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ON THE

POISON OF VENOMOUS SNAKES

AND

THE METHODS OF PREVENTING
DEATH FROM THEIR BITE

REPRINTED PAPERS

BY

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PREFACE.

SCIENTIFIC literature is increasing at such a pace at present that it is difficult to keep completely acquainted with even one branch of it. In consequence, some workers publish their own results without taking the trouble to ascertain what other men have been doing in the same field. Others, again, belong to the "Ten Year School," who systematically neglect all work except that done within the last ten years. But there are many more, thoroughly conscientious workers, who try to find out all that has been done in their own field of investigation, so that their own observations may be rightly fitted in and help to build up a solid structure of knowledge. But even these are often hampered by the difficulty of obtaining the original papers to which they would like to refer, and consequently remain unacquainted with observations which may be of considerable importance. This seems to have been the case with the papers here reprinted by Sir Joseph Fayrer and myself, because in his admirable work on Venoms, Calmette credits Lacerda with the discovery of the antidotal power of permanganate of potash and himself with that of chloride of gold, although both of these substances, as will be seen from pages 137 and 149 of these reprints, were shown by us to be active a good many years ago.

With the concurrence of Lady Fayrer and Major Leonard Rogers, and by permission of the Royal Society, I thought it would be advantageous to republish these papers, not only for the purpose of giving wider circulation to the work of the late Sir Joseph Fayrer, but in the hope that they may be useful to other workers in the same field.

LAUDER BRUNTON.

LONDON,

January, 1909.

ON THE NATURE AND PHYSIOLOGICAL
ACTION OF THE POISON OF *NAJA*
TRIPUDIANS AND OTHER INDIAN
VENOMOUS SNAKES.—PART I.

By T. LAUDER BRUNTON, M.D., Sc.D., M.R.C.P., and J. FAYRER,
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(Reprinted from the *Proceedings of the Royal Society*, No. 145, 1873.)

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 neutralising 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 connection 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 cœruleus*) the second place; whilst under the headings of "other snakes" and "unknown" must be included many deaths due to cobra, *Bungarus cœruleus*, *Ophiophagus*, *Daboia*, *Echis carinata*, *Bungarus fasciatus*, *Hydrophida*, 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. Fayerer 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 neutralising 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 realise 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 localised 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 neutralise 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 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, neutralise, 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.

* 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 spécifique 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.

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, paralysing 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), secondary 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, antagonising, 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 syrupy 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.

* *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.

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 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	7·0	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

* 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.

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. 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 guinea-pigs and rabbits peculiar twitching movements occur, which seem to represent vomiting in them, and occasionally, in fact, guinea-pigs 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 co-ordinating power of the muscles of locomotion.

Hæmorrhage, relaxation of the sphincters, and involuntary evacuations, not unfrequently of a sanguineous or mucosanguineous 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, guinea-pigs, 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 paralysed.

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.

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

* 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 paralysed; at all events the heart suddenly ceases to beat.

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 c.c. 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 away. 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 towards 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 $1\frac{1}{2}$ c.c. of water, and injected it under the skin of the left hip of a guinea-pig, 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 $\frac{1}{2}$ c.c. 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 paralysed 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 c.c. of water. It dissolved easily and formed a somewhat opalescent solution.

Injected about one-third 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.

Four 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: $5\frac{1}{2}$ 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 an interrupted 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 guinea-pig.

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

Six minutes 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 guinea-pig.

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 half a grain of fresh but coagulated and cheese-like cobra-poison was suspended in

distilled water and injected into the back of a guinea-pig, weighing about a pound and a quarter.

2.23. Injection made.

2.26. The animal looks scared and is twitching. This guinea-pig 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 paralysing the nerve-centres or other portion of the nervous apparatus, and thus causing arrest of respiration, or by partially paralysing 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.*

* Our experiments in England have not confirmed these observations made in India. The blood of animals dead from *Daboia*-poisoning has been found to

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 neutralise 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 vein 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; 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
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.

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 (Experiments 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 paralysed. Artificial respiration begun. Temperature in the rectum, $101^{\circ}8$.

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, $100^{\circ}8$.

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

2.30. Cardiac pulsations as before. Temperature, $98^{\circ}6$ F.

2.32. Heart as before. Temperature, 97° .

4.10. Heart still beats vigorously. Temperature, $95^{\circ}4$. 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 paralysed. 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.

ON THE NATURE AND PHYSIOLOGICAL
ACTION OF THE POISON OF *NAJA*
TRIPUDIANS AND OTHER INDIAN
VENOMOUS SNAKES.—PART II.

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THE effects of the poison of *Naja tripudians* are probably the same as those of *Ophiophagus elaps*, *Bungarus*, Hydrophidæ, and other poisonous colubrine snakes, whilst that of *Daboia Russellii* is similar to that of *Echis carinata*, and also of the *Trimeresuri*, which represent the viperine snakes in India.

Just as the *Naja* may be regarded as among the most virulent of the colubrine, the *Daboia* is probably as venomous as any of the viperine snakes, it being very deadly; whilst the Crotalidæ are but feebly represented in India by the *Trimeresuri*.

The venomous colubrine snakes in India are represented by the *Naja tripudians*, *Ophiophagus elaps*, *Bungarus fasciatus*, *B. cæruleus*, *Xenurelaps bungaroides*, and the various species of *Callophis* and Hydrophidæ; whilst among the viperine snakes the Viperidæ, or vipers, are represented in India by only two genera, each with a single species, *Daboia Russellii*, *Echis carinata*; the Crotalidæ, or pit-vipers, by the various *Trimeresuri*, *Peltopelor*, *Halys*, *Hypnale*, though these are much less active than their American congeners.

The *Daboia*, however, may be considered as virulent as the most deadly form of the Viperidæ of Africa, or probably as the *Crotalus* or *Uraspedocephalus* of the pit-vipers of America and the West Indies.

In a previous communication we have described the effect of the poison of *Naja tripudians* upon warm-blooded animals, and have illustrated it by experiments on the dog, rabbit, guinea-pig, and fowl.

We purpose in the present paper to compare its action with that of the poison of the *Daboia Russellii*, a viperine snake, to describe its effects upon cold-blooded animals and invertebrata, and to examine in detail its action upon the various organs of the body.

In our former paper we stated that the general symptoms of poisoning by cobra-venom are depression, faintness, hurried respiration and exhaustion, lethargy, unconsciousness, nausea, and vomiting. In dogs, guinea-pigs, and rabbits, peculiar twitching movements occur, which seem to represent vomiting in them; occasionally, in fact, dogs and guinea-pigs (Experiment XX) do vomit, and dogs are profusely salivated. 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 co-ordinating power of the muscles of locomotion.

Hæmorrhage, relaxation of the sphincters, and involuntary evacuations, not unfrequently of a sanguineous or mucosanguineous character, often precede death, and are generally accompanied by convulsions.

