On the nature and physiological action of the poison of Naja tripudians and other Indian venomous snakes / by T. Lauder Brunton and J. Fayrer.

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ON THE

NATURE AND PHYSIOLOGICAL ACTION

OF THE

POISON OF *NAJA TRIPUDIANS*

AND OTHER

INDIAN VENOMOUS SNAKES.

PART I.

BY

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On the Poison of Naja tripudians.

The destruction of life in India by snake-bites is so great, that, with the hope of preventing or diminishing the mortality, in 1867 Dr. Fayrer began, and has recently completed, a protracted and systematic series of investigations on the subject in all its aspects; and, in a work entitled the 'Thanatophidia of India,' has published a description of the venomous snakes found in British India, with an account of a series of experiments on the lower animals, conducted for the purpose of studying the nature of the poison, its *modus operandi*, and the value of the numerous remedies that have been from time to time reputed as antidotes—that is, as having the power of neutralizing the lethal effects of the virus, and of saving life.

His object in carrying out these investigations has been:—

1st. To ascertain the nature and relative effects of the bite of the different forms of Indian venomous snakes, and the conditions and degrees of intensity under which the activity of the virus is most marked.

2nd. The physiological action of the virus, and its mode of causing death.

3rd. The value of remedies, and the extent to which we may, by preventive or therapeutic measures, hope to save life.

4th. To ascertain and make known the actual state of our information in connexion with these three points of inquiry, and to substitute scientific and rational knowledge for vague, empirical, and dangerous theories.

He has had the honour of submitting a copy of this work to the Royal Society; and it is therefore unnecessary to occupy its time by repeating much of what is therein related on the 1st, the 3rd, and part of the 4th heads.

But on that which is involved in the 2nd, and partly in the 4th, much is still required to be done; and therefore on the question of the nature and physiological action of the virus on life, and the application of that knowledge in the treatment of those poisoned, the following investigations have been made.

That the subject is one of interest in a purely scientific as well as sanitary point of view we believe will be admitted; for it is as important to humanity as to science that the nature and properties of a poison which, in India alone, probably destroys over 20,000 human beings annually should be determined.

We are aware that these figures may excite astonishment and even mistrust; but the sources from which the information is derived place it, we think, beyond a doubt, being derived from official returns for the year 1869, supplied to Dr. Fayrer by the Government of India.

He has received reports from Bengal, the North-west Provinces, Punjaub, Oude, Central Provinces, Central India, Rajpootana, British Burmah, showing the loss of life from snake-poisoning in those provinces in the year 1869.

These records represent, it is true, only a portion of India, as the Madras and Bombay Presidencies, as well as other parts of India, are not included. Had similar information been obtained from these provinces, the list of mortality would doubtless have been much larger; as it is, the number of deaths is perfectly appalling, and the subject merits consideration, with the view of providing, if possible, some remedy.

He has roughly classified the deaths under the headings of the snakes that inflicted the fatal wound; but the records are rather vague on this point, and the information not perhaps always very reliable. Still they are sufficiently explicit to make it clear that, in order of destructiveness, the cobra (*Naja tripudians*) occupies the first place on the list; the krait (*Bungarus cæruleus*) the second place; whilst under the headings of "other snakes" and "unknown" must be included many deaths due to cobra, *Bungarus cæruleus*, *Ophiophagus*, *Daboia*, *Echis carinata*, *Bungarus fasciatus*, *Hydrophidæ*, and some perhaps to the *Trimeresuri*, though, as to the last, there is reason to believe that deaths from their bites are comparatively very rare.

The total number of deaths recorded therefore stands thus:—

Bengal, including Assam and Orissa	6,645
North-west Provinces	1,995
Punjaub	755
Oude	1,205
Central Provinces	606
Central India	90
British Burmah	120
Total	11,416

of a population (according to Dr. Hunter) of 120,972,263, or, in round numbers, about one person in every 10,000.

This total, large as it is, we fear cannot be regarded as the real mortality in these provinces, nor may the numbers be accepted as an absolutely true indication of the relative frequency of deaths in each.

The information from which these records were framed was, though official, probably only partial and imperfect. Dr. Fayrer believes that if systematic returns could be kept, as he has suggested that they should be, by the police in every district, subdivision, and municipality, the number of deaths would be, excluding all doubtful cases, much larger. He believes also that were such information collected throughout the whole of Hindoostan, it would be found that more than 20,000 persons die annually from snake-bite.

