

FIG. 3868.—Solenoglypha; Viperidæ. *a*, Fang of banded rattlesnake, three feet long (natural size); *b*, fang of diamond-back rattlesnake, six feet long (natural size); *c*, the same enlarged (2 diam.); *d*, front view of the latter; *e*, cross section.

poison is always acid. The color of the latter varies from a light straw or greenish-yellow to a deep orange. The viscous fluid, either clear or turbid (bitter in Naja) is not odorless as often asserted; it has a specific smell for every species, which is not easy to describe, but easy to recognize. Thus the odor of crotalus poison may be called "mousy"; that of the *fer de lance* is said to resemble the odor of fresh salt water. Its specific gravity varies from 1.030 to 1.077; the solids are variously stated as from twelve to sixty-seven per cent.; my own samples are mostly dried down to twenty-five or twenty per cent. of the original weight. The dry poison cracks on scaly transiucent chips of a light yellow or deep brown color and also has a characteristic odor. Fresh poison under the microscope shows nothing but a few scaly epithelia and a number of finely granulated, amorphous, albuminoid masses, which undergo no change in a hanging drop, even after a long while. It was often, and even is to-day, asserted that bacteria or cocci exist in the poison. After thoroughly sterilizing the collecting apparatus I was not able to see the least sign of bacterial life in broth or gelatin cultures of the fresh poison; also in acid media in which the experiments were repeated no trace of life was to be found. In order to determine whether the poison, which itself destroys life, might for that reason be free from microbes, I mixed fresh poison with B. subtilis and B. coli for one-half hour and then inoculated it on gelatin. The growth was lively, even more so than in the control plates, probably because the gelatin was liquefied at the points of contact with the poison.* A bacterial action, therefore, cannot be assumed; the rapidity alone with which the poison acts in the system would exclude bacterial influence.

Chemistry of the Venom.—The first chemical analysis was made in 1843 by Prince Lucien Bonaparte, who established the proteid nature of viper poison and called the poison "viperin." Almost twenty years later (1861) Weir Mitchell found a similar proteid in crotalus poison, which he named "crotalin." Other investigators claimed to have found alkaloids or ptomains, when Weir Mitchell, associated with Reichert, published in 1883 the results of their studies, that the active principle of snake poison was of an albuminoid nature; but instead of one ingredient they had discovered two. One of them, easily dialyzable and not coagulable by heat, was called venom peptone; the other, not dialyzable but coagulable by heat, venom globulin. The proportions of both were not alike in cobra and crotalus poison; even among the Crotalidæ they found wide differences. Thus cobra poison had 98 per cent. of peptone and 2 per cent. of globulin; but moccasin venom had 92 per cent. of peptone and 8 per cent. of globulin, diamond-back only 75 per cent. of peptone and 25 per cent. of globulin. Besides the proteid there are a coloring substance, several salts, and some fat. Mitchell's report was mainly corroborated in 1886 by Wolfenden, who discovered globulin and several albumins in variable proportion in the poison of cobra and daboia; one of the latter he designated serum albumin; the other, corresponding to Mitchell's peptone, syntonin, or albumose. Kanthack's analyses likewise demonstrated the presence of a proto- and heteroalbumose in cobra poison. Martin and McGarvey Smith found a harmless albumin and two very toxic albumoses in the poison of the Australian snakes. It may be asserted that in no instance, up to the present time, has a definitive analysis of any poison been worked out; but all investigations centre in this one fact, that the active principle in all snake poisons is some form of albumose.†

Although probably both of Weir Mitchell's bodies are albumoses, we may still, in default of accurate analyses, use the convenient terms venom peptone and venom globulin in our further discussion. Not only do the various poisons differ in the percentage of peptone and globulin, but also in the toxicity of the constituents themselves. The venoms retain their efficacy for long periods of time under suitable conditions. Poison, when dried or mixed with glycerin, has proved itself as active as fresh poison, even after a lapse of twenty-two and twenty years respectively. Putrefaction destroys it after a long time; freezing, continued through weeks, does not alter it, but it is soon changed by heating when the temperature is raised to different heights, according to the different chemical composition. The globulins are rendered innocuous at 80° C. after fifteen minutes, while the peptones are destroyed only by applying higher temperatures for hours. The coagulated proteids are inert in this state, but they regain their toxicity when redissolved.* It is the more or less evident capability of chemicals to coagulate proteids which determines their relative power of destroying the efficacy of venoms, when they are mixed with the poison

FIG. 3869.—Location of the Poison Gland in Tragops belonging to the Opisthoglypha. *a*, Poison gland; *b*, supralabial gland.

in a test tube for experimental purposes. Alcohol renders it inert for a time only. Absolute alcohol seems to coagulate all poisonous ingredients, but the presence of an infinitesimal part of water is sufficient to retain the toxicity of the supernatant fluid. Poisonous serpents, when preserved in alcohol, have to be handled, even after years, with the greatest care, as has been demonstrated by a fatal accident to an assistant in the St. Petersburg Museum.