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

The following experiments upon pigeons and guinea-pigs show that the general symptoms produced by the poison of the *Daboia* are nearly the same as by that of the *Naja*. The local symptoms are greater extravasation of blood and effusion into areolar tissue. In Experiment III it was noted that greater lethargy and less violent convulsions occurred in the pigeon poisoned by cobra-venom than in that poisoned by *Daboia*; but this might readily be due to individual difference in the bird; and an opposite result is noted in Experiment VII upon a

guinea-pig. In one pigeon, killed by *Daboia*-venom, the blood remained permanently fluid after death; but in the other, and also in the guinea-pigs, it coagulated firmly. This is an exception to the rule which has been noticed in experiments made in India, that the blood after *Daboia*-poisoning remains fluid—in marked contradistinction to death from cobra-venom, in which the blood almost invariably coagulates. Coagulation, however, of the blood of a fowl after death from the bite of a *Daboia* has also been noticed by one of us (Dr. Fayrer) in India; and therefore the coagulation in our experiments was not due to the lower temperature of the atmosphere.

Experiment I.

August 27th, 1873.—Three milligrammes of dried *Daboia*-poison, received some weeks ago from Balasore, were injected into the thigh of an old and vigorous pigeon at 2.48.

2.53. No apparent effect, except that the bird is lame on that leg.

3.2. The bird is sluggish. Respirations hurried. Lameness continues.

3.18. Still sluggish, but it is not deeply affected.

3.30. Disinclined to move. When placed on the table it sank on its breast. No nodding of the head.

3.45. Sudden and violent convulsions.

3.46. Dead in 58 minutes from the time of injection.

Electrodes inserted into the spinal cord soon after death caused movements of the wings, but not of the legs. Blood taken from the bird just before death partially coagulated after death. Blood taken from it after death coagulated more firmly, but less firmly than some taken from another pigeon poisoned with cobra-venom.

Experiment II.

A young full-grown pigeon had 3 milligrammes of dried *Daboia*-poison injected into the peritoneum at 3.5 P.M.

At 3.13 it was observed to pass suddenly into violent convulsions, flapping its wings strongly. It continued in this state

for a minute; and at 3.14 it died, 9 minutes after the injection.

Electrodes inserted into the spinal cord, in the neck, caused violent muscular contractions all over the wings and legs. The cord was thus evidently not paralysed; but its irritability soon ceased. The blood remained permanently fluid, and became bright red on exposure to air; under the microscope (400 diameters) the corpuscles seemed normal. *Rigor mortis* came on.

Experiment III.

A full-grown young pigeon had 3 milligrammes of dried cobra-poison injected into the thigh at 2.49 P.M.,

2.53. The respiration is very hurried; the bird presents a sluggish appearance and begins to droop.

3.2. The eyes are now closed and the bird is crouching; legs extended.

3.6. Convulsions; head and back resting on the ground; legs extended and paralysed.

3.10. Dead in 21 minutes from the injection.

Electrodes inserted into the cord soon after death caused general contractions of the extremities, showing that the cord was not paralysed. Its irritability soon disappeared. The symptoms in this bird are different from those in the one poisoned by *Daboia*-virus; there is more lethargy, nodding of the head, and apparent drowsiness before the convulsions, which are not so sudden or so violent.

Experiment IV.

A full-grown pigeon had 3 milligrammes of dried cobra-poison injected into the peritoneum at 3.5 P.M.

3.15. The bird is sluggish, nodding its head.

3.17. Gaping; the head is twitching, and the bird can hardly stand.

3.22. Convulsions. Several grains of Indian corn are vomited.

3.25. Quite paralysed. Convulsions.

3.26. Dead in 21 minutes from the injection.

Electrodes in the cord soon after death caused movements in

the limbs. The irritability rapidly disappeared, and at 3.33 was entirely gone.

The blood coagulated firmly after death.

When examined after death with a magnifying power of 400 diameters, crenation of some of the red corpuscles was observed, but no other change was noticed.

Experiment V.

February 11th.—About $\frac{1}{2}$ —1 c.c. of a mixture of *Daboia*-poison with alcohol (1 part poison with 4 of alcohol) was injected into the left thigh of a small guinea-pig at 1.45 P.M.

Immediately afterwards it became very restless, and the nose began to be twitched inwards towards the breast.

1.48. The left leg drags somewhat.

1.54. The hind legs are jerked backwards regularly every few seconds.

1.55. It bites at its left leg.

1.58. It has drawn itself together almost into a ball.

2.2. The twitching still continues.

2.23. Its hind quarters have become nearly paralysed. It lies on its side, and convulsive movements occur from time to time.

2.28 $\frac{1}{2}$. It is apparently dead. The heart continues to beat strongly. On opening it, the lungs were slightly congested. Peristaltic movements of intestine active. The blood from the heart was allowed to run into a clean beaker. It was of a dark colour, but became red on exposure to air. It shortly afterwards coagulated and formed a firm clot.

Experiment VI.

February 11th.—About 1 c.c. of *Daboia*-poison (1 part poison mixed with 4 parts of alcohol) was injected under the skin of the left thigh of a guinea-pig at 1.13.

1.17. Animal rubbing its mouth with its fore-paws. It is restless and moves about. There are slight twitchings, and it sits on its hind legs like a cat.

1.22. Very restless.

1.27. Head is drawn towards legs in a twitching fashion. Animal bites at the left leg. When it moves about, the left leg drags somewhat.

1.45. Has been very quiet and disinclined to move for some time.

1.55. About 1 c.c. more was injected into the right thigh.

1.56. Both hind legs drag slightly.

1.58. The animal is very unsteady and tottering on its legs.

2.2. Both hind legs completely paralysed, and, when the animal draws itself forward with its fore-paws, the hind legs trail out behind it. There are twitchings of the fore part of the body.

2.17. Hind legs and loins quite paralysed. The posterior part of the body lies flat on the ground, the abdomen being flattened out upon it. Paralysis seems gradually extending to the fore limbs. There is general twitching. It tries to crawl, but cannot drag itself forward, though it can still move the fore legs. Gnaws the bottom of the box in which it lies.

2.20. Almost motionless. Eye is still sensitive. Fluid has issued from the mouth. The animal can still move its head.

2.23. Convulsive movements.

2.24. Cornea insensible. Weak twitches of the trunk still occasionally occur; they seem to be of the nature of respiratory movements. Heart beats strongly.

In a minute or two afterwards the animal was opened. The heart was irritable and contracted when touched. The ventricle did not contract unless touched. The auricles were beating. The lungs were (I think) slightly congested. Blood from the large trunks in the thorax was collected in a vessel: it was of a dark colour; on exposure to air it became bright red and formed a firm coagulum. Peristaltic movements of the intestine were observed.

Experiment VII.

February 11th.—About $\frac{1}{2}$ c.c. of milky-looking cobra-poison was injected into the right thigh of a guinea-pig of moderate size at 2.20. It became restless immediately, and the hind legs began to twitch backwards. Shortly afterwards it again became quiet and sat quite still.

3.12. The animal did not seem to be much affected by the poison. Some more injected into left thigh.

4. Both hind legs became paralysed, and the animal lay with them spread out behind it. The hind part of the body also sank down, so that the abdomen became flattened on the floor, just as with the *Daboia*-poison.

4.23. Convulsive twitches occur. The animal lies on its side. It is more convulsed than the one killed with *Daboia*-poison.