The result of his investigations in India has been, we think, to show that, so far, no agent or antidote, as that term is commonly understood, has been found effective in neutralizing the action of snake-poison. We think it is also pretty clearly demonstrated that death is caused in most cases, at all events where a full quantity of the virus has been injected, by its action on the nerve-centres, though whether on them alone, or also on the peripheral distribution of the nerves, or on the muscles themselves, or the exact extent to which each is affected, there may be some difficulty in determining. The futility of all the methods of treatment hitherto had recourse to is probably explained by the mode of death: their inutility had long since been demonstrated by Fontana, who, ninety years ago, among other things, showed that the outward and inward use of ammonia, as well as its injection into the veins, was as powerless for good as were all other remedies.

There is apparently some analogy between the nature of the action of the cobra-virus and that of curara, death in both cases being brought about by arrest of respiration through paralysis of the respiratory apparatus.

In the case of the curara it has been demonstrated by experiment that this is due to paralysis of the peripheral distribution of the motor nerves; and it has been further shown that if respiration be continued artificially for a sufficient length of time, perfect recovery may take place, as we have ourselves observed, the poison being eliminated from the system, and not having, during its presence, so far compromised the integrity of the parts of the nervous system where it took effect as to interfere with a resumption of their functions after its removal. Now it is evident that artificial respiration and the use of any remedies that may expedite elimination, with the application of artificial warmth to sustain temperature up to the normal standard, are the measures which may be regarded as antidotal in a rational sense to this form of poisoning; and such they have proved themselves to be; for if an animal apparently dead from curara-poisoning be kept warm and artificial respiration be kept up for some hours, it will perfectly recover.

It is in the application of similar principles that we may hope to realize a similar result in cases of snake-poisoning; and it is with this object that the investigations by Dr. Lauder Brunton and Dr. Fayrer, since his return to England, of which the present paper is an instalment, have been pursued.

Our investigations so far confirm the opinion by Dr. Fayrer already recorded, that death is due to the action of the poison on the nerve-centres, to which it is conveyed by the blood with terrible rapidity when the injection of the poison takes place into a large vein like the crural or jugular. But we have not yet arrived at absolute conclusions as to the extent to which this neurotic action is carried, whether it be localized in the nerve-centres only, or whether there be, and to what extent, any action on other portions of the nerve-apparatus.

Our experiments so far, though pointing distinctly to the centres as the seat of its action, in some cases seem to imply that the nerve-periphery and perhaps even the muscles themselves are involved; but on this head, for the present, we reserve the expression of a positive opinion.

With reference to remedial measures in cobra-poisoning, we would remark that, so far as our experiments have as yet gone, artificial respiration has certainly had the effect of prolonging life; and without committing ourselves to any opinion, we would say that we would not yet abandon hope that it may, as in the case of the curara, even save it altogether. This must of course depend on, first, the nature of the action of the poison on the nerve-apparatus—that is, whether it be of a transient or permanent character. Is it, for example, like curara, which though it destroys the power of the peripheral extremity of the motor nerves during its presence, yet leaves them uninjured and capable of resuming their functions after the poison is removed (as it may be) by elimination, life being supported by artificial respiration during that process.

If so, and the cobra-poison, even though antagonistic and annihilative of the action of the nerve-centres and peripheral distribution, or of the muscular irritability itself, be only so whilst it is present, and would, if removed within reasonable time, leave the nervous apparatus or muscles in a condition to resume their operations, then, if elimination could be carried on whilst respiration is artificially sustained, we might hope to succeed eventually in cobra as in curara poisoning.

Or could we, indeed, conceive of and find any agent so subtle as to overtake and neutralize the virus whilst it is in the system, and before it should have compromised the nerve-centres or other parts, then we should have the antidote which has been so long sought for, but yet, we fear, not found*. We do not now wish to speak of the action of the cobra-virus as it

* Fontana thought he had discovered such an agent in the "pierre à cautère" (caustic potash). He says of it:—"Mais on peut point douter cependant de l'efficacité de ce remède, et on peut affirmer que la pierre à cautère est le vrai specifique de ce terrible venin."—*Sur les Poisons*, p. 324 (Florence, 1781).

This agent has been tried in India, but has not proved of any service in cobra-poisoning.

operates secondarily on the blood, either in those cases where great vigour of the animal or smallness of the dose have enabled the creature to resist the immediate and deadly neurotic effects of the poison. Such cases are to be classed among other septicæmiæ, and are apart from that we are now discussing.

The question resolves itself into three points of inquiry:—

1st. Is the nature of the virus such that we may hope to find any agent that may overtake, neutralize, and so render it (the virus) harmless or inert?