Physiological Effects.—Absorption of venom from connective tissue, whether introduced by hypodermic injection or by the bite of a snake, takes place through the blood-vessels, more rapidly when the blood-vessel is wounded directly. Serous membranes absorb it very readily. Its resorption through mucous membranes varies; rattlesnake venom seems not to be absorbed in this way; cobra venom, however, passes through the ileum and conjunctiva, but not through the stomach and rectum. Gastric juice and bile do not affect it, but the pancreatic secretion destroys it. The resulting complex of symptoms varies partly on account of the varying rapidity of absorption, but more so because of the difference in the nature of the several venoms.

The physiological effects of both ingredients named, whenever they are tested separately in animals, are widely different. The peptone, though causing some local œdema, is more productive of general nervous symptoms, which, commencing as irritation, twitching, and convulsions, finally end in paralysis; paralysis of the respiratory centre is especially characteristic. The globulin, on the contrary, incites a violent local reaction with hemorrhages around the point of injection, hemorrhages of the mucous membranes, and destruction of the coagulability of the blood. The latter phenomenon recalls to us the results of experiments performed on animals with pure peptones and albumoses of digestion; these excite not only characteristic hemorrhages and necroses, but also paralyses, the intensity of which is in correspondence with the higher hydrolysis of the albumoses. And thus, to go one step farther: all the symptoms produced by snake venoms classify them distinctly among the toxins, especially those of bacterial origin.

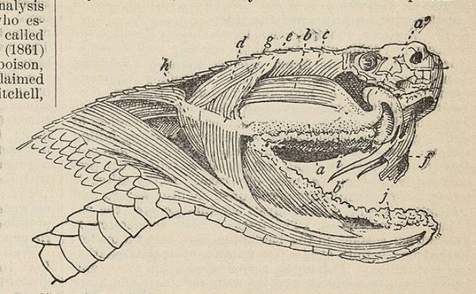

FIG. 3870.—Head of Crotalus. *a*, Poison gland; *a'*, poison duct with sphincter muscle; *b*, *d*, portions of temporal muscle; *f*, plica of mucous membrane.

SYMPTOMATOLOGY.—From the foregoing remarks it will be perceived that different cases of snake poisoning cannot have an identical course, and that the numerous contradictions of the mostly incomplete records of snakebites are to be explained only when we consider each

* Experiments with sterile snake poison have demonstrated that it liquefies gelatin like some digestive ferments, *e.g.*, trypsin. Wehrmann finds that it peptonizes fibrin weakly and does not clarify amylum. Flexner states that in agar culture of B. anthracis, B. coli, and B. typhi the bacteria underwent rapid involution. My own numerous observations, recorded above, do not confirm this view.

† It is well known that albumoses, the products of the hydration of albumin, formerly called proneptones and accurately defined by Kühne and Chittenden in 1884, differ widely as to their toxicity. While our modern means do not allow yet a chemical differentiation of those albumoses which are generated by superheated steam, by gastric digestion, by bacilli, or—as in our case—by the parenchyma cell of a gland, the varying reaction of the more sensitive living organism toward them demonstrates decisively their different nature.

* Recent advices of researches going on in Germany assure me that the toxic principle does not belong to the albumoses, in fact, that it is not at all of a proteid nature.

type of poisoning separately. Leaving aside the cases of almost instantaneous death which are due to general thrombosis, especially when the venom has been accidentally injected into a large blood-vessel, we have first to make a distinction between the two great classes of snakes, the colubrines and the vipers.