Action of Cobra-poison on Frogs.

When cobra-poison is injected under the skin of frogs they occasionally become very restless immediately after the injection. This, however, is by no means always the case; and as similar agitation occurs, often to a much greater extent, after the injection of other substances, it is to be attributed rather to the insertion of the needle than to the action of the venom. A gradually increasing torpor then comes over the animal, sometimes beginning some time after the injection, and then proceeding uninterruptedly, at other times being interrupted by occasional movements. The limbs are drawn close up to the body, and the head gradually sinks down between the hands in most instances; but sometimes, as in Experiment VIII, the head is held at first much more erect than usual. The power of motion is lost before that of sensation; for the movements caused by painful stimuli become weaker and weaker, although they may still follow each application of the irritant. The progressive weakness is well shown in the movements of the hind legs. After the frog has sunk down and is lying flat upon the table, pinching the toes causes it to kick vigorously; but by-and-by, instead of kicking, it merely draws away the foot from the irritant with a slow wriggling motion. If it is then lifted up from the table, so as to remove the resistance occasioned by friction, the wriggling entirely disappears, and the foot is promptly and easily drawn up to the body when pinched. This weakness seems to depend on the nervous system rather than on the muscles; for, even in this state of apparent paralysis, the animal occasionally displays considerable muscular power, and is able to spring to a

considerable height, as in the following experiment. A similar condition is sometimes observed in warm-blooded animals, as in Experiment LX. The motor paralysis increases, no motion follows the application of any irritant, however powerful; but even then sensation exists, as is seen from Experiment LXXVI. The heart continues to beat after all motion in the body has ceased; but its pulsations become gradually slower, and at last cease altogether.

Experiment VIII.

September 12th, 1873.—Three frogs of nearly equal size were selected, and a dose of dried cobra-poison dissolved in water was injected into the dorsal lymph-sac of each. The quantity injected into No. 1 was estimated to be equal to three or four drops of the fresh poison, that into No. 2 about a drop, and into No. 3 about half a drop. These estimates, however, are not to be absolutely depended on.

The injection was made into all three about 3 P.M.

3.17. Nos. 1 and 2 are sitting with the head much more erect than usual and the belly depressed. No. 3 has the head depressed between the fore paws.

3.22. No. 3 is now sitting up in the normal posture.

4. No. 1 lies quite quiet; when moved its limbs give a slight wriggle. Applied strong acetic acid to its legs; after many seconds it gave a faint wriggle. No. 2 also lies quiet. When its legs are pulled back it can still wriggle them up towards its body. When held up it can kick well. After being placed on the table it suddenly, and without any apparent reason, sprung up to a considerable height. No. 3 presents the same appearance as No. 2, but seems more paralysed.

4.5. No. 1 does not react at all to any painful stimulus. Nos. 2 and 3 wriggle their legs when pinched. The observation was now discontinued. Next morning all three were dead.

Action on Lizards.

The action of cobra-poison upon lizards seems very similar to that which it has upon frogs; the animal becomes sluggish and difficult to rouse; and the bitten part is affected by

paralysis, so that, if a limb has been thus wounded, it is dragged by the animal. The paralysis afterwards extends to the rest of the body, and death ensues. Experiments on this subject have been recorded by one of us (Dr. Fayrer) in the *Thanatophidia of India*.

Effect of Serpent-venom on Snakes.

The bite of venomous serpents, such as the cobra, *Daboia*, and *Bungarus*, generally proves fatal to innocuous serpents, but not always. The occasional escape of the latter is probably due to the quantity of poison absorbed having been small, either absolutely, or relatively to the size of the bitten snake. The effect of the size of the innocuous snake upon the time required by the poison to produce a fatal effect is illustrated by Experiment *f*, in which a small rat-snake was killed by the bite of a *Bungarus caeruleus* (less poisonous than a cobra) in 7 hours 17 minutes, while a large snake of the same species was not killed by the bite of a cobra till after about 36 hours (Experiment *a*); and another still larger one was unaffected by the cobra-venom (Experiment *g*). Venomous snakes are not generally affected either by their own poison or that of another sort of snake, no less than 15 drops of venom having been injected hypodermically into a cobra (Experiment *r*) without effect; but small ones are occasionally killed by large individuals belonging either to the same or to a different species.*

The symptoms caused by the poison were the same in both the innocuous and the venomous snakes killed by it, and consisted chiefly of sluggishness and indisposition to move, which probably signifies in the snake, as it does in the frog, a progressive paralysis. Only in Experiment *b* were convulsive movements noticed. The movements of the tail in Experiment *c*, after motion had ceased in every other part of the body, are remarkable.

The poisonous action of the venom of the cobra, *Daboia*, and *Bungarus* upon innocuous snakes is shown in the following

* It is probable death may be due to other causes, especially in the case of a *Daboia*-bite, where the fangs are so large that the wound and internal hæmorrhage might cause death.

experiments selected from a number recorded in the *Thanatophidia of India* :—

Experiment *a*.—March 10th, 1868.—A rat-snake (*Ptyas mucosa*), about 6 feet in length, was bitten by a large cobra at 12.54. Before closing the snake's jaws on the part the scales were scraped off. Blood was freely drawn by the snake's fangs from bites inflicted in two places.

1.8 P.M. Appears sluggish; wound bleeding freely.

1.16. Perfectly active, and moves about rapidly in the cage.

1.35. No change.

There was no apparent change in the snake all that day or the next, except that it may have been a little more sluggish. It died in the night of the 11th, being found dead on the morning of the 12th.

Experiment *b*.—A small grass-snake (*Tropidonotus quincunciatus*) was bitten by a cobra at 1.12 P.M.

1.11. Very sluggish.

1.20. Tosses its head about in a convulsive manner.

1.25. Dead 13 minutes after the bite.

Experiment *c*.—Two tree-snakes (*Dendrophis picta*), one about 3 feet 4 inches long, and the other somewhat smaller, were bitten by a cobra.

1.7. The larger snake bitten.

1.8. The smaller one bitten.

1.12. Both sluggish.

1.15. The smaller snake dead 7 minutes after the bite.

1.16. The larger one dead 9 minutes after the bite.

They simply seemed to become sluggish and powerless; there were no convulsions, no writhings or contortions. After they had appeared quite dead for a moment or two, the tail of each moved slightly.

Experiment *d*.—A green whip-snake (*Passerita mycterizans*) more than 3 feet long, was bitten by a cobra about 10 inches from the head, at 12.37 P.M.

12.38. Sluggish, moves less actively; gapes, keeping the mouth wide open.

12.39. Almost paralysed; mouth now closed; head lying on the side. The body is swollen where bitten.

12.43. Dead 7 minutes after the bite. This snake was peculiarly active and vigorous though innocuous.

Experiment *c*.—A green whip-snake (*Passerita mycterizans*), somewhat smaller than the former one, was bitten in the body by a *Daboia* at 1.40.

1.45. Almost powerless. It gradually became more and more exhausted, gaped like the one bitten by the cobra, and at 2.2 it was dead, 22 minutes after the bite. The *Daboia* had been in confinement for some time and was probably exhausted.