2nd. Does the virus exert only a temporarily pernicious action on the ultimate structure of the nerve-centres or other parts of the nerve-apparatus? *i. e.* is it only inhibitory or hurtful during its presence in the blood, but if removed would leave the nerve-apparatus in a condition to resume its functions (such is curara), or does it enter into some permanent composition or union with the nerve-elements? or, 3rd, does it so modify their arrangements as to render them permanently incapable of resuming their functions, even after the poison has been eliminated, if it may be so removed, as we know other poisons may? Such, we fear, may be snake-poison!

If the first proposition be correct, then in some subtle chemical agent, or, if the second, in artificial respiration and eliminant action we may have hope of success.

If the third, what chance have we beyond that of sustaining life as long as artificial respiration be maintained? for if the nerve-apparatus be permanently injured, no resumption of its functions can take place. Whichever of these propositions be nearest the truth, there must still be a condition in which, from the smallness of the quantity of virus inoculated, recovery is possible—one in which the full lethal effect of the virus is not produced. In such cases, no doubt, remedial measures may be of avail.

The results of investigations in India have led to the conclusion, then, that death is brought about by the action of the poison on the cerebro-spinal nerve-centres, paralyzing them, and in some cases, where the quantity of virus was large and introduced into the circulation through the medium of a large vein, acting directly on the ganglia of the heart, causing arrest of its action. In those cases where the quantity of virus inoculated is smaller and of less intensity, according to the condition of the snake or its species (the poison of some genera being less active than that of others), econdary changes, though of what precise kind we are not yet prepared to say, occur in the blood itself, but allied in character to that of other blood-poisons and probably of a zymotic nature. We would merely for the present remark that, in the first class of cases, we believe that remedies or means of treatment other than those which may be of a preventive character are as yet of no avail, whilst in the second it is probable that they may be of some efficacy. So far we believe little more has been done than to go over ground that has

already been traversed by previous observers, who have come to similar conclusions that most of the reputed antidotes have been powerless, and that where there has been an appearance of success, it has depended not on any antidotal or antagonistic action of the remedy so much as on the fact that the quantity or quality of the poison was defective; and how this may be explained, Dr. Fayrer has endeavoured to prove by showing that the snake may have been exhausted, that its poison may be deficient in quantity or in quality, or that it may have wounded without inoculating sufficient of the poison to cause death, or more than to cause slight poisoning, and probably that, by a sphincteral arrangement of fibres, as pointed out by Dr. Weir Mitchell to exist in the rattlesnake, the snake may have the power of imbedding its fangs without shedding its poison at all.

Much virtue has been recently attributed to one of the oldest and most trusted of all antidotes—ammonia; but it was long ago shown by Fontana by repeated experiments that the injection of this agent into the veins, as well as its internal administration and external application, were powerless (as may be seen by reference to the following* pages of his works), so it has proved in all the experiments made with it in India. Any complete and satisfactory means of resisting, antagonizing, or eliminating the poison and of saving life are, we fear, still unknown; and it is in the hope that by determining the physiological action of the poison we may make some advance in our knowledge of this important subject, that the following investigations have been undertaken with cobra-virus sent to us from Bengal, and of which we hope to receive continued supplies from Mr. Vincent Richards, of Balasore, who, at our request, is also carrying on a series of experiments on the subject.

Appearance and Chemical Characters of Cobra-poison.

The poison when fresh is a transparent, almost colourless fluid, of a somewhat sirupy consistence, and not unlike glycerine in its appearance. When quickly dried it forms a transparent mass of a yellowish-brown colour, and resembling some kinds of gum-arabic. The poison may be kept in a fluid state for some months without undergoing any change, but after a certain time it decomposes.

During decomposition it gives off a quantity of gas, which has been ascertained by Dr. Armstrong to be carbonic anhydride, and at the same time acquires a dark brown colour and a disagreeable odour. The dried poison may be kept for a much longer time without undergoing any apparent change.

The chemical constitution of the poison has been examined by Dr. Armstrong. He has not been able to separate from it any crystalline principle. It is partially coagulated by heat; mineral acids produce in it

* 'Traité sur le venin de la Vipère,' vol. i. pp. 108, 109, 118, 120, 124, 129; vol. ii. pp. 5, 6, 7 (Florence, 1781). 'Opusculi Scientifici,' Letter iv. pp. 125 *et seq.*

a gelatinous precipitate; absolute alcohol throws down a white gelatinous precipitate; a drop of it evaporated with a little sulphate of copper solution and then treated with caustic potash gives a violent coloration. These reactions show that the chief constituent of the poison is an albuminoid body. On an ultimate analysis being made, very little difference was found to exist between the fresh poison, the alcoholic precipitate, and the alcoholic extract. This is the only ultimate analysis of the poison of any snake which has yet been made, so far as we know. We quote the results of it, and give the composition of albumen for comparison*.