To illustrate the first class, let us briefly describe the effects of a cobra bite: two small, scarcely visible punctures in the skin are found, whence radiates a burning and stinging pain with gradually extending moderate œdema. Within an hour, on an average, the first constitutional symptoms appear—a pronounced vertigo, like that of drunkenness, quickly followed by weakness of the legs, which is increaseed to paraplegia, ptosis, falling of the lower jaw with paralysis of the tongue and epiglottis, inability to speak and swallow, with fully preserved sensorium. A mass of viscous, frothy saliva is constantly dribbling from the open mouth; nausea and vomiting set in; the paralysis becomes general, the patient lies motionless. The pulse, a little accelerated, is somewhat weaker in the beginning, but keeps a moderate strength until even a few minutes after the cessation of respiration. The latter, also accelerated in the beginning, soon becomes slower, labored, and more and more superficial, until it dies out almost imperceptibly. The pupils, somewhat contracted, react up to the last moment. Slight convulsions, which we are accustomed to see in asphyxia, sometimes occur shortly before death. Absorption is exceedingly rapid; already after thirty seconds a distinct areola is visible around the bite. Death occurs at the latest within fifteen hours, in thirty-two per cent. in the first three hours. When the patients do not die of paralysis, they recover remarkably quickly and without later consequences. The autopsy reveals no changes in the skin at the point of injection; the subcutaneous tissue, however, is thickly infiltrated with reddish serum; the surrounding blood-vessels are congested. All the internal organs are congested, and the bronchi are filled with frothy mucus and perhaps with fluids which have been forced into the patient's throat. The blood is mostly liquid and dark.

Viper.—After the bite of a viper, *e.g.*, a rattlesnake, the local disturbance is most pronounced; violent pains at the bleeding wound, hemorrhagic discoloration of its surroundings, and later also of more distant parts; bloody exudations on all the mucous membranes (nose, mouth, conjunctiva), and hæmaturia or rather hæmoglobinuria. Usually, somewhat later than after cobra poisoning, but possibly within fifteen minutes, constitutional symptoms develop, viz., great prostration with nausea and vomiting. A continuous fall of blood pressure is noticed. Respiration, in the beginning accelerated, grows slow and stertorous. After a temporary increase of reflexes, which in susceptible animals and after large doses may rise to convulsions, opisthotonos, and tetanus, paresis supervenes, with paraplegia of the lower extremities, which progresses in an upward direction, ending in complete paralysis. Albuminuria appears after about six hours. In such a condition death may result inside of twelve hours. If the patient recovers from the paralysis, a septic fever may develop in consequence of the enormous and multiple hemorrhages, to which he may succumb after a lapse of time. Eventual recovery sets in very suddenly, even in the most desperate cases. Not rarely, however, there remain suppurating gangrenous wounds which granulate poorly, break open repeatedly, and may lead later on to a deep necrosis, even of the bones.

The effect of the bite of the tropical vipers, especially the East Indian Daboia Russelii, is undoubtedly more pronounced and violent. Sanious discharges from all mucous membranes are prominent features; such hemorrhagic extravasations from lungs and bowels may persist even during recovery. Albuminuria is never missed; even hæmaturia is observed as a rule. The autopsy shows a deep bloody infiltration at the bite, down into the necrotic muscles, hemorrhages of distant muscles, particularly of the intercostals; all serous membranes, chiefly the endocardium and the peritoneum, are completely covered by countless ecchymoses of all sizes; the lungs show subpleural ecchymoses and infarctions; the kidneys are hemorrhagic in the glomeruli and pelvis, and there is cloudy swelling of the epithelium of the canaliculi. Hemorrhages have been observed also in the serosa and in the substance of the central nervous system. The blood is fluid and does not clot, even after a long time.

A disproportionate swelling is to be noted in poisoning by the European viper; it sometimes extends over the whole body. The poison of the African viper, the puff-adder, acts in a stupefying manner from the very beginning; the animal stricken stands without motion or reaction as if the whole cerebral cortex were eliminated; complete sensory and motor paraplegia ascends gradually with sharply defined limits.

The Australian snakes occupy an intermediate position between the two types just described, for, besides a prominent cobra effect, they produce moderate hemorrhage and always hæmoglobinuria.

Wall relates a peculiar variation after the bite of the East Indian Bungarus fasciatus. Some cases cannot be distinguished from the acute cobra poisoning, yet in others a certain chronicity of symptoms is seen which can be compared only to the incubation period of infectious diseases. From two to six days may have elapsed after the bite without any symptoms, when unexpectedly a general debility sets in with albuminuria and a sanious discharge from the eyes, nose, and rectum. The patient invariably succumbs within a short time.