Experiment *f*.—A small rat-snake (*Ptyas mucosa*), about 2 feet long, was bitten by a *Bungarus caeruleus*, 42½ inches long, in the muscles of the back at 1.8 P.M.; blood drawn.

2.30. Sluggish; has lost all its vivacity.

8.25. Found dead 7 hours and 17 minutes after the bite.

The occasional escape of an innocuous snake after the bite of a poisonous one is illustrated by Experiment *g*. Several others were made with a like result.

Experiment *g*.—A full-grown rat-snake (*Ptyas mucosa*), about 8 feet long, was bitten by a fresh cobra about two-thirds grown and about half its own size. About 13 minutes after the bite it seemed restless and uneasy, but remained perfectly active, and was perfectly well on the third day after the bite.

The power of one venomous snake to kill another appears from the following experiments:—

Experiment *h*.—A *Bungarus fasciatus*, nearly full grown, was bitten by a very large and powerful cobra, 5 feet 8 inches in length. It was bitten twice, about 8 inches from the head, at 12.22 P.M. The cobra took firm hold and implanted the fangs deeply. It seemed to be unaffected; and 22½ hours after the bite it still seemed well; but it died about the 29th hour.

Experiment *i*.—A *Bungarus caeruleus*, 28 inches long, was bitten by a very large and powerful cobra. It died in 40 minutes,

presenting the same symptoms as those of an innocuous snake killed by a cobra-bite.

Experiment *j*.—A young and very small, though lively, cobra, 14 inches long, was bitten in the muscular part of the body by a large krait (*Bungarus caruleus*), 48 inches long, at 12.50.

At 1 P.M. the cobra is very sluggish.

1.8. So sluggish that it moves with difficulty and can be easily handled; it makes no effort at resistance.

1.20. Apparently dying; movements scarcely perceptible.

1.22. Dead 32 minutes after the bite.

Experiment *k*.—July 10th, 1869. A young cobra, about 10 inches long, was bitten at 3.45 P.M. by a fresh full-grown cobra near the tail, so that the viscera might not be injured. The fangs were seen to penetrate; and no doubt could exist that the poison was fairly inserted. Being put on the ground, it crawled away vigorously, and seemed unaffected by the bite. On the 13th it seemed well; but on the 17th it was found dead, and had apparently been so for about 12 hours.

As this snake was young it may have died partly from want of food and partly from the wound, as well as from the effects of the poison.

Though small snakes of a venomous species may be killed by large ones, either of the same or of another species, full-grown individuals are rarely injured by the bite of another, either of their own or another species. This is illustrated by the following experiments, which are taken from numerous others of the same sort.

Experiment *l*.—A *Bungarus fasciatus* was fairly and deeply bitten by a fresh cobra near the tail; there was no doubt of the penetration of the fangs and inoculation of the poison. No effect was produced, and the *Bungarus* was alive and well five days after the bite.

Experiment *m*.—A *Bungarus fasciatus* was thoroughly bitten in a similar manner by a fresh *Daboia*. The bite produced no

effect, and five days afterwards the snake was in its normal condition.

Experiment *n*.—A *Daboia* was bitten by a fresh cobra near the tail, the scales having been previously scraped off. The snake bit fiercely and repeatedly. Two days afterwards no effect could be noticed.

Experiment *o*.—A large black cobra was bitten in two places 1 foot 6 inches from the head, and also on the head, by a large and vicious *Daboia*. Blood was slightly drawn; and there could be no doubt that the fangs had penetrated and the poison been inoculated. Six days after the bite there was no change in the snake.

Experiment *p*.—A full-grown cobra was bitten by another full-grown, fresh, and vigorous cobra in two places about 6 inches from the head, and also in the mouth. They both bit each other freely in this situation, and blood was freely drawn. They were both well a week afterwards.

Experiment *q*.—A cobra had 15 drops of his own venom injected hypodermically about 8 inches from the head. A week afterwards it seemed sluggish; but this might be from other causes.

Experiment *r*.—A cobra had 15 drops of the venom from another cobra injected hypodermically in the same situation as the last. A week afterwards he was perfectly well.

Effects on Fish.

Cobra-poison seems to produce paralysis, indicated by the fish turning on its side in the water—and also great excitement, the fish struggling and plunging violently.

Experiment IX.

A fish (*Ophiocephalus marulius*), about 10 inches in length, was bitten by a fresh cobra at 11.20 A.M. in two places on the dorsal and ventral surfaces.

11.22. It turned over on its side in the water.

11.23. Struggling and plunging violently in the water.

11.25. Turned over on its side.

11.26. On being roused it plunges violently.

11.40. Dead in 20 minutes from the bite.

For the purpose of comparison the following experiment with curare was made. It will be seen that there was no plunging. The failure of muscular action, except when a more than ordinarily powerful stimulus from the nerve-centres called it into play, is very evident.

Experiment X.

November, 1873.—Injected a solution of curare under the skin of a carp near the tail. A great part of the solution came out on withdrawing the needle of the syringe.

11.25. Injection made.

11.26. The fish lies obliquely in the water, inclining to the opposite side from the injection. It can move when irritated, and can remain perfectly upright in the water; but in a very short time its position becomes oblique again.

11.35. Injected some more curare. A great part of this also returned.

11.50. Lies obliquely, but can move tolerably vigorously when roused.

11.55. Moves more feebly when roused.

12.10. Seemed dead, but did not lie flat on its side, and still preserved the oblique position.

12.20. It suddenly started up without any apparent cause, swam across the vessel, a distance of several inches, and then relapsed into its former state.

Action on Snails.

Cobra-venom seems to destroy their irritability. It first causes them to shrink within their shells, and finally lessens their movements when stimulated.

Effect of Reagents, etc., on the Action of the Poison.

The activity of the poison is not destroyed, and scarcely impaired, by drying. We have made no comparative experi-

ments with perfectly fresh poison and the dried residue of a similar quantity; but there are few, if any, instances on record of death from the fresh poison in less than half a minute, the time in which the dried poison killed a guinea-pig in Experiment XXVIII.

The local action of the poison, however, seems to be altered by drying; for extravasation of blood around the part where a snake has inserted its fangs, or venom has been injected, is one of the most prominent effects produced by the fresh poison, whereas it is very slight, or absent altogether, when the dried venom has been employed, except in occasional instances, such as Experiment LVII.

Dilution seems also to have no effect in lessening the activity of the venom, except so far as it retards absorption; for it is evident that a drop of pure poison, injected subcutaneously, is likely to find its way into the circulation more quickly than the same quantity diluted with a hundred times its bulk of water.

Coagulation of the venom by alcohol does not destroy its activity, as we have shown in our former communication. The coagulum thrown down by the alcohol is innocuous, or nearly so; but the poisonous principle remains in solution, and the alcoholic extract possesses similar properties to the poison itself. A specimen of poison was received from India in a coagulated state; but we are uncertain whether this occurred spontaneously or was produced by the action of reagents. It is probable, however, that it was due to its having been mixed, in order to preserve it, with alcohol, which had evaporated before we received it. It was active, as Experiment XI shows. Coagulation by boiling does not destroy the activity of the poison (Experiment XII); but a portion which was boiled for more than half an hour under pressure corresponding to a temperature of 102° C., had no effect when injected under the thigh of a lark. The notes of this experiment have unfortunately been lost. Admixture with liquor ammoniæ and liquor potassæ does not alter the effects of the poison. This appears from Experiment XIII, and from several made by Dr. Fayerer in India.