Crude poison.	Alcoholic precipitate.	Alcoholic extract.	Albumen.
Carbon, 43·55 . .	45·76	43·04	53·5
Nitrogen, 43·30	14·30	12·45	15·7
Hydrogen	6·60	7·	7·1
Sulphur	2·5		
Ash	traces.		

We have recently received from Bengal some cobra-poison dried and in appearance resembling dried gum. On this we hope to report on a future occasion.

Although there is little difference between the composition of the alcoholic precipitate and extract, there is an immense difference between their physiological actions, the extract being a virulent poison and the precipitate almost inert. It is to be observed that the poison examined by Dr. Armstrong had already begun to undergo decomposition; but if it should be found by further experiments that the properties of the extract and precipitate from perfectly fresh cobra-poison are the same as those of the poison he used, it will form a notable distinction between the poison of the cobra and that of the rattlesnake. The precipitate thrown down by alcohol from the poison of the rattlesnake has been ascertained to be active, while the alcoholic extract is inert (*vide* Weir Mitchell, "Physiology and Toxicology of the Venom of the Rattlesnake," Smithsonian Contributions, 1860, p. 36).

We have experimented on four different samples of poison sent from Bengal. The first was originally a clear transparent fluid; but after keeping it decomposed and became almost black, as already described.

* Dr. Armstrong in his analysis does not appear to have arrived at the same conclusions as the Prince of Canino (L. Buonaparte), who detected the presence of a peculiar principle perhaps allied to ptyaline, to which he gave the name Echidnine or Viperine, in addition to fatty matter, salts, albuminous and mucous substance. It has been suggested by Prof. Busk (*vide* Holmes's 'System of Surgery,' vol. v. p. 941) that the venom may reside in a principle analogous to, though differing from, ptyaline. We would not, however, regard Dr. Armstrong's analysis as conclusive, but hope to have the result of further examination of larger quantities of the virus.

It retained its fluidity and activity to the last. The third sample was of a light-brown colour, quite solid, and resembling dry hard cheese in its consistency. The second and fourth consisted of a clear, thin, transparent fluid and a white curdy precipitate. None of these specimens had the same activity as the first; they produced similar symptoms, but much less marked.

Effects of the poison.—The local effects of the poison are partial paralysis of the bitten part, occasionally pain in it, ecchymosis around the spot where the poison has been introduced, and sometimes in other and distant parts, and, if the animal survives for some hours, infiltration and perhaps incipient decomposition of the tissues and hæmorrhagic discharge.

The general symptoms are depression, faintness, hurried respiration and exhaustion, lethargy, nausea, and vomiting. In guineapigs and rabbits peculiar twitching movements occur, which seem to represent vomiting in them, and occasionally, in fact, guineapigs do vomit. Dogs vomit, are salivated, and present an appearance as if the hair had all been rubbed the wrong way, "staring." As the poisoning proceeds paralysis appears, sometimes affecting the hind legs first and seeming to creep up the body, and sometimes affecting the whole animal nearly at the same time. There is loss of coordinating power of the muscles of locomotion.

Hæmorrhage, relaxation of the sphincters, and involuntary evacuations, not unfrequently of a sanguineous or muco-sanguineous character, often precede death, and it is generally accompanied by convulsions.

In fowls the appearance is one of extreme drowsiness; the head falls forwards, rests on the beak, and gradually the bird, no longer able to support itself, rolls over on its side. There are frequent startings, as if of sudden awaking from the drowsy state*.

The effects of the poison upon dogs, guineapigs, and rabbits are illustrated by the following experiments.

The poison which was first sent home and still remained perfectly liquid, but had become of a dark brown, almost black colour, and somewhat inspissated, was used.

Experiment I.

1.30. Three drops of this, diluted with water, were injected into the flank of a small dog. Immediately after the injection the corresponding leg was drawn up, partially paralyzed.

1.32. He walks less steadily. Tail rigidly held out.

1.35. Is restless and whining. Walks about and then sits down again. Walks unsteadily.

* In cases where the quantity of poison injected is large, and it is at the same time very active, the bitten animal small and weak, or if inoculation has taken place into a large vein, death is almost sudden, as if it were from shock. In such cases the cardiac ganglia are also probably paralyzed; at all events the heart suddenly ceases to beat.

1.45. There are distinct muscular twitches in the shoulder. General tremor.

1.47. There are twitching movements of the back.

2.8. Has been standing perfectly still. Is now pawing and licking his lips. Vomits.

2.10. Vomits again, but licks up part of what he had ejected.

2.22. Has been continually vomiting. The ejection consisted at first of food, afterwards of tenacious mucus. He now lies down apparently exhausted. He is still trying to vomit, but can bring nothing up. He tries to rise, but cannot. Convulsive struggles occur.

2.25. Breathing has ceased, but the cornea is still sensitive. Convulsive attempts to vomit.

2.27. Cornea insensible. Heart is still beating strongly. Death soon followed.

Experiment II.

A young rabbit, weighing 900 grammes, was used. An incision had been previously made through the skin of the neck and the wound again sown up, but the animal was otherwise uninjured. Two drops of cobra-poison, weighing 12 centigrammes, were diluted with 1 cubic centimetre of water.

At 4.6 the diluted poison was ejected under the skin of the left hip.

4.7. Washed out the watch-glass in which the poison had been placed with water, and injected it under the skin of the back. The animal sat quiet after the injection, occasionally licking its fore paws.

8′ 30″. Respiration seems hurried. The rabbit occasionally makes a jerking motion with its hind feet.

10′. Has been restless, running about, occasionally licking its fore feet.

13′ 30″. Still very restless, and when held makes convulsive efforts to get oway. Ears are much congested.

17′. The animal is now quiet. Its ears are no longer congested.

About 20′. Quiet, with occasional starts. Disinclined to move, but can walk quite well.

25′. Movements seem difficult, and hind legs seem weak when it tries to walk.

26′. Paralysis of hind feet is increasing.

26′ 15″. The rabbit lays its head down on the table.

28′. When laid on its side it merely makes a few slight movements with its fore paws and then lies still. The eyes remain in a half-closed condition, and have done so for some time. When the cornea is touched the head gives a jerk, but the eyelids move very little. Respiration slow and laboured.

4.30. The chin is twitched inwards, the sternum once or twice, the hind feet at the same time being twitched backwards. The eyes open widely. Slight convulsive extension of limbs.

4.31. Respiration has stopped, cornea is insensible; thorax opened

immediately. There were large extravasations of blood under the skin of abdomen and thorax, and under the skin of the left hip. Heart beating vigorously.

The muscles contracted on direct irritation. The foot twitched when the sciatic nerve was exposed and irritated by an interrupted current. The peristaltic movements of the intestine were active after the abdomen was opened.

Experiment III.

Dissolved 5 milligrammes of dried cobra-poison which had collected round the stopper of the bottle containing it in $1\frac{1}{2}$ cubic centimetre of water, and injected it under the skin of the left hip of a guineapig, weighing 790 grammes.

In $\frac{3}{4}$ of a minute after the injection the animal became restless and uneasy and began to cry.

$1\frac{1}{2}$ minute it began to give little starts.

$3\frac{1}{4}'$. The starting motions became greater, the hind quarters of the animal being jerked upwards, and the chin drawn in towards the body; continues to cry.

$4\frac{1}{4}'$. Passes water.

7′. Less restless.

15′. Washed out the watch-glass in which the cobra-poison had been placed with about $\frac{1}{2}$ a cubic centimetre of water, and injected it as before. Immediately afterwards the restlessness increased.

24′. Seems to be trying to vomit.

27′. It cannot walk rightly.

28′. The hind legs are paralyzed and spread out laterally from beneath it.

29′. Respiration very slow and deep. The animal lies quiet, but convulsive twitches of the limb follow almost every respiration.

Respiration 8 in $\frac{1}{2}$ a minute.

30′. Cornea insensible. Respiration has ceased. Post-mortem examination made immediately. The left ventricle was much dilated, the right ventricle empty. There were two beats of the left auricle for every one of the ventricle, and the ventricular beat was weak and imperfect.

Experiment IV.

Dissolved 1 centigramme of a substance like gum, and labelled "alcoholic extract of cobra-poison," in 1 cubic centimetre of water. It dissolved easily and formed a somewhat opalescent solution.

Injected about $\frac{1}{3}$ of this (equal to $3\frac{1}{2}$ milligrammes of the dried extract) under the skin of the thigh of a rabbit weighing about a kilogramme.

4 minutes after the injection there was no apparent effect; so a similar quantity was again injected, making the total amount received by the

rabbit 7 milligrammes of extract: 5½ minutes after the first injection the animal became very restless.

7′. Respiration rapid. The vessels of the ears were noticed to be much injected. On continuing to observe them the injection disappeared and then returned again. The alternate filling and emptying of the vessels was much more perceptible than in the normal condition. The rabbit sits quietly, but every now and then gives a start.

22′. The condition of the ears has continued the same. The eyes are becoming half shut and the eyeballs turned up.

The animal now begins to tremble. The head is laid down on the table and then raised again: this is succeeded by a nodding motion of the head. The head is next laid down on the table.

Respirations 22 in 15 seconds.

24′. The animal has sunk down on its face, and paws as if its fore legs would no longer support it. The hind legs, however, still support the posterior part of the body. Respirations 11 in 10 seconds. It seems to be trying in vain to raise its head.

26′. Respirations 8 in 10 seconds. Convulsions. The cornea is sensitive. The rabbit is now lying on its side. Respirations 5 in 15 seconds. Pulse 12 in 18 seconds.

31′. Cornea is nearly but not quite insensible. The eyeball is protruding.

About 31½′ respiration has stopped. The heart is still beating vigorously.

32′. Cornea insensible. The animal opened immediately. The heart was beating vigorously; 21 beats in 10 seconds.

An attempt was made to insert electrodes into the spinal cord and pass uninterrupted current through them. No effect followed; but it is not certain that they were well in the cord. Irritation of the nerves going to the hind legs by uninterrupted current had but a slight effect. Direct irritation of the muscles caused them to contract. After the irritation was discontinued, a fibrillary twitching was observed in one of the extensions of the thigh.

42′. Heart still feebly pulsating. Irritation of the brachial, sciatic, and crural nerves has very little effect.

45′. Heart still feebly pulsating.

Experiment V.

Two drops of cobra-poison were injected under the skin of the thigh of a guineapig.

One or two minutes after the injection the legs of the animal began to twitch. It was then covered with a glass bell-jar.

6′ after injection. The legs are again twitching. This is a peculiar motion of the hind legs, in which they seem to make an abortive attempt to kick involuntarily.

7′. Respirations are deeper than usual.

9′. Legs again twitching.

10′. The animal is restless and moves round and round inside the bell-jar. Grunts occasionally and grinds its teeth. The hind-quarters are twitched upwards, and the nose is drawn in towards the chin at the same time.

13′. Bites at the spot where the injection was made and passes water.

22. It can no longer walk.

23. It has sunk down and lies flat on the table, leaning rather to one side. Respirations are deep. There are occasional twitches of the legs.

25′. Cornea is sensitive. Occasional convulsive stretches.

27′. Cornea almost insensible. Respiratory movement of nostrils continues.

28′. Cornea completely insensible. Post-mortem examination made immediately. The muscles of the abdomen were dark-coloured. Peristaltic movements of the intestines occurred when the abdominal cavity was opened. The heart was dark and slightly dilated; all its cavities were contracting, though feebly. There were three beats of the auricles to each one of the ventricles. Irritation of the nerves in the pelvis caused contractions of the legs.

35′ after injection. The heart is still feebly contracting.

Experiment VI.

October 28th.—Injected about a grain and a half, or two grains, of the precipitate, which was thrown down from cobra-poison by alcohol, into the thigh of a guineapig.

2.30. Injection made. A few minutes afterwards it passed some milky-looking water, and then remained perfectly quiet.

3.8½. Passed water, which was quite clear.

3.33. Injected about two grains into the right femoral vein. It passed clear water almost at once.

3.35. Its nose gave a jerk inwards. Wounded leg drawn up.

3.38. Nose twitches frequently and the animal emits a faint barking sound.

3.40. Slight tremors.

3.50. Begins to eat a piece of bread placed near it.

3.58. Still twitches.

4.8. Is still sluggish, but seems nearly well. Recovered.

Experiment VII.

October 29th, 1872.—About ½ a grain of fresh but coagulated and cheese-like cobra-poison was suspended in distilled water and injected into the back of a guineapig, weighing about a pound and a quarter.

2.23. Injection made.

2.26. The animal looks scared and is twitching. This guineapig is very active.

2.30. Another dose injected. The animal is twitching much. It jumped out of the deep box in which it had been placed for observation. Breathing is hurried.

2.36. It seems better. Another dose injected into the thigh.

2.45. Not much effect. Another dose injected.

2.46. Twitching continues; animal remains active. It recovered.

Means of preventing the Effects of the Poison.

There are three ways in which the toxic effects of a poison may be entirely prevented or greatly diminished. These are:—1st, by preventing its admission into the blood; 2nd, by counteracting the effects it produces while it is circulating in the body and sustaining life by artificial respiration; 3rd, by quickening its elimination. The first of these methods is the only one which has hitherto been of any great service in cases of poisoning by the bite of cobras. Various attempts have been made to counteract the effects of cobra-poison by means of antidotes; but the advantage derived from their use is still, to say the least, doubtful. No special attempts, so far as we know, have been made to hasten the elimination of the poison, or at least none have been made avowedly for this purpose, though it is possible that some of the antidotes may have had that effect. This part of the subject we will treat in a future paper.

The subject of prevention of entry of the virus by ligature or other mechanical measures has been fully discussed in the 'Thanatophidia'; it is unnecessary to recur to it here, for the present at all events.

For the purpose of attempting to counteract the effects of the cobra-poison while it is circulating in the blood, it is necessary to have some idea of its mode of action.

Mode of Action of the Poison.

Snake-poison probably produces its fatal or deleterious effects either by completely paralyzing the nerve-centres or other portion of the nervous apparatus, and thus causing arrest of respiration, or by partially paralyzing them and also poisoning the blood, thereby inducing pathological conditions of a secondary nature, which may, according to circumstances, cause the slightest or the most dangerous symptoms.

The effect produced depends on two sets of conditions:—first, the species of the snake, its actual state at the time, the quantity and quality of its poison, and the circumstances under which it inflicts the bite; second, the species, size, and vigour of the living creature, and the circumstances under which it is bitten.

Snake-poison is essentially a neurotic, and, when it takes full effect,

it appears to kill by annihilating, in some unknown way, the source or distribution of nerve-force. It is also an irritant; for if applied to a mucous membrane or to the conjunctiva, it soon induces violent inflammation; absorption at the same time takes place, and symptoms of poisoning are produced. It is also, to a certain extent, a septic; for if the bitten creature survive, the wound and the parts about it are apt to slough and to induce septicæmia. The poison acts by absorption—that is, by entering the circulation, and so reaching the nerve-centres, it produces, according to the quantity or intensity of the venom, either death or severe local and constitutional symptoms. If it find entry by a large vein, such as the femoral or jugular, life may be destroyed in a few seconds.

The blood itself is affected by the poison.

Dr. Fayrer has not been able to detect any corpuscular changes, nor has he any exact information on the chemical changes it undergoes, or may have undergone; but that it is altered there can be little doubt; and in poisoning of the lower animals, at all events by the Viperidæ, its coagulability after death is generally destroyed, whilst after death by poisoning by the colubrine snakes the blood generally coagulates *.

As the blood is the channel through which the poison acts, it is obvious that the first object should be to arrest, destroy, or prevent its entry into the circulation; or if it has already entered, to neutralize or counteract its action, or to procure its elimination by the agency of the natural depurating organs and their secretions, and to treat local, consecutive, and constitutional symptoms by such remedial measures as may be required by the patient's condition.

Absorption takes place with extreme rapidity, so fast, indeed, that it was formerly supposed, in the case of some of the more active poisons, that they acted by transmission of a shock through the nervous system; and, so far as we know at present, it is not improbable that such, in some instances, may be the case. But rapid as the effect of snake-bite sometimes is, there is no reason to believe that generally it operates on the nerve-centres through any other channel than that of the vascular system. The experiments of Blake, Hering, and, later, of Claude Bernard show that absorption takes place with such rapidity as to explain the most rapid deaths from such cause. Blake (*vide* Guy's 'Forensic Medicine,' 3rd edition, p. 388) found that a poison passed from the jugular veins to the lungs of a dog in from four to six seconds, from the jugular vein to the coronary arteries of the heart in seven seconds;

* Our experiments in England have not confirmed these observations made in India. The blood of animals dead from *Daboia*-poisoning has been found to coagulate. This is a point that needs much further and repeated observation, as, indeed, does the question of the chemistry of the blood of animals affected by snake-poison, and we hope to report further on it.

a poison injected into the jugular vein was distributed throughout the circulation in nine seconds. Claude Bernard found that a saturated solution of sulphuretted hydrogen introduced into the jugular vein of a dog began to be eliminated from the lungs in three seconds, and when injected into the femoral vein of the same dog in six seconds.

We have neither seen nor heard of any case of snake-poisoning, in man or the lower animals, so rapid (though in some Dr. Fayrer has observed the first symptoms in a few seconds) as to justify the conclusion that poisoning had occurred otherwise than through the medium of the circulation.

Some preliminary experiments made in England by one of us (Dr. Brunton) with the poison before it had undergone decomposition seemed to show that it produced paralysis of the spinal cord, of the ends of the motor nerves, and of the muscles themselves. The experiments which we made together with the same poison a few months afterwards, as well as with other samples of poison sent from India, have not given concordant results. We therefore propose to postpone the consideration of this subject to a future paper, and to confine ourselves at present to the mode in which death is produced by the poison, especially in mammals.

Somatic death, according to Bichat, may commence in the brain, lungs, or heart; but the experiments of Fontana and Legallois show that so long as circulation and respiration are kept up the body remains alive although the head be absent. The brain is only necessary to life, inasmuch as the respiratory movements cease when it is removed or destroyed, either mechanically or by the action of a poison upon it. The causes of somatic death are thus limited to failure of the circulation and failure of the respiration.

The long continuance of the cardiac pulsations after apparent death (Expts. I., III., IV., V., IX., X.) excludes failure of the circulation as the usual cause of death; and we are thus brought by exclusion to regard death caused by the bite of a cobra, or by its poison introduced into the body in any other way, as death from failure of the respiration, or, in other words, death by asphyxia. The truth of this view is well illustrated by the following experiments*, which show that the vitality of the heart may be retained for a considerable time if the respiration is kept up. It shows also that the convulsions which have been remarked by Russell and all subsequent observers as almost always preceding death are not due so much to the action of the poison itself on the nervous centres, as that they depend on the irritation which is produced in them by the venosity of the blood.

* Excepting those cases in which the poison is injected into a large vein, such as the jugular, and causes sudden arrest of the heart's action.

Experiment VIII.

July, 1872.—A drop or two of cobra-poison diluted with water was injected into the thigh of a strong fowl. Shortly after it began to droop. It then seemed drowsy, and crouched down with the beak resting on the ground: it then fell over on its side. The comb and wattles lost their bright red colour and became dusky. Almost simultaneously convulsions occurred. A cannula was quickly inserted into the trachea, and artificial respiration commenced. The comb rapidly regained its bright colour, and the convulsions ceased. On the artificial respiration being discontinued the lividity of the comb reappeared, and convulsions again began. The experiment was repeated about ten times, and on each occasion the convulsions disappeared whenever the blood became arterial, as shown by the bright colour of the comb, and reappeared when the blood became venous. After discontinuing artificial respiration, the convulsions returned and the fowl died.

Experiment IX.

November 7th, 1872.—A cannula was placed in the trachea of a rabbit.

12.57. A small quantity of cobra-poison was injected into the hip. Symptoms of poisoning came on slowly.

1.25. The animal is still breathing, but the limbs are almost completely paralyzed. Artificial respiration begun. Temperature in the rectum 101°·8.

1.37. Paralysis is now complete. The animal is perfectly motionless, and not the slightest movement of the eyelids occurs when the cornea is touched. Temperature in rectum 100°·8.

1.55. The animal appears quite dead, but the heart pulsates vigorously.

2.30. Cardiac pulsations as before. Temperature 98°·6 F.

2·32. Heart as before. Temperature 97°.

4.10. Heart still beats vigorously. Temperature 95°·4. The continuance of the artificial respiration was now entrusted to an assistant.

5. Heart beating well.

5.20. Heart beating feebly and its action jumping.

5.30. Heart beating slowly.

6.30. Heart beating a little quicker.

7.30. Heart as before.

8. Heart beating more slowly.

8.30. Cardiac pulsations are very feeble.

9.30. Very feeble and slow.

The hour was now late, the rabbit was still completely motionless, and its body felt cold to the touch. The artificial respiration was therefore discontinued, although the cardiac pulsations had not ceased. Life was evidently prolonged for some hours in this case by artificial respiration.

Experiment X.

November 28th, 1872.—One fifth of a drop of cobra-poison (the first supply), diluted with about 2 cub. centims. of $\frac{1}{2}$ per cent. salt, was injected into the external jugular of a rabbit.

12.5. Injection made.

12.20. The animal has been convulsed and paralyzed. Sensibility of the cornea has disappeared; cannula placed in trachea and artificial respiration commenced. Temperature 100°.

1.15. Temperature 96°·3. Heart is beating vigorously.

3.13. Heart is beating as before.

3.20. In order to try if possible to quicken elimination milk was injected into the stomach.

4.5. Heart is beating as well as ever.

4.40. Heart still beating vigorously. Respiration discontinued. Death soon followed. In this case also life was prolonged by artificial respiration.