An interesting incident is the periodical relapse of inflammation and suppuration which is said to occur mostly annually, almost to the day of the first injury. The cases reported are too numerous, and have been observed by too good authorities, to admit of a doubt. While in some instances there appeared only a scaly or vesicular eruption of the skin, in others a suppurating inflammation set in, *e.g.*, with regular loss of a nail. All the cases on record are from the United States and include all species of snakes—copperhead, rattlesnakes, and Elaps. They have been watched for six, ten, twelve, and even eighteen successive years. Perhaps the best authenticated case is that of a draughtsman of the Smithsonian Institution, who, according to Yarrow and Stejneger, for ten years had the same inflammation of the finger, bitten by an Elaps, almost to the date of the accident. A cure was finally effected by the use of the South American herb, Micania guacho.

To use for comparison a well-known and familiar complex of symptoms, we might call the sequelæ of a cobra bite an *acute bulbar paralysis* of the most furious and vehement type. Likewise, for the second type, that of viper poisoning, an analogy is found in *acute ascending spinal paralysis*, the last stage of which exhibits alike bulbar symptoms and inhibition of respiration. It should be remembered that the common ascending spinal paralysis is also ascribed to an infection. Yet, whereas in the two diseases named, the development of the nervous symptoms is very slow and gradual, and they may take years or at least weeks to advance to a fatal exitus, in snake poisoning the effect is almost instantaneous. It may, therefore, be considered firmly established that snake venoms affect the motor ganglia of the anterior horns and chiefly the medulla oblongata, exercising a selective influence upon the adjacent centres of respiration and deglutition. There exist records of a few accurate microscopic examinations of all organs after snake poisoning (Nowak). In general they resemble the changes which we are wont to find in all kinds of poisoning of whatever origin, especially by the toxins of zymotic diseases—*e.g.*, fatty degeneration of the liver with inflammation of the bile ducts, beginning as early as thirty-five minutes after poisoning; in chronic cases focal necrotic destruction of liver cells, acute parenchymatous nephritis, disseminated pneumonic patches, slight beginning of fatty degeneration of the heart muscle, etc. Of the pathological changes in the central nervous organs, we

also have some accurate records (Ewing, Bailey). As we may expect, they demonstrate a pronounced acute degeneration of the ganglion cells throughout the central nervous system. The chromatic bodies generally disintegrate with some loss of the chromatic substance, the outlines of the Nissl bodies being completely obscured; the nucleus and nucleolus may be normal or swollen and opaque; the dendrites irregular, shrunken, or detached. These changes are to be found in the cells of the cortex, the cerebellum, olfactory lobe, basal ganglia, medullary nuclei, anterior horns, and spinal ganglia, most marked, however, in the anterior horn and in the Purkinje cells and the mitral cells of the olfactory lobe. These changes were exhibited only in their beginning in those animals which had been killed in a short time by a large dose of venom, but were more advanced and involved a much greater number of cells in the cases of more chronic poisoning. Alt, after poisoning with puff-adder venom, finds the changes in the posterior columns so marked that they are perceivable to the naked eye.

The old question whether snake venom is a nerve or a blood poison, therefore, must receive the answer that it is both a neurotoxic and a hæmolytic substance. Nay, recent investigations have shown that both principles are physiologically distinct, for Flexner has demonstrated *in vitro* that in a mixture of venom with an emulsion of brain substance, the chief (neuro) toxic constituent unites with nerve cells while the agglutinating and hæmolytic element combines with blood corpuscles. It is of considerable interest to analyze more accurately its influence upon the circulatory system, which is such a prominent feature in viperine poisoning, but is nevertheless of paramount influence in cobra poisoning as well. The assumption that the action on nervous tissue is but a secondary sequela of its primary action upon the circulation must be positively denied, inasmuch as extremities whose circulation is entirely obstructed by constriction respond readily to the action of the venom upon the nervous centres; neither do we miss any of the characteristic nervous symptoms in frogs, in which the blood has been entirely replaced by decinormal saline solution.

Notwithstanding the facts just related, some of the phenomena might be referred to a disturbance of the vaso-motor centres. Some investigators ascribe them to an enormously increased diapedesis, as is seen after the local application of poison to a capillary area; while others consider it to be a rupture of the capillary walls. The blood cells escape after a hypodermic injection of venom, and are destroyed to such an extent that a few hours later but one-half of the normal blood corpuscles may be counted.

