

On the nature of snake-poison / [Sir Joseph Fayrer].

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ON THE NATURE OF SNAKE-POISON.

THE communication which I have the honour of making to you this evening is in fulfilment of a promise made last April, after the discussion of a paper on a similar subject by Dr. Badaloni of Nocera, which excited considerable interest and some criticism with regard to the purely scientific aspect of snake-poisoning, its treatment, and its relation to the vital statistics of countries in which venomous snakes are more numerous than in our own (in this respect) more highly favoured one.

I purpose to describe the nature and the mode of action of snake-poison on living creatures; and, being most familiar with the Ophidia of India, I shall select some illustrations from that source, especially as it affords typical examples of snakes which are endowed with this terrible power of destroying life.

Let me ask your attention to some points in the structure of the apparatus which is concerned with the elaboration and inoculation of the poison which it is the purpose of this paper to describe.

The order Ophidia has three subdivisions:

1. Ophidii Colubriiformes (innocent).
2. Ophidii Colubriiformes Venenosi.
3. Ophidii Viperiformes.

The two latter are all poisonous—they are the Thanatophidia, and well merit this name in India, where they destroy, probably, 20,000 human beings annually.

The general anatomical structure and distinctive characters of a snake are well known, but I will ask you to notice certain differences between:

1. An innocuous and a poisonous snake.
2. Between a poisonous colubrine and a viperine snake.

The crania drawings and dissections before you illustrate these differences. Snakes are provided with sharp re-curved teeth, which are firmly fixed in the maxillary palatine, and pterygoid bones; by the form and arrangement of these teeth, poisonous may be distinguished from innocent snakes.

The harmless snake has two complete rows of ungrooved

small teeth, one outer or maxillary, and one inner or palatine row ; in the majority, there are from 20 to 25 teeth in the outer row.

In the venomous snakes, the outer row is represented by one or more large tubular fangs, firmly anchylosed to the maxillary bone, which is movable, and by its movement causes the erection or reclination of the fang which is so marked in viperidæ. In the innocent snake, the maxillary bone is elongated, and gives insertion to a row of teeth ; in the poisonous colubrine, it is much shorter, giving insertion to only one or more teeth, the anterior and largest of which is the poison-fang.

In the viperine snakes, the maxillary bone is reduced to a mere wedge, giving insertion to a long curved and tubular fang, which is a much more formidable weapon than the fang of the cobra, or other colubrine snake.

These fangs, when reclined, are covered by a sheath of mucous membrane, in which lie also several loose reserve fangs, in different stages of growth. When the working fang is lost by accident, or is shed, one of the reserve fangs takes its place, becoming fixed to the maxillary bone, and placed in communication with the duct of the poison-gland.

The teeth vary considerably in the different subdivisions of the order. They are described as being perforated. Though this is apparently the case, it is not really so. They are dense and compact, enclosing the usual pulp-cavity ; but being folded on themselves form either an open groove, as in the hydrophidæ ; a complete canal, as in cobra ; or a more complete tube still, as in viperidæ.

During development, the laminated tooth folds like a leaf on itself, and so forms the channel along which the virus is conveyed ; and thus the tooth makes a most complete hypodermic syringe.

The poison is secreted by a conglobate racemose gland situated in the temporal region behind the eye. It is of considerable size—about that of an almond in the cobra—and is furnished with a duct which opens into the capsule of mucous membrane enveloping the base of the fang ; the venom thence flows into the dental canal, and is injected into the wound when the tooth penetrates the bitten object. At the orifice of the duct it seems probable that there may be a sphincteral arrangement of muscular fibres which would enable the snake to control the ejaculation of the virus.

I have not been able to make out such a sphincter in the elapidæ; but Dr. Weir Mitchell says it exists in crotalus. I may have overlooked it, and think it probable that further examination may detect it in other poisonous snakes. I may here just refer to the remarkable mechanism by which, the ectopterygoid bone being pushed forwards, the maxillary is made to rotate, and to erect the fang in the viperine snakes; and to the action of the temporal and masseter muscles, which, whilst they close the jaw in the act of biting, at the same time compress the gland, and force the poison through the duct. Time does not admit of anatomical details; but they are fully described in the *Thanatophidia* (pp. 1 to 5), and are represented in the sketches and specimens before you.

Before I pass on to consider the poison, let me say a few words about the poisonous snakes themselves. Here I may remind you that the only poisonous snake in Great Britain, and, indeed, in a great part of Europe, is the adder—*Pelias berus*—a viper (or some variety of it); and that, in comparison with the cobras and vipers of India and the Tropics, it is feeble in its venomous power.

The venomous colubrine snakes of India are: of elapidæ, the naja tripudians or cobra, ophiophagus elaps or hamadryad, bungarus ceruleus or krait, bungarus fasciatus or raj-samp, sankni; of xenurelaps, x. bungaroides, and the various species of callophis; hydrophidæ a very numerous family of sea-snakes all are very poisonous, but, being confined entirely to a marine or estuarial life, are not so dangerous to human life as others.

The viperine snakes are represented by daboia russelii (or tic polonga, or chain-viper); echis carinata (or kupur, or phoorsa-snake); these are true vipers; whilst the crotalidæ, or pit-vipers, are only feebly represented by the trimeresuri, peltopelor, halys, and hypnale; these are much less poisonous than their American congeners, crotalus, lachesis, craspedocephalus, and others.

The najadæ are the most virulent of the colubrine snakes; none are more deadly than the cobra or hamadryad. Of viperidæ the daboia and echis are probably as deadly as any of the African forms.*

In 1868, I resumed an investigation, begun in 1854, on

* Of American elapidæ, elaps corallinus, and lemniscatus. Of American crotalidæ, crotalus, (rattle-snake), lachesis-mutua; craspedocephalus (West Indian). Of African elapidæ, naja-haje, naja-hæmachates: of viperidæ, cerastes, and four or five others are very dangerous.

the subject of poisonous snakes and the nature and effects of their venom. During that inquiry, which continued till 1871, I ascertained from official sources that out of a population of 120,972,263 (Dr. Hunter), 11,416 persons died of snake-bite in the year 1869. Subsequent returns show that the mortality continues at very much the same rate. The Sanitary Commissioner, in his report on the North-West Provinces and Oude for 1882, tells us that 6,515 persons were killed in that year by snakes and wild beasts, out of a population of 44,107,869. In 1881, in all India, there were 22,377 deaths from the same cause.

In destructiveness the snakes stand in about the following order : cobra, krait, echis, daboia.

The ophiophagus elaps, bungarus fasciatus, and hydrophidæ are deadly but less numerous, and therefore less destructive to life.

The returns cited represent only a portion of India, and there is good reason to believe that the total annual mortality of the whole peninsula is not much, if at all, under 20,000 persons, or roughly about one in every 10,000.

The subject is of much general interest, and it is as important to humanity as to science to ascertain the nature and properties of the poison, and to discover what may best counteract it.

Snake-poison is secreted by glands which represent the parotids in other creatures (a small gland is connected with the duct of the poison-gland in daboia, and was figured in a drawing by me, made in 1869. Dr. Wall suggests that its secretion may in some way modify the action of the poison, perhaps giving it the peculiarity in which it differs from the cobra-venom) and is probably a modification of the saliva, though different in its action from that innocent and indispensable secretion. The analogy is more probable if, as suggested by some physiologists, Mr. Busk and others, there be an active principle in it, closely allied to the ptyaline of saliva.

The virus is a transparent, slightly viscid fluid, faintly acid in reaction, of varying specific gravity, 1.058 being the average (according to Wall) of a mixture of virus taken from several cobras. It has a bitter taste in the cobra, but not bitter in daboia. It is of a faintly straw-coloured hue in cobra ; in the ophiophagus of a golden yellow. When dried it loses from 50 to 75 per cent. of water (Wall) and forms a semi-crystalline substance like gum-arabic. It is secreted in considerable quantities, and if a fresh and

vigorous cobra be made to bite through a leaf stretched across a spoon or shell, several drops can be thus obtained. Examined under the microscope it is structureless, but a few cell-forms and micrococci may be detected. The mucus of the mouth may be the origin of these organisms, and it is probable that there is nothing characteristic in them (Wall), for the most active venom is free from them. The poison is exhausted when the snake has bitten frequently, and it is then comparatively harmless; but it rapidly becomes dangerous again.

"If the virus be kept in the liquid state it first becomes neutral, then alkaline, and a few feathery cubic crystals form; if preserved in a loosely corked test-tube, it will become cloudy, smell offensively, and swarm with bacteria, but still it is poisonous.

"The alkalinity now lessens, and the reaction becomes again acid; the fluid then coagulates into a firm whitish opaque substance, somewhat like the coagulated white of an egg, but of a lemon colour.

"If a small quantity of fluid be left uncoagulated it is poisonous, and the washings of the coagulum are also poisonous." (Wall)

Heating cobra-poison to boiling point (Wall says) does not destroy its physiological action, though less local inflammation is caused by it so treated.

Snake-poison has been examined by chemists, but a complete or exhaustive analysis has not yet been given.

Fontana, in 1781, and Prince L. Bonaparte, in 1843, made an analysis of the virus of the adder (*Pelias berus*), and came to the conclusion that it contained an active principle, to which he gave the name of echidine or viperine, which he succeeded in separating. The paper in which he describes the process was read before the Union degli Scienziati Italiani at Lucca in 1843, and is in our library; so far as I know but little has been added since Prince Louis Bonaparte's investigations; further analysis will probably confirm or modify his views, and perhaps add to our information. The Prince laboured under the disadvantage of having only adder-poison to analyse. With a better supply of cobra, daboia, or crotalus virus, which might now be obtained, there are good grounds for hoping that the chemistry of snake-poison will be exhaustively worked out. This is now being done in America by Drs. Weir Mitchell and J. E. Reichardt, who have published some results of their work.

In 1873, cobra-poison from Bengal was submitted to Dr. Armstrong, F.R.S., for analysis, and he obtained the following results :—

Crude Poison.	Alcohol Precip.	Alcohol Extract.	Albumen for Comparison.	
				(Ralfe)
Carbon, 43.56	45.76	43.04	53.5	53.5
Nitrogen, 40.30	14.30	12.45	15.7	15.5
Hydrogen.....	6.60	7.0	7.1	7.0
Sulphur.....	2.5	...	...	1.6
Oxygen.....	...	...	...	22.0
Phosphorous	...	...	...	0.4

This is an incomplete analysis, but it is to be hoped that the same eminent chemist may be disposed to continue the investigation when supplied with more virus.

The following is an epitome of Weir Mitchell and Reichardt's investigations, which relate chiefly to crotaline poison, but include a partial analysis of some dried (colubrine) poison from India. They find that the venom of the crotaline snakes can be subjected to the action of the temperature of boiling water, without completely losing its poisonous powers. The activity of the venom, however, of *crotalus adamanteus* seems to be destroyed by a temperature below 176 deg. Fahr. Mitchell, some years ago, showed that the venom of *crotalus durissus* is not destroyed by boiling, and the curious fact is noted that the venom of *crotalus adamanteus* should thus differ from the venom of other snakes.

The symptoms caused by the venom of the different snakes with which they have operated do not, they say, differ radically, save in degree, but there are symptoms which suggest that further investigation may enable them to point out certain differences by which it will be possible to discriminate one form of poisoning from the other. This is partly in accordance with what has already been observed in India, and notably by Dr. Wall.

The investigations, so far, lead them to conclude that the poison of the cobra is the most active, next the copper-head, then the mocassin, and lastly, the rattle-snake; but their researches on this head are not yet complete.

They are unable to confirm the statement of Gautier of Paris, that an alkaloid, resembling a ptomaine, exists in cobra poison. Professor Wolcott Gibbs, they say, was unable to find an alkaloid in the poison of *crotalus*, but they have satisfied themselves that the venom contains

three distinct proteid bodies, two of which are soluble in distilled water, one which is not soluble. These bodies have certain properties and reactions, which are detailed in their monograph on the subject.

Hitherto, observers have regarded the venom of different snakes as each representing a single poison; but it appears that, of the three proteids before mentioned, one is analogous to peptones, and is a putrefacient poison; another is allied to globulin, and is a most fatal poison, probably attacking the respiratory centres, and destroying the power of blood to clot, while the third resembles albumen, and is probably innocuous. The separation of the poisons necessitates a long and elaborate series of researches, the results of which will be subsequently reported. They have also ascertained that the poison of the rattle-snake (*crotalus adamanteus*), copper-head (*Trigonocephalus contortrix*), and mocassin (*Toxicophis piscivorus*), are destroyed by bromine, iodine, hydrobromic acid (33 per cent.), sodium hydrate, and potassium permanganate.

It appears that the activity of the venom differs not only in character and intensity in different genera and species, but also in the same individual under varying conditions of temperature, climate, health, and state of vigour or exhaustion at the time. It is a most virulent poison, and it takes effect when absorbed into the circulation, either by inoculation, or as I demonstrated in India (quite against all former and universal belief) when applied to a mucous or serous membrane, proving that it may neither be sucked from a bite, nor swallowed with impunity.

It acts most rapidly on warm-blooded creatures, sometimes with lightning-like rapidity, when it enters a vein; it is deadly also to cold-blooded creatures, and to the lowest forms of invertebrate life. Strange to say, and this, to me, is one of the greatest of its mysteries, a snake cannot poison itself, or one of its own species, scarcely its own congeners, and only slightly any other genus of venomous snake, but it kills innocent snakes quickly. It has been ascertained that a vigorous cobra can kill several dogs, or from a dozen to twenty fowls before its bite becomes impotent, and then the immunity is of brief duration, for the virus is rapidly reformed.

In 1868 and 1869 I observed that, whilst the general characters of the effects of snake-poison are alike, yet viperine differs from colubrine poison. The poison of naja kills without destroying coagulability of the blood, whilst that

of the daboia (viper) produces complete permanent fluidity (*Thanatophidia*, p. 4), and, in connection with this, "the blood of an animal killed by snake-poison is itself poisonous, and, if injected into an animal, rapidly produces its poisonous effects. I have transmitted the venom through a series of three animals with fatal results."

In 1868 I described the difference of the action of cobra and daboia-venom in the case of two horses bitten by these snakes (*Thanatophidia*, p. 79). At pp. 72-73, *op. cit.*, I also pointed out the peculiar action of daboia-venom in causing early convulsions. In some the convulsions are more marked, and, in others, death is preceded by a more decided state of lethargy. In the bite of the echis the local symptoms are peculiarly severe, so (*Thanatophidia*, p. 631) Dr. Wall gives a more complete exposition of the varying effects, and shows them to be greater than I supposed.

Snake-poison is a narcotic, and kills by extinguishing in some way (some molecular change) the source of nerve-energy. It is also a blood-poison and an irritant, if applied to mucous and serous surfaces it causes inflammation; absorption then takes place, and the symptoms of general poisoning are induced. It causes great local disturbance as well as blood-change; for, if the bitten creature survive long enough, the areolar tissue may inflame, suppurate, and slough. If it enter by a large vein, life may be destroyed in a few seconds. It was supposed the more active poisons acted by shock through the nervous system, but the rapidity with which a poison can be distributed through the circulation would account for the most rapid death from snake-bite. The chief effect is on the respiratory apparatus, and death occurs by asphyxia; but the whole voluntary muscular system is also affected, and general paralysis results; whilst the long continuation of cardiac pulsation after apparent death, proves that it is not due to failure of circulation.

The action of snake-poison is discussed at full length in the *Proceedings of the Royal Society* by Dr. T. L. Brunton and myself (1873-74-75-78). These researches led us to conclude that the action of the poison is: (1) on the cerebral and spinal centres, especially the medulla, inducing general paralysis, especially of respiration; (2) in some cases, where the poison has been conveyed through a large vein directly to the heart by tetanic arrest of cardiac action, probably owing to action in the cardiac ganglia; (3) by a

combination of these causes ; (4) by blood-poisoning of a secondary character.

The phenomena vary according to the nature of the snake, and the individual peculiarities of the creature injured, the chief difference being observed in viperine as contrasted with colubrine poison. The latter is a nerve-poison of great deadliness ; but as a blood-poison it is not of much power. Viperine poison, on the other hand, is a more potent blood-poison. Dr. Wall summarises the difference in the action of daboia (viperine) or cobra (colubrine) poison as follows : "Cobra-poison, when introduced slowly into the circulation, produces gradual general paralysis, but, at the same time, shows a preference for certain nerve-centres ; paralysis of the tongue, lips, and larynx being very marked symptoms, and respiration is very quickly extinguished after the paralysis shows itself. Death is often attended with convulsions, which are clearly due to carbonic acid poisoning. Introduced with a fair amount of rapidity, these symptoms are rapidly developed, the paralysis being preceded by gentle stimulation, which causes slight muscular twitchings. Injected in a large quantity into the circulation, the stimulation is so violent as to cause general convulsions, of which, however, the respiratory muscles have the chief share, and which are immediately followed by paralysis and death.

"Daboia-poison, though not injected directly into the circulation, causes the most violent convulsions, which are in no way necessarily followed by paralysis and death, but may be, for the time, completely recovered from. They do not depend on carbonic acid poisoning. The paralysis that succeeds is general, and lasts a very considerable time before respiration is extinguished. There is no evidence of the tongue, lips, and larynx being especially paralysed ; they probably only suffer in the same degree as other parts. Cobra-poison very quickly destroys the respiratory functions—after slight acceleration the respiration becomes slower, and the excursus is lessened. Daboia-poison at first quickens the respiration very much more than cobra-poison does, and the lessening of the excursus and the slowing of the breathing does not occur so soon. The respiration generally in daboia-poisoning has a peculiarly irregular character. This function certainly exists longer under the influence of daboia-poison than under that of cobra-poison. The effect of cobra-poison on the pupil is so slight as to be a matter of doubt. Daboia-poison

nearly always causes wide dilatation in the earlier stages of the poisoning. Salivation is a constant symptom of cobra-poisoning; it is exceedingly rare in daboia-poisoning.

"The effect of cobra-poison in the blood is not very great, Sanious discharges are rare, albuminuria has not been seen, and recovery is striking and complete when it takes place. In daboia-poisoning, on the other hand, sanious discharges are the rule. Albuminuria is usual should the victim live any time; and, after the nerve symptoms have passed away, the subject has to go through a period of blood-poisoning little, if at all, less dangerous than the primary symptoms; we have, in addition, the greater local mischief caused by daboia-poisoning, and the greater power it has of destroying the coagulation of the blood.

"The physiological properties of daboia-poison undergo great change by its being heated to 100C. in solution, losing the power of producing primary convulsions, whereas cobra-poison remains unaltered. Daboia-poison kills birds at once in convulsions, whereas, with cobra-poison, unless the poison has been directly injected into the circulation, death occurs only after paralysis.

"Lastly, amphibia recover from an amount of daiboia-poison that would be necessarily fatal in the case of cobra-poison."

Without unreservedly accepting Dr. Wall's conclusions, I regard them as an able summary of the action of different kinds of snake-poisons, and they confirm the deadly nature of Indian as compared with European snake-poison.

The local effects of the poison are partial paralysis of the bitten part, pain, infiltration, swelling, inflammation, and ecchymosis round the spot where the poison has been introduced, and sometimes in other and distant parts, and, if the animal survive for some hours, infiltration and incipient decomposition of the tissues and hæmorrhagic discharges. The general symptoms are depression, faintness, cold sweats, nausea, vomiting, exhaustion, lethargy, unconsciousness.

Dogs vomit, and are profusely salivated. They present an appearance as if the hair were "staring." As the poisoning proceeds, paralysis appears in the limbs, commencing generally in the hinder parts, with a tendency to creep over the whole body, involving the muscles of deglutition, and loss of co-ordinating power of muscles of locomotion. Albuminuria (especially in viperine poisoning), hæmorrhagic dis-

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charges, relaxation of sphincters; exhaustion, lethargy, and convulsions precede death.

In fowls the appearance is that of great drowsiness. The head falls forwards, rests on the point of the beak, and gradually the fowl, no longer able to support itself, rolls over on its side. There are frequent startings, as if of sudden awaking from the drowsy state, then convulsions and death.

In cases where the quantity of poison injected is large, and it is at the same time very active (as in cobra), the bitten animal small and weak, or if it have entered a vein death is almost instantaneous, as from shock. In such case, the cardiac ganglia are probably paralysed; at all events, the heart suddenly ceases to beat.

The effects of snake-poison on man are much of the same character, and may be studied in the details of sixty-five cases recorded in the *Thanatophidia*, which also give an idea of the duration of life. Dr. Wall has summarised them as follows: "The average length of time of the sixty-five cases is 15.17 hours; but the average is raised by the exceptionally long duration of a few cases of viperine poisoning, so that a better estimate of the probable duration of time will be obtained by dividing the period in spaces of one hour each, and determining what percentage of deaths occur in each.

	Per centage.		Per centage.
One hour and under	... 10.76	Between 7 and 8 hours...	4.61
Between 1 & 2 hours	... 12.3	" 8 " 9 "	... 3.07
" 2 " 3 "	... 13.84	" 9 " 10 "	... 7.69
" 3 " 4 "	... 7.61	" 10 " 12 "	... 4.61
" 4 " 5 "	... 1.54	" 12 " 24 "	... 9.36
" 5 " 6 "	... 1.54	Over 24 hours	... 20.00
" 6 " 7 "	... 3.07		

"The most fatal periods appear to be between two and three hours, and more than twenty-five per cent. of the total deaths take place between one and three hours after the infliction of the bite."

It appears, also, from the above report in which, in fifty-four cases the exact spot is described, that 94.54 per cent. are wounded in the extremities.

Place of Bite.	Per centage of Cases.	Place of Bite.	Per centage of Cases.
Fingers and wrist	... 31.48	Leg	... 3.70
Fore arm	... 1.85	Thigh	... 1.85
Elbow	... 5.56	Breast	... 1.85
Shoulder	... 1.85	Ear	... 1.85
Feet, toes, ankle	... 48.15	Perinæum	... 1.85

This is a matter of some interest, as the hope of success lies in preventing access to the circulation, and in the facility of removing the part injured, and with it the inoculated venom.

The greater proportion of deaths recorded, result from the direct effects of the poison; chronic cases, in which death or recovery resulted after protracted periods, are less frequently referred to.

Snake-poisoning in this country is of the viperine character, and though happily the activity of our viper is feeble compared with that of the tropical viperidæ, and except in the case of very weak or young creatures, its immediate effects as a nerve poison are feeble; yet the effects on the blood, and, locally, on the tissues, may be productive of severe and even dangerous symptoms.

The result of my experience is that, so far, no physiological antidote to snake-virus is known, and that when the full effect on the respiratory centres is produced, remedies are of little, if any, avail; albeit, when the poison has entered in smaller quantities, treatment may be of service on general principles.

Viewing the apparent analogy between curare and snake-poisoning, death in both being caused by paralysis of the respiratory apparatus, Dr. L. Brunton and I hoped that, by keeping up artificial respiration, and supporting the body-temperature, we might keep an animal poisoned by snake-virus alive until elimination had taken place; and the result of some experiments justified the anticipation to some extent, for animals were kept alive for many hours, but succumbed at length when the artificial respiration was withdrawn. Mr. V. Richards, who repeated our experiments in India, succeeded in thus keeping an animal alive for days, though it, too, succumbed finally. In the case of curare, artificial respiration is completely successful, though not so in snake-poisoning. This seems to show that the damage done by the snake-poison is of a more serious and permanent nature than that by curare, as indeed I am inclined to believe, though I do not say that a physiological antidote is impossible; all I assert is, that it has not yet been found. I would encourage efforts to devise a method of treating snake-poisoning in whatever degree it presents itself, for some means of neutralising the poison, or of restoring the damaged nervous system and blood, may still be found; at any rate, it is with snake-virus as with other deadly poisons: there must be a quantity, however

small, which, though dangerous, is not of necessity fatal, in such cases we may influence the result by treatment, and save life in some. But after long and repeated observation in India, and subsequently in England, I am forced to the conclusion that all the remedies hitherto regarded as antidotes are absolutely without any specific effect on the condition produced by the poison, and that such aid as we can give must depend on preventive and local treatment.

I will now briefly describe the measures to be adopted in the treatment of snake-poisoning, and especially refer to the permanganate of potash as a remedy, and shall read a letter from Dr. M. de Lacerda, of Rio de Janeiro, written by that distinguished physician as a commentary on the discussion which took place here last April on Dr. Badaloni's paper.

The first and most important indication is to prevent the poison entering into the circulation; to this all else is subsidiary. The rapidity with which this takes place depends a good deal on the part of the body bitten, and on its vascularity. When the poison enters a vein, if the bite be inflicted by a vigorous snake, the result is generally rapidly fatal. Experiments on animals show that bites inflicted on parts, even where large veins are not implicated may produce their effects so rapidly, that only immediate severance of the part, or complete constriction, prevents absorption.

It is necessary, therefore, as quickly as possible after a bite has been inflicted, to apply a ligature above it, and so tighten it as to completely arrest the circulation. As it happens in 94 per cent. of cases that the bite is inflicted on an extremity, this may frequently be accomplished; but, in parts where no ligature or elastic bandage or cord can be applied, proceed at once to excise the bitten part; this, indeed, should be done in all cases, ligatured or not; then make an incision through the bite, and reflect the skin; expose the tissue wherever that is altered in colour, dissect it out, and be careful to remove every part of it; then apply cautery, some escharotic, or the permanganate solution, taking care that it reaches, as much as possible, in every direction where the poison may have infiltrated. After this is done, the ligature may be relaxed; for, if the virus be destroyed, the danger of its entering the circulation is past. Should it have already entered, as is only too probable, all that can be done is to give stimulants, keep the patient warm, at rest, and, when the respiration begins

to fail, use artificial respiration, and endeavour to keep the patient alive till the poison be eliminated.

In 1869 I gave instructions for the treatment of snake-bite, and, excepting that I would substitute Esmarch's bandage for the ligature, as recommended by Dr. Wall;—that permanganate, five per cent. solution, should be applied to the wound when the venom has been carefully dissected out, or injected when it has not been cut out, I have nothing to alter in these suggestions.

Suction, being unlikely to be of much avail, is practically useless to the patient and dangerous to the operator, and should neither be encouraged nor relied on. Insist on the importance of quiet and perfect rest; the temperature should be kept up; the respiration, if it begin to fail, supported by artificial methods. Where the poison has happily been limited to the seat of inoculation, and in cases where no great quantity of virus has been absorbed, we may hope to do good; but where the poison has entered the circulation in larger quantities, and the physiological symptoms are developed, the prognosis is exceedingly unsatisfactory.

As soon as possible after a person is bitten by a snake, apply a ligature made of a piece of cord, or elastic bandage, round the limb or part, at about two or three inches above the bite. Introduce a piece of stick or other lever between the cord and the part, and, by twisting, tighten the ligature to the utmost. After the ligature has been applied, cut the punctures, to the depth of a quarter of an inch, with a penknife, or other similar cutting instrument; let the wounds bleed freely; or, better still, excise the punctured part and all the infiltrated areolar tissue subjacent to it. Apply either a hot iron or a live coal to the bottom of these wounds as quickly as possible, or inject into the subcutaneous cellular tissue a solution of permanganate of potash, five per cent., or some carbolic or nitric acid. If the bite be where a ligature cannot be applied, with a sharp penknife, cut out the bitten part and all the infiltrated cellular tissue to the depth of a quarter or half of an inch; then apply a hot coal or hot iron to the very bottom of the wound, or, better, the permanganate of potash. Give fifteen drops of liquor ammoniæ diluted with an ounce of water immediately, and repeat it every quarter of an hour for three or four doses, or longer if symptoms of poisoning appear; or give hot brandy, or rum, or whisky, or spirits with equal parts of water, about an ounce of each (for an adult), at the same intervals. Suction of the wounds is not very

likely to be beneficial, and as it may be dangerous to the operator, it cannot be recommended.

If symptoms of poisoning set in and increase, if the patient become faint or depressed, unconscious, nauseated, or sick, and respiration begin to fail, with symptoms of paralysis of tongue and fauces, apply mustard poultices, or liq. ammoniæ on a cloth, on the stomach and heart; continue the stimulants, and keep the patient warm; but do not shut him up in a hot stifling room, or a small native hut; rather leave him in the fresh air than do this.

Chronic, *i.e.*, milder cases, must be treated on the same and general principles. Do not make the patient walk about; if depressed, rouse him with stimulants, mustard poultices, or ammonia, but let him rest.

If the person be brought, as he or she probably will be, some time after the bite has been inflicted, and symptoms of poisoning are present, the same measures are to be resorted to. They are less likely to be successful, but nothing else can be done.

In many cases the prostration is due to fear; the bite may have been that of a harmless or exhausted snake, and such will rapidly recover if so treated and encouraged. If poisoned, but, as frequently is the case, not fatally, these measures are still the most expedient.

A plain summary or translation of these suggestions might be hung up in public places. The people should be warned against incantations, popular antidotes, and delay in seeking for aid. Every police inspector, of whatever grade, might be taught the application of the simple measures I have described, and should be enjoined to make them known as widely as possible among the police and the people.

There can be little doubt that recoveries from Indian snake-poisoning occur chiefly in cases where the snake has been exhausted or harmless, or has bitten imperfectly, and in a few cases where prompt interference has prevented the entry of the poison into the circulation.

Let me now make some remarks on the remedial value of permanganate of potash. During my investigation of the value of remedies for snake-poisoning, permanganate of potash was not omitted, and I made the following experiments:—

June 12th, 1869.—First, a fowl was bitten by a cobra in the thigh at 3 p.m.; at 3.1 fifteen drops of liq. potass. permanganate were injected into the spot; dead in seven

minutes, 3.35. Second, forty drops of liq. pot. permanganate injected into the external jugular of a dog. This produced no apparent effect on the animal. At 3.48, bitten by a cobra (which had bitten before and was not fresh) in the thigh; the fang punctures were at once washed with the strong solution of permanganate, which was well rubbed in; 3.52, sixty more drops injected into the vein; 3.54, two drachms injected into the bowel, all the symptoms of cobra-poisoning advancing rapidly; 4.12, forty more drops injected into jugular vein; 4.25, dead in thirty-seven minutes.

In 1878 Dr. Brunton and I made the following experiments, which confirm the power of the permanganate to neutralise the poison before it has entered the circulation, but show its inefficiency when it follows it.

Experiment 1.—Five milligrammes of poison were dissolved in one cubic centimètre of water, and mixed with one cubic centimètre of liquor potassæ permanganatis, and injected under the skin of a guinea-pig. No symptoms were produced, and the animal remained quite unaffected.

Experiment 2.—Two rabbits of the same litter, each weighing exactly 2 lbs., were taken. Five centigrammes of cobra-poison, dissolved in one cubic centimètre of liquor potassæ permanganatis, and allowed to stand for about eight minutes. The mixture was then injected under the skin of the flank of one rabbit. No symptoms whatever were produced, and the animal though kept under observation for some weeks, remained quite unaffected by the poison. Five milligrammes of cobra-poison, dissolved in two cubic centimètres of water, were injected into the other rabbit at the same time. During the injection a little of the poison was lost, so that the animal did not receive the full dose, yet it died in thirty minutes.

Experiment 3.—April 4th, 1878. Guinea-pig, weighing $1\frac{1}{2}$ lbs.; injected four centigrammes of cobra-poison into leg. 4.1 p.m., ligature applied immediately; permanganate of potash applied immediately. 4.5 p.m., twitching; 4.10 p.m., dying; 4.13 p.m., convulsion; 4.14 p.m., dead.

Experiment 4.—April 4th, 1878. Guinea-pig weighing 1 lb. 3.45' 20" p.m. Injected $\frac{3}{4}$ grain (= 4 centigrammes) of cobra poison, under skin of leg. A ligature was applied round the leg in one minute, and in five minutes permanganate of potash was rubbed into an incision made over the site of injection. 3.52 p.m., ligature cut; 3.53, twitching violently, leg paralysed; 3.57 p.m., dying; 3.58 p.m., dead—less than thirteen minutes.

Dr. Wall, who has carefully investigated the subject, makes the following pertinent remarks *Indian Snake-Poisons*, p. 129) : "As it was found that potassium permanganate does destroy the poison, steps were taken to see if it would be of any practical use in the treatment of animals suffering from snake-bite. It was found, by experiment, that a considerable quantity of potassium permanganate, dissolved in a weak saline solution, could be injected into the circulation of an animal without producing any immediate effect (I found the same with a strong solution). A dog, suffering from cobra-poisoning, had a cannula placed in its saphena vein ; a solution of potash was injected, but though a large quantity was cautiously and gradually introduced into the circulation, and though at the same time life was prolonged by artificial respiration, in no way was the least benefit to be perceived from the remedy. The reason is obvious. It is quite true that potassium permanganate destroys the active agent of cobra-poison by oxidising it ; but, when introduced into the blood, it of course commences oxidising indifferently all the organic matter with which it comes in contact ; but it has no power of selecting one organic substance for oxidation rather than another. The oxidising power of the permanganate is, therefore, exerted on the constituents of the blood generally, instead of being reserved for the cobra-poison in it alone ; so, if cobra-poison is dissolved in an organic solution, and the permanganate is added before injection, the poison suffers little, if any, diminution in strength, for oxidation has taken place chiefly at the expense of the other organic matter. Thus, it would be necessary to destroy all the constituents of the blood by oxidation before all the poison in it could be destroyed too. If a substance should be found having the power of oxidation, with a special affinity of exercising it on snake-poison, the problem of the treatment of snake-bite would be solved, but potassium permanganate has not the special power."

It has been pointed out that there are other substances which greatly diminish or destroy the action of snake-poison when mixed with it out of the body. Of all such agents, permanganate of potash is probably the best ; still it seems to be of little practical use.

Wall further remarks : "It may be asked why, if metallic salts, tannic acid, hydrate of potash, and permanganate of potash, destroy snake-poison, should not these substances be used in preference to excision. The reply is obvious.

If we could know the exact position of the poison, and if there were only one deposit, we might probably succeed in destroying it by injection. But to remove the poison deposited by the bite of a snake requires a most intelligent observation, guided by eye-sight and judgment, but an injection of a chemical agent must be, to a great extent, made by guess-work, and the solution, instead of following the poison, takes the line of least resistance in the tissues, often leading it far from the poison."

In a pamphlet (*Experiments on Permanganate of Potash and its Use in Snake-poisoning*) dated 1882, Richards says: "A solution of 5 per cent. of permanganate of potash is able to neutralise the poison;" and recommends that this should be injected into the bitten part after a ligature has been applied; it is less likely to cause sloughing of the tissues than any other agent which could neutralise the venom. In his letter dated July 22nd, 1882, he says: "It is, in my experience, the best local application we possess. It is not a physiological antidote, but is a chemical one, and is utterly powerless to effect any influence on the lethal action of snake-poisoning." (He means the constitutional action.) He is of opinion "that whenever opportunity offers, the injection of permanganate of potash should be resorted to, assuming that a ligature has been efficiently applied (where it can be applied at all) within five minutes from the bite. In the average run of cases, the permanganate will certainly destroy the poison lying beyond the ligatured part," if it come in contact with it; but, as Wall pointed out, the difficulty of insuring its contact with the poison is so great as to render it practically unreliable. I agree with Richards that, so far as it goes, it is a good local application, and as such it ought to be used, or, in its absence, tannic acid or liquor potassæ might be resorted to with the same object; but as a constitutional remedy, as a physiological antidote, it is powerless, like all others that have been tried and failed to do good. Dr. de Lacerda himself, although he attributes the highest value to it as a chemical antidote, both as a powerful oxidising agent, and by the action of the potash, says; "as to the idea of finding a physiological antidote for snake-poisoning, I entirely agree with you that it is a Utopia."

Dr. de Lacerda's letter is most interesting and instructive. He says that he has been led to write it by reading the report of a discussion at this Society on April 16th, 1883. With some preliminary observations, he continues:

"I beg leave to protest against an opinion attributed to me by some of your colleagues, but which I have never sustained. I refer to the opinion that attributes to bacteria the effects of the poison. I have weighty reasons for considering such an hypothesis as entirely false. I recognised, indeed, by means of repeated and careful observations that the venom contains micrococcus in great numbers, and I made a communication on this subject some three years ago to the Academy of Sciences of Paris. These corpuscles, however, exist in the venom in an accidental manner, as also in the human saliva, and play no important part in the effects of the poison. This last acts as a chemical agent producing a rapid alteration in the molecular composition of the albumina which enters into the formation of almost all animal tissues. On the blood, given certain conditions, its effects are very rapid, almost instantaneous; the same happens with the nervous and other elements whose functions are disturbed immediately that the venom comes in contact with them. Now, such immediate action can never be attributed to bacteria. You see, therefore, that this unsustainable theory cannot be invoked in endeavouring to explain the neutralising effects of perman-ganate of potash.

"Having made this protest, I will proceed to indicate the points on which I cannot agree with certain of your colleagues and with yourself, in regard to certain questions relative to snake-poisons. In the first place, I do not consider it exact to say that this venom inoculated in the tissues of an animal, invades rapidly the organism.* On the contrary, numerous experiments made during three years have proved to me that the venom is slowly absorbed by fractions, acting first locally on the tissues in which it has been innoculated, the elements of which imbibe the venom little by little and fix it. This destructive local action is at times, of itself alone, sufficient to produce, a short time after the inoculation has been effected, general disorders of a reflex character which are not unfrequently confounded with the disorders due to the generalisation of the venom which require a greater time for their manifestation.

* Dr. de Lacerda may possibly have operated only with the crotaline snakes, and if so, he has not had the opportunity of witnessing the different action excited by colubrine poison. In my experience, frequent experiments showed that direct general contamination follows the bite even when no large vein has been wounded.

"In those cases in which the effects of a generalisation of the venom were produced within a short time after the inoculation, some vessel had been opened by the inoculating instrument, giving the venom free entrance into the circulation.

"Another point in regard to which I cannot agree with some of your colleagues, is that there are species of snakes whose venom actuates principally upon the blood, while others act specially upon the nervous centres. For the Brazilian species, at least, I can affirm that this opinion is erroneous, and it does not appear to me probable that the species inhabiting India furnish an exception to the rule of unity of action of the venom, that I have verified for Brazil. With the venom from a single species, I may even say, of a single individual, an animal may be made to succumb by causing profound perturbations in the central nervous system, without apparent alteration in the blood ; or *vice versâ*, with slightly pronounced disorders of the nerve-centres and profound alteration of the blood. Everything depends on the conditions in which the experiment is made.

"Passing now to the essential point of the discussion that took place in the Medical Society, I will give in a few words how I comprehend and how I judge that the efficacious effect of permanganate of potash should be comprehended. You yourself, by experiments made in 1869, recognised that permanganate of potash mixed with the venom, took from it its noxious properties. Certain conditions of the experiments led you, however, to deny the efficacy of this chemical agent in the cases in which the venom had been inoculated in the tissues. As you know, however, I have demonstrated by numerous experiments and innumerable clinical facts that the neutralisation takes place even in the midst of the tissues, which makes this substance a chemical antidote of great value.

"The permanganate of potash acts upon the venom, destroying it in two ways : first, as a powerful oxidising agent ; second, by the potash that forms the base of the salt. Passing a current of nascent oxygen through a concentrated solution of the venom, this loses entirely its noxious properties. This experiment, which I have repeated many times, gave me always the same result. Let us suppose now that an individual is bitten. If injections are made in the place of the bite from five to ten minutes after the inoculation of the venom, this is promptly neutralised *in situ*, and the individual runs no further danger.

A great number of facts like this have been observed in Brazil. If aid is given late, hours after the bite, when the tumefaction of the wounded part is very pronounced, and the phenomena that indicate the entrance of the venom into the circulation have already declared themselves, injections repeated in various parts of the wounded member, parting from the wounds made by the fangs of the reptile, still give very good results. Nor is it difficult to explain the good results in this case. The venom, as I have said, acts first locally, and only enters the general circulation after the lapse of a certain time, and by portions. The permanganate of potash, meeting in the tissues with the venom, which is little by little diffusing itself, neutralises it in the various points where it has been diffused, and thus stops the source of supply. The entrance of new and successive portions of the venom into the general circulation being thus impeded, the organism takes charge of the elimination of what has already been introduced, and which was insufficient to compromise the life of the individual.

"We will now suppose a case of greater gravity, in which a vein is wounded, and there is a rapid penetration of a large quantity of venom into the circulation. Even here, an injection of a solution of one-hundredth of permanganate of potash may be practised in the vein, since we have recognised that no bad effects are produced in dogs by a dose of from two to three cubic centimètres. In this case, the good results are problematic, in view of the rapid diffusion of the venom in the organism; but then, if permanganate of potash does no good, no other substance could be useful. These cases, fortunately uncommon, are beyond all help.

"As to the idea of finding a physiological antidote for snake-poison, I entirely agree with you that it is a Utopia."

After careful consideration, fully admitting that in permanganate of potash we have an agent which can chemically neutralise snake-poison (as indeed was shown by Dr. Brunton and myself in 1878), I do not see that more has been done than to draw attention to a local remedy already known as a chemical antidote, the value of which depends on its efficient application to the contaminated part, which, Dr. Wall has pointed out, is too uncertain to be reliable. We are still then as far off an antidote as ever; and the remarks made by me in 1868 are as applicable now as they were then; they were as follows:—

"To conceive of an antidote, as that term is usually

understood, we must imagine a substance so subtle as to follow, overtake, and neutralise the venom in the blood, and that shall have the power of counteracting or neutralising the poisonous and deadly influence it has exerted on the vital force. Such a substance has still to be found, nor does our present experience of drugs give hopeful anticipations that we shall find it. But I repeat that where the poisonous effects are produced in a minor degree, or where the secondary consequences are to be dealt with, we may do much to aid the natural powers in bringing about recovery."

In conclusion, fully acknowledging the value of recent researches, I would express a hope that the subject may receive further vigorous investigation, and that efforts may be prosecuted, especially in the direction of search for some method of increasing elimination of the poison, of ascertaining the exact nature of the lesion of the nervous system and blood, and how far they are removable; that, as to local measures, with the view of preventing entry of the virus into the circulation, and of neutralising it *in situ*, improvements on present methods may be sought for. As to advance in the investigation of the physiological and chemical aspects of the question, much may still be done, as also in respect of the chemistry and microscopical character of the virus itself, and the blood and tissues of the poisoned. But these inquiries, of such importance to the human race, can, I fear, make but little progress whilst the present restriction on all physiological research continues to be maintained.

A review of the subject of snake-poisoning would be quite incomplete without acknowledgement of the valuable labours of such Indian observers as Dr. Short, Dr. Nicholson, and Dr. Stradling; Drs. Stuart, Ewart, Richards, and Wall, who have added materially to our knowledge, as also have Dr. Halford, in Australia, Dr. de Lacerda, in Rio de Janeiro, Dr. Lauder Brunton, F.R.S., in London, and Drs. Weir Mitchell and Reichardt, in America, who are now engaged in the most important and much needed investigations into the chemistry of the poison, and the condition of the blood and tissues of the poisoned.

I am indebted to the Director-General of the Army Medical Department for the following interesting case, which will appear in the next *Army Medical Department Report*.

Colonel M., while serving in Zululand, near the lower

Tugela river, was bitten in the leg just below the knee, and, after the lapse of a few seconds, became sensible of extreme shock, and at once felt certain that a snake had bitten him. He rode back to camp, and, when first seen, ten minutes after the infliction of the injury, was in the following condition. There was pain, ecchymosis, swelling, and partial paralysis of the bitten part. He was so exhausted that he had nearly fallen off his horse. The forehead and hands were bathed in cold perspiration; the extremities were cold and pale; there was great nervous depression, with sense of impending death; respiration was hurried. Quickly following this, bilious vomiting set in, with loss of co-ordinating power; numbness of extremities and lips, and dragging sensation of the face; intense pain in neck, troublesome cough, with thick viscid expectoration. The pulse was, from the first, weak and rapid, rising from 120 to 150; restlessness and anxiety became very distressing. Vomiting ceased at 9 p.m., but soon afterwards still graver symptoms developed; vision rapidly failed; the eyelids drooped, the speech became thick and nasal; there was paralysis of the tongue and soft palate, with dysphagia. There were also chronic convulsions of the upper extremities of the muscles of the chest; the breathing was stertorous, with low muttering. At 12.45, he spoke for the last time, and then lapsed into a semi-comatose condition, and died at 2 a.m., ten hours after the bite.

Tight compression was made above the seat of injury, between the bite and the heart; wound enlarged, and an attempt made to remove all the blood and poison from it. Nitrate of silver and ammonia were applied freely to the surface of the wound. Ammonia and diffusible stimulants were administered by mouth. To relieve the distressing vomiting, sinapisms were applied to region of stomach, and brandy, with soda-water, given; the restlessness was combated with hypodermic injections of morphia (half a grain for a dose); the morphia gave great relief, which, however, was only transitory. Hot water-bottles were applied to the feet, and stimulants were given with an unsparing hand, but were not always retained. Ammonia was also injected subcutaneously.

Post mortem examination made nine hours after death; body well nourished. Cadaveric rigidity well marked. Hypostatic congestion. Great discolouration of scrotum and finger-nails. Situation of bite on left leg at upper and inner side of calf, about three inches below internal con-

dyle of femur, and immediately over internal saphena vein. Appearance that of a small pin-puncture; lower part of leg rather swollen. On removing the skin from the region of the wound, there was found great sero-sanguineous extravasation into the surrounding tissues, and the muscles were soft and infiltrated with blood; the internal saphena vein was punctured. The venous system on the left side much congested. The glands in left groin, in long axis of limb, enormously enlarged and congested. Glands in right groin normal; pericardium normal. Heart, right cavities of, full of fluid blood; left cavities empty; valves healthy; no clots. Lungs normal. Liver congested, and slightly enlarged. Gall-bladder fully distended. Spleen somewhat enlarged, otherwise normal. Stomach slightly congested, rugæ well marked; contents, a small quantity of glairy mucus. Kidneys normal. Omentum contained much adipose tissue. Intestines normal. Bladder normal, contained a small quantity of urine. Brain somewhat congested, otherwise normal. Blood in a fluid state.

The snake which inflicted the fatal wound was not seen; in all probability Colonel M. trod on one asleep, which then struck at him. The systemic shock was at once apparent after receipt of the injury, which is accounted for by the puncture of the internal saphena vein, and the introduction of the poison direct into the general circulation. The clothing traversed by the fang of the snake was, first, cloth garter; second, khakee riding-breeches; third, drawers of light material. From the high situation of the puncture, the opinion of competent judges was that the snake which inflicted the wound was a "black mamba," one of the large African vipers, species not determined.

The following were exhibited :—

Crania of innocent snakes.

Crania of venomous colubrine snakes.

Crania of viperine snakes.

Dissections of muscular apparatus for erecting fangs.

Dissections of poison gland and duct.

Models of fangs.

Drawings of the above.

Also coloured figures of venomous snakes of India.

The following snakes were exhibited :—

Naja tripudians, *bungarus ceruleus*, *bungarus fasciatus*, *callophis*, *elaps corallinus*, *daboia russellii*, *echis carinata*, *vipera rhinoceros*, *vipera cerastes*, *lachesis mutus*, *crotalus durissus*, *pelias berus*, and several non-venomous snakes.