Experiment XI.

October 28th, 1872.—A fresh supply of poison was received from India. It was of a yellowish colour, and was hard and dry, like tough cheese. About half a grain diluted with alcohol (in which it was only imperfectly soluble), was injected into the thigh of the same guinea-pig at 4h. 14' 30''.

4.15. Twitchings of an emprosthotonic character. The animal is apparently attempting to vomit.

4.20. The twitchings continue. The animal throws up its head. It seems sluggish, and will not walk.

4.22. A mixture of 5 minims of liquor ammoniæ with 10 of water was injected into the animal. Almost immediately afterwards it became convulsed, and fell over on its side, paralysed.

4.25. It is dying.

4.26. Quite dead.

4.27. The cardiac pulsations and peristaltic action of the bowels still continue. The blood, when collected in a vessel, formed a firm coagulum.

4.32. Peristaltic action diminished. The muscles of the leg contract when the sciatic nerve is stimulated by an induced current. Electrodes were then placed in the cord. The muscles of the legs contracted readily when an induced current was passed through the cord. One cell was employed, and the distance of the secondary from the primary coil was 44 cm.

Experiment XII.

May 19th.—A full dose of dried cobra-poison was diluted with distilled water, and heated until it was filled with white flocculent coagula.

The solution was injected into a guinea-pig's hip at 3.25. Twitching began almost immediately.

3.30. Restless. Hind leg paralysed.

4. Twitching acute in hind leg.

4.10. Active hip-twitching, but hind leg still paralysed.

4.15. Making efforts to vomit.

4.25. Vomiting repeatedly.

4.30. Distinct repeated convulsive attempts to vomit. Limbs

becoming weaker; began to be convulsed; gradually becoming more and more paralysed.

4.45. In convulsions. Dead.

Experiment XIII.

May 19th.—Dried cobra-poison, dissolved in liquor ammoniaë, injected into a guinea-pig's hip at 3.42.

Twitching at 3.43. Restless.

4. Twitching; restless; weak in hind leg.

4.8. A little more injected with a full quantity of ammonia. The guinea-pig becomes immediately very restless.

4.15. Paralysed. Going into convulsions. Pinching foot at once causes reflex action; marked reflex actions all over the body.

4.20. Nearly dead. Heart disturbed; continued to beat regularly for some minutes after death. Lungs much congested.

Influence of Constitution on the Action of the Poison. Supposed immunity of the Mongoose.

With cobra-venom, as with other poisons, there is a general correspondence between the size of the animal and the intensity of the effects of a given quantity of poison, a small animal being more readily affected by it than a large one. There are, however, some exceptions to this rule; for a cat will resist the action of cobra-poison as much as, or more than, a dog five or six times its size. (Compare Experiment LVII with Experiment XLIV.)

The mongoose (*Herpestes griseus*) has long been supposed to be unaffected by the poison of venomous snakes, either on account of some peculiarity in the constitution of the animal, or, as the story used to run, on account of its knowledge of some herb which it used to eat as an antidote; but such is not the case. If fairly bitten, it succumbs like any other creature, as proved by experiments in India (*Thanatophidia*, pp. 68, 69, and 134). Its great activity and vigour enable it to elude the snake; and generally, when it is wounded, it is merely

scratched, not pierced by the fangs. If the poison is inoculated, it dies.

The same is true of the pig, which escapes probably by receiving the wound in the foot, where absorption is not rapid or vigorous. This animal, like others, yields to the poison when the fangs are embedded and the virus thoroughly inoculated (*vide Thanatophidia*, p. 134).

Action on Germination.

In order to see whether cobra-poison had any effect on the germination of seeds, the following experiments were made. It will be seen from them that the venom does not prevent germination, but interferes with it, especially when strong. In this it agrees with rattlesnake-poison. (Weir-Mitchell *On Rattlesnake Venom*, p. 52.)

Experiment XIV.

A piece of flannel was doubled, and, 12 cress-seeds being laid between the folds, it was placed in a small beaker with 10 c.c. of water. Another piece, treated in the same way, was laid in 9 c.c. of water and 1 of a 2-per-cent. solution of dried cobra-poison.

Some time after the water had evaporated, so as to leave the flannel soaked with water but not covered, nine of those seeds which had been treated with water and poison had germinated and grown to about half-an-inch in length, while seven of those treated by water alone had germinated and had grown somewhat larger than the others.

Experiment XV.

The preceding experiment was repeated with lettuce-seeds. Seven of those treated with water alone had germinated, but only one of those treated with water and poison.

Experiment XVI.

A small piece of cotton-wool was placed in the bottom of each of two short test-tubes, and 10 lettuce- and 10 cress-seeds

were dropped into each. Ten drops of a solution of dried cobra-poison, containing 0.0355 gramme in 3 c.c. of water, were then used to moisten those in one tube, and as nearly as possible the same quantity of pure water for those in the other. The seeds were then covered with a few fibres of cotton-wool; the tubes were stopped with a plug of the same substance, and placed in a warm room.

Three days afterwards, all the cress-seeds which had been moistened with water had sprouted and sent out a radicle, varying from $\frac{1}{4}$ to $\frac{1}{2}$ an inch in length. Eight out of the 10 lettuce-seeds had sprouted and sent out a radicle more than $\frac{1}{8}$ of an inch long. All the cress-seeds moistened with poison had also sprouted, but the radicles were only about $\frac{1}{10}$ of an inch long. Five lettuce-seeds had begun to sprout, but the radicles were barely visible.

It is not improbable that the delay caused by the poison in the germination of the seeds, in this experiment, is not to be attributed entirely to its poisonous action; and it may be due in great measure to the solution of the poison having matted the fibres of cotton-wool more closely than the water, and thus rendered the conditions of air and moisture less favourable to the seeds placed in it.

Effect of the Poison when introduced through different channels.

The action of the poison is most rapid when it is introduced directly into the circulation, as by injection into the jugular vein; and in such instances death may occur in less than a minute. When injected into the thoracic cavity, as in Experiment XXVIII, death occurred almost as quickly; but this may have been due to puncture of the lung and introduction of the poison directly into some of the pulmonary vessels.

Injection into the peritoneal cavity comes next in order of rapidity, but a good deal behind the last; and it is followed by subcutaneous injection.

Whatever may be the effect of the venom of the viper or crotalus, the cobra-virus produces its poisonous effects tolerably rapidly when swallowed, both in the frog and in warm-blooded animals, as is seen from Experiments XVII and XIX.

It is also absorbed from the conjunctiva, and produces the characteristic symptoms of poisoning. In Experiment XX the animal, though affected by the poison, recovered; but in several experiments made by one of us in India, death rapidly occurred after the application of the fresh poison to the conjunctiva (*Thanatophidia of India*, pp. 108, 115, 127, 128, 135).

Experiment XVII.

May 21st, 1873.—2.23 P.M. A small bit of dried cobra-poison put into a frog's mouth and swallowed.

3.25. Frog not much, if at all, affected.

4.5. Frog not so vigorous. Appears to be paralysed in fore legs, but moves his hind legs freely. On irritating his fore legs there are vigorous contractions in his hind legs, but none in the fore legs.

4.10. The anterior part of the body and fore legs seem to be quite paralysed. No reaction is noticed in the eyelids when the cornea is irritated. Hind legs are still vigorous.

4.20. Hind legs vigorous. All the fore part of the body quite paralysed. Mouth gaping. Tongue swollen.

4.25. Hind legs now becoming weaker.

4.30. The application of acid causes slight reflex movements in the hind legs.

4.35. Acid causes no reflex action. Complete paralysis and death have thus occurred in two hours and a quarter.

4.40. Thorax opened. Heart still contracting rhythmically and steadily.

4.55. Heart still contracting, but less vigorously. There is no movement apparent in the intestines.

5.5. Heart still contracting slowly.

5.25. Heart still contracting. The heart and liver were now removed and given to another frog.

Experiment XVIII.

The heart and liver of the former frog were given to a large and strong frog. It was kept under observation for many days, but did not seem in the least affected.

Experiment XIX.

A small quantity of dried cobra-poison dissolved in water was given to a young rabbit at 2.53 P.M. It was readily swallowed. In seven minutes all the symptoms of poisoning were developed. The rabbit died in convulsions in 11 minutes, just as when the poison is injected hypodermically. The thorax was opened a few minutes afterwards. The heart had ceased to beat. *Rigor mortis* came on very rapidly.

Experiment XX.

November 28th, 1872.—1.49. One-quarter of a drop of cobra-poison put into a guinea-pig's eye.

3.12. The eye is much congested. The animal has twitchings.

3.14. Has been making efforts to vomit, and now vomits frothy clear fluid. Has been purged also.

4.5. Still retching, but not vomiting.

November 29th.—Found to have recovered.

Local Action of the Poison.

Cobra-poison acts as a local irritant, and produces chemosis of the conjunctiva and swelling of the eyelids when applied to the eye, and occasionally congestion of the peritoneal vessels when injected into the abdominal cavity (Experiments XX and XLIV).

It paralyses the ends of the motor nerves, and also the muscles of the part into which it has been injected (Experiment XXV). The muscles are not only deprived of their irritability, but become prone to putrefy (Experiment LVII). The fresh cobra-poison produces great extravasation of blood around the wound through which it has been introduced; but this is not so marked when dried poison is used.

If death do not rapidly follow, great swelling from infiltration of the areolar tissue may occur, or, in some cases, gangrene of the skin and subjacent cellular tissue and subsequent changes indicative of general blood-poisoning.

The local action of viperine is probably more active than that of colubrine virus.

Action of Cobra-poison upon the Blood.

The blood of animals killed by cobra-poison generally presents a dark colour, as death is due to failure of the respiration and not of the circulation; but it readily assumes a florid colour when exposed to air. The same is the case with the blood of animals poisoned by *Daboia*-venom (Experiments II, V, and VI).

Coagulation usually occurs readily and firmly in the blood of animals killed by cobra-poison, while it is frequently absent from the blood of those killed by that of the *Daboia*. In experiments made in India, this occurred almost invariably; and it is illustrated by Experiments II and IV. In Experiments I, V, and VI, however, coagulation occurred in the blood of a pigeon and guinea-pig poisoned by *Daboia*-venom; and a similar occurrence has been sometimes observed by one of us (Dr. Fayrer) in fowls bitten by this snake in India.*

In numerous instances we have been unable to detect any alteration in the blood-corpuscles after death from cobra-poison; but in Experiments XXI and XXII we observed a most distinct crenation in the corpuscles of rats poisoned by it. This was probably due in some degree to evaporation, as in Experiment XXI it was to a great extent prevented by surrounding the preparation with oil; but it indicates a change in the blood, as the corpuscles did not present this appearance before the injection of the poison—although they were prepared for observation in exactly the same way, and were as much exposed to evaporation in the one case as in the other.

Experiment XXI.

A drop of blood from the tail of a white rat was examined microscopically. The corpuscles did not form rouleaux; but no trace of crenation could be observed in them.

12.10. P.M. 0.018 gramme of dried cobra-poison, dissolved in 1 c.c. of water, was injected into the flank. Almost immediately the nose of the animal began to twitch up every few seconds.

* *Thanatophidia of India*, pp. 80, 100, 101, 104. *Vide* Mr. Cunningham's remarks.

12.15. Head has sunk down. The breathing was laboured. The animal made a sudden start forwards. The hind legs dragged behind. It did not move readily when irritated. The breathing was laboured; the expiration convulsive. General convulsive movements occurred.

12.18. The animal seemed dead. The heart was still beating. A drop of blood was taken from the tail; and, the thorax being opened, another was taken from the right ventricle. On being examined microscopically, the corpuscles in both were seen to be very much crenated. They did not form rouleaux. Another drop was taken from the right ventricle, and surrounded with oil to prevent evaporation. Hardly a trace of crenation could be observed in this drop; but several branching crystals of a reddish colour were observed, and some of them appeared to grow while under observation. Numerous granular masses were also seen.

Experiment XXII.

August 27th.—Injected 1 c.c. of a 2-per-cent. solution of cobra-poison under the skin of the hip of a white rat.

1.35. Injection made.

1.37. Respiration quick. The end of the tail snipped off, and a drop of blood examined by Dr. Klein. The red corpuscles are much crenated, and have no tendency to form rouleaux, but adhere together in flat masses. The plasma contains numerous lumps of a granular material, probably coagula of some sort.

2.5. The animal lies stretched out. Makes a curious squeaking noise. It does not rise when the tail is pinched.

2.13. Lies with nose on ground. Convulsive movements of hind legs.

2.15. Head sinks to one side. Convulsive movements.

2.18. Breathing slow. Marked interval between inspiration and expiration.

2.19. Stopped breathing. Heart still beating.

2.20. The animal lay on its back. A few weak respirations were made, and then ceased. The heart was beating steadily. Thorax opened and heart exposed. A little blood drawn from the ventricles by a fine pipette was examined microscopically

by Dr. Klein. It presented exactly the same characters as those of the former specimen. Blood from another healthy rat showed numerous rouleaux, and the corpuscles were not crenated.

Action on Muscles.

Cobra-poison has the power of destroying the irritability of voluntary muscular fibre when applied directly to it, either in a concentrated or diluted condition. It does not produce any quivering of the fibres; and in this particular it differs from the poison of the rattlesnake as described by Dr. Weir Mitchell.

The local action of cobra-poison on muscle is illustrated by Experiments XXIII, XXIV, XXV, and XXVI.

Experiment XXIII.

September 4th.—A frog was decapitated, and the skin removed from both hind legs. A longitudinal cut was then made in the muscle of both thighs. A strong solution of dried cobra-poison in distilled water, of such a strength as to resemble the fresh poison closely in appearance, was then applied to the cut in one thigh, while the other was moistened with distilled water. Immediately after the application an almost imperceptible trembling in the muscles occurred *equally* in both thighs; but it ceased after a few seconds, and did not reappear. On testing the muscles soon afterwards, by an induced current applied directly to them, those of the poisoned leg contracted feebly, but those of the non-poisoned leg, forcibly.

In this experiment, the quivering occurred equally in both thighs, and was therefore obviously due to the water in which the poison was dissolved, and not to the poison itself.

As Weir Mitchell found that the quivering produced by the poison of the rattlesnake was not prevented by paralysis of the motor nerves by curare, the previous experiment was repeated on a curarised frog.

Experiment XXIV.

September 4th.—The motor nerves having been tested and found to be completely paralysed, a strong solution of cobra-poison was applied to a cut in the back of the right thigh. No quivering of the muscles could be observed after its application. The poison was only applied to the middle of the back of the right thigh. After a few minutes, those muscles with which it had come into contact did not contract when irritated by the direct application of an induced current. Distance of secondary from the primary coil 0. The muscles of the sides and front of the poisoned thigh, as well as those of the other thigh, contracted well when irritated in the same way, with the coil at 13 cm.

The poison paralyses the muscles of warm-blooded animals in much the same way as those of frogs; and it seems probable from the following experiment, that the paralysis of the wounded limb, which is very frequently noticed in cases of snake-bite, is partly due to the local action of the poison upon the muscles.

Experiment XXV.

September 4th.—Injected five or six drops of a strong but not perfectly concentrated solution of dried cobra-poison into the muscles of the left thigh of a guinea-pig.

12.43 P.M. Injection made. The animal immediately became much excited, and rushed about wildly, crying loudly.

12.47. The leg seemed paralysed and dragged behind the animal.

12.48. It ground its teeth and cried.

12.50. Began to start, and cried more loudly. Took it in my arms. It then became quiet.

12.52. Shivered.

12.58. Laid the guinea-pig on its side on the table. It lay still and did not attempt to rise. Respiration was still going on.

12.59. Cut off the head of this guinea-pig (No. 1), and immediately after decapitated another healthy guinea-pig of nearly the same size (No. 2).

1.7. Exposed both sciatics of No. 1, and irritated them by an induced current.

Left leg. Coil at 0. No contraction.

Right leg. Coil at 17.5. Movement of toes.

The muscles of both legs twitch well when irritated by single shocks (coil at 17.5), except those in the middle of the inside of the left thigh, near the place to which the point of the syringe had penetrated. These muscles contract when the coil is at 3.

1.13. The muscles of the hip of No. 2 twitch distinctly when irritated by single shocks, coil at 24.

The toes move distinctly when the sciatic is irritated; coil at 37.

1.15. The ventricles of the heart of No. 1 are firmly contracted and motionless. The auricles are still pulsating vigorously.

The ventricles of the heart of No. 2 are only moderately contracted, and there is no pulsation either in them or the auricles.

1.22. The toes of the right leg of No. 1 move when the sciatic is irritated, coil at 18.

Those of No. 2 do so, coil at 37.

Put the electrodes in the cervical part of the spinal cord of both guinea-pigs, and irritated it by an induced current, coil at 0. No contraction took place in the hind legs of either animal. Contractions occurred in the muscles of the fore legs with much the same force in both.

1.45. On irritating the muscles by single induced shocks:—left leg of No. 1, vastus externus contracts, coil at 9.5; rectus femoris, a pale muscle, 12.5.

No. 1. Right leg, vastus 15.5, rectus 25. No. 2. Right leg, vastus 11, rectus 15.

1.53. No. 1. Left leg, vastus at 16; right leg, vastus at 20. No. 2. Left leg, vastus at 20; right leg, vastus at 20. The vastus contracts rather more strongly in the right leg of No. 1 than in those of No. 2.

2.23. No. 1. Left leg, vastus at 4; right leg, vastus at 11. No. 2. Left leg, vastus at 11; right leg, vastus at 11.

This experiment shows that the venom paralyses the motor nerves when applied to them locally, a strong current applied to the sciatic causing no contraction in the left leg of No. 1, while a moderate one caused movement in the right foot, at a time when the muscles of both were nearly equally irritable.

Its deleterious action on the muscles, when conveyed by the blood, is also evident in the rapid loss of irritability after death in both legs of No. 1 as compared with No. 2. The pale muscles seemed to retain their irritability longer than those having a deep colour.

The power of cobra-poison to paralyse muscle when applied to it, even in a diluted condition, is shown by the following experiment.

Experiment XXVI.

July 18th, 1873.—The legs of a large frog were cut off close to the body, and the skin removed. Each was then placed in a glass, and a sufficient quantity of fresh ox-blood serum poured over it to cover it. In one glass, the serum contained about 5 centigrams of cobra-poison dissolved in about 20 c.c. of serum; but, with this exception, all the conditions under which the two legs were placed were exactly alike.

July 19th.—About 19 hours after the immersion of the legs in serum their irritability was examined.

The muscles of the leg in the pure serum did not contract at all when the strongest irritation was applied to the sciatic nerve, but contracted very vigorously when irritated directly. The muscles of the leg in the poisoned serum were whiter than those of the other one. They had a faint yellowish tinge, and were somewhat stiff. They did not contract in the least when the strongest irritation by a Du-bois coil was applied either to them or the sciatic nerve.

When the poison is injected directly into the circulation, or is very rapidly absorbed, so that the quantity circulating in the blood is large, it destroys the irritability of the voluntary muscles rapidly, and, occasionally at least, hastens in a most remarkable manner the occurrence of *rigor mortis*. This is well seen in the Experiment XXV, where *rigor mortis* super-

vened in half an hour after the injection of the poison, while the muscles of another animal killed at the same time by decapitation retained their irritability for many hours.

Experiment XXVII.

May 8th, 1873.—Right thigh of a frog ligatured, with the exception of the sciatic nerve. Animal poisoned by the introduction of some dried cobra-poison dissolved in water into the lymph-sac of the back. After the animal had become completely paralysed, the gastrocnemii of the two legs were irritated by an induced current (1 bichromate cell).

Left leg (poisoned), distance of coil 13·5, contraction; right, 24·0, contraction.

Experiment XXVII (a).

Another frog prepared in the same way gave at first:—left leg (poisoned), distance of coil 42·2, contraction; right (ligatured), distance 21·0, contraction.

After some time:—left leg, distance 6·0, contraction; right, distance 25·0, contraction.

Some time later:—left leg, distance 0, almost no contraction; right leg, distance 14·5, contraction.

In this experiment, the poisoned muscle at first responded more readily to the irritation than the one which had been deprived of blood by the application of a ligature; and this renders more apparent the effect of the poison, in causing rapid diminution and final extinction of irritability in the muscle to which it had access, since the other lost its excitability very slowly.

Experiment XXVIII.

September 5th.—About 2.35 P.M. injected $\frac{3}{4}$ c.c. of a 2-per-cent. solution of dried cobra-poison into the thoracic cavity of a guinea-pig. It was uncertain whether the lung (right one) was pierced by the point of the needle or not. Within a few seconds the animal gave several convulsive struggles, and died in half a minute or so. The head was then cut off. Immediately afterwards a second guinea-pig was killed by decapitation.

On opening the thorax of No. 1 (the poisoned guinea-pig) the lungs were found congested. The heart was tetanically contracted and quite still. The heart of No. 2 was contracting vigorously. The vena cava contained a few bubbles of air. The lungs were pale.

2.40. Peristaltic movements are going on very actively in the intestines of both animals.

2.42. The muscles of the abdominal wall irritated by single induced shocks.

Guinea-pig, No. 1. No contraction. Coil at 0.

Guinea-pig, No. 2. Contraction. Coil at 14.5.

Muscles of the hip irritated in the same way:—

No. 1. { Trace of contraction of muscle. Coil 13.
 { Contraction still slight. Coil 0.

No. 2. { Contraction. Coil 37.
 { Powerful kick. Coil 0.

2.50. *Rigor mortis* is coming on in No. 1. The legs are quite stiff. A trace of peristaltic movement still going on in the small intestine.

The muscles of No. 2 are quite flexible.

2.55. No. 1. Muscles of back of thigh and of abdominal wall irritated directly as before. No contraction. Coil at 0. Muscles of the front of thigh twitch slightly. Coil at 0.

No. 2. Muscles of back of thigh twitch decidedly. Coil at 37.

3.12. No. 1. No contraction in any muscles. Coil at 0. The animal is stiff.

No. 2. Muscles are quite limp. Muscles of back of thigh twitch decidedly. Coil at 25.

All the muscles do not lose their irritability with the same rapidity, some of them becoming paralysed before others. The intercostal muscles, serrati, and abdominal muscles seem to lose their irritability first; and such muscles of the limbs as have a dark colour become paralysed sooner than those which are paler (Experiment XXV).

Experiment XXIX.

September 4th.—A cannula was placed in the carotid of a large guinea-pig, and $\frac{1}{2}$ c.c. of a 2-per-cent. solution of cobra-poison injected into it towards the heart. The animal was seized with violent convulsions, passing into complete opisthotonos in about 20 seconds after the injection of the poison. These ceased, and the animal seemed quite dead in rather less than a minute from the injection. The thorax was then opened. The lungs were somewhat congested. The heart was quite still in tetanic contraction. A strong interrupted current applied to it caused no contraction of any of the fibres. The muscles lost their irritability very quickly; the intercostals of both sides, and the serratus and subscapularis of the right side, seemed to lose their irritability before the other muscles.

When the poison is more slowly absorbed, so that a less quantity of it circulates in the blood, its action on the muscles is much less marked, as is evident from a comparison of the irritability of those in the poisoned and non-poisoned limbs in Experiments XXXVII, XXXVIII, XXXIX, XLVII. If the poison has undergone such changes as render it less active, it has no action, or only a feeble one, on the muscles, as seen in Experiments XI, XXX, XXXI, and XXXII, where poison, which had undergone partial coagulation was employed.

Experiment XXX.

January 14th.—In order to test the local action of the poison on the muscles and nerves, a ligature was tied round the base of a frog's heart so as entirely to arrest the circulation.

12.0. About a drop of cobra-poison was injected into one leg.

1.30. Laid bare the lumbar nerves in the abdomen, and irritated them by an induced current. Both legs contracted nearly equally.

Experiment XXXI.

January 14th.—At 12.15. One or two drops of cobra-poison were injected into the leg of a frog. The wound bled freely.

Immediately after the injection the frog became very excited and jumped about very much.

12.20. Frog quiet. Respiration quick.

2.30. Frog quiet, but jumps when irritated. It seems to use both legs equally well.

January 15th.—The frog is not dead, but is feeble. On killing and opening it, both legs contracted nearly equally when the lumbar nerves were stimulated by an induced current.

Experiment XXXII.

January 15th.—Tied the heart of a frog, and, 12.55 P.M., injected into the right leg a drop of water, and into the left leg a drop or two of cobra-poison.

1.55.—Irritated the back of the frog by an induced current. Both legs contracted nearly equally.

Experiment XXXIII.

May 9th.—A frog (*Rana temporaria*) was poisoned with curare. After complete paralysis had set in, the right leg was ligatured, with the exception of the sciatic nerve. The animal was then poisoned by the introduction of a solution of dried cobra-poison in water into the lymph-sac on the back, at about 12.30 P.M. The irritability of the muscles was tested by single induced currents applied to the denuded muscles, about 2.30.

Distance of Coil.

Left leg.....	7·5	Contraction.
Right leg	7·2-7·5	do.

Another frog was curarised and similarly prepared, with this exception—that the vessels of the right leg only were ligatured, the muscles, as well as the nerve, being left free. This frog was also examined in the same way; and the irritability of the muscles in both legs was found to be almost exactly the same three to four hours after poisoning. Both contracted with the coil at about 7·5.

Secondary Action of the Poison on Muscles.

The muscles of the part into which the poison has been introduced are very apt to undergo rapid decomposition. We have already shown that their irritability is either lessened, or completely destroyed, by the action of the venom; and it seems very probable that the mere contact of any other foreign body, containing bacteria or their germs (as the water in which the cobra-poison was dissolved in our experiments certainly did) would suffice to explain the decomposition of the muscle without assuming any special putrefactive action on the part of the poison; for the muscle, which has been at least temporarily killed by the poison, is placed in the body in the most favourable conditions of temperature and moisture for the occurrence of decomposition whenever any germs are brought into contact with it. However, Weir Mitchell found that the venom of the rattlesnake had a curious influence upon muscle, which could hardly be explained without the supposition that the poison had a peculiar disorganising action upon the muscular tissue. In every instance the venom softened the muscle in proportion to the length of time it remained in contact with it; so that, even after a few hours, in warm-blooded animals, and after a rather longer time in the frog, the wounded muscle became almost diffuent, and assumed a dark colour and somewhat jelly-like appearance. The structure remained entire until it was pressed upon or stretched, when it lost all regularity, and offered, under the microscope, the appearance of a minute granular mass. In order to ascertain whether cobra-poison had a similar action, the following experiment was tried.

Experiment XXXIV.

September, 1873.—The gastrocnemii of a frog were removed and laid in two watch-glasses. One was then covered with several drops of a solution of dried cobra-poison, dissolved in a sufficient quantity of $\frac{3}{4}$ -per-cent. salt solution to form a mixture about the consistence of fresh poison, while the other was covered with a few drops of salt solution alone. They were then protected from dust by two other watch-glasses inverted

over them. The temperature of the room was moderately warm. The poisoned muscle underwent no change. Both muscles gradually dried up; but at no time could one be distinguished from the other, except by the label on the watch-glass.

The influence of cobra-poison in causing decomposition within the body is evident from the following experiment.

Experiment XXXV.

January 17th.—About three drops of cobra-poison were injected under the skin of the flank of a guinea-pig at 12.48 P.M. Immediately afterwards the guinea-pig became restless and cried. In two minutes its head began to twitch. An hour after the injection the animal was quiet