The point which has been creating the greatest diversity of opinions is the poison's influence upon the coagulability of the blood. Formerly it was an accepted dogma that cobra venom increased and viper venom inhibited clotting, until recent investigations of Heidenschild and the more accurate experiments of Martin, of Sydney, have cleared up the matter. The doses as well as the mode and rapidity of introduction are matters of the greatest importance. As a rule coagulation is inhibited for a long period. A small dose injected intravenously causes a positive phase of coagulability of two or three minutes, which is followed by a negative phase of longer duration. A second larger injection brings on the same positive and a much longer negative phase. A third still larger injection, which is borne remarkably well, destroys coagulability for a long period and, as it were, immunizes the blood against further coagulative influence of the poison. At the same time the leucocytes disappear almost entirely from the circulating blood; they are massed in the liver, lungs, and bone marrow, and reappear only when the blood regains its coagulability (or perhaps inversely). Auché found the bone marrow much congested soon after poisoning, and regards it as evidence of a reaction of the blood-forming organs,—a reaction which, within a few hours, floods the circulation with an abundance of leucocytes. A hypodermic injection, and therefore the majority of all snake bites, acts in the same way as a small intravenous injection. Immediate introduction of a larger quantity of poison into a blood-vessel may cause a sudden complete clotting of the whole mass of blood, with the exception of that in the pulmonary veins and the left heart. Many contradictory reports of the blood pressure, sudden stoppage of respiration, etc., are explained by the sudden massive thrombosis. The immediate cause of coagulation is probably a nucleo-albumin, analogous to the fibrinogenic substance of Wooldridge, also a nucleo-albumin. It is not preformed in the venom, but, as Martin has it, is liberated instantaneously by the action of the poison, from the stroma of the destroyed erythrocytes and from the endothelium of the blood-vessels; it brings on extensive thrombosis at one stroke. Or, according to the theory of Delezenne, which would explain the different phases of coagulability and fluidity, nucleo-histon is formed which splits into leuconuclein and histon; the former, which is retained by the liver, accelerates coagulation; the latter, which remains, retards it.

Many of the symptoms noted in former experiments are now explained by the recent interesting methods of study in hæmolysis. The first effect of snake venom upon blood *in vitro* is agglutination, speedily followed by hæmolysis; the escaping hæmoglobin is not changed, the spectrum remaining normal. A great variation in susceptibility to this latter reaction is distinguished in the different animals, but most noticeable is the difference of hæmolytic power in the several varieties of venom. Contrary to what we should expect from the prominent symptoms, cobra venom is most actively hæmolytic; those of moccasin, copperhead, and rattlesnake are hæmolytic in less degree, in the order named. The action upon leucocytes is similar to that upon erythrocytes, although the several varieties of white cells show different susceptibility.

Another important effect of snake venom is the loss of the germicidal property of the blood plasma. It is well known that normal blood serum destroys micro-organisms, or at least retards their growth. Ewing, of Washington, was the first to show, in 1894, that this faculty was annihilated in the blood of animals killed by crotalus poison, and Martin has confirmed it for the venom of the Australian black snake. This explains both the well-known rapid putrefaction of the poisoned organs and the danger of subsequent decomposition of the extravasated blood, and the resulting sepsis during convalescence. The recent hæmolytic studies mentioned above have shown that the germicidal power of serum is rendered inactive through the fixation of the serum complements by the venom.

A closer similarity in the two types of poison can be created in an artificial way by heating. The agglutinating power is destroyed by a temperature of from 75° to 80° C., a temperature which leaves the hæmolytic power undisturbed. The latter is somewhat reduced in crotalus poison by 90° to 96° C., while it requires 100° C. for at least fifteen minutes to make an impression on cobra, copperhead, and moccasin venom. A prolonged heating, however, of viperine poison destroys the intense influence upon the circulation to be ascribed to the globulin; after such heating it approaches cobra venom in character.

In briefly summarizing the mode of dying from snake poison, we might say that death occurring within a few minutes is due to general thrombosis; a patient who dies within twenty-four hours may succumb in the first hours to paralysis of the respiratory centre, later to general paralysis; lethal exitus, after such a period, days or even weeks after the bite, may be the result of sepsis or of general prostration following prolonged suppuration.

From what has been said, it will be seen that the danger of a snake-bite must vary considerably. Statistics cannot give us an adequate idea as regards this point. Not all cases are reported, and not all bites reported are those of venomous snakes. Moreover, chance is an important factor as regards the sequelæ: *e.g.*, in what condition was the snake when biting? Were one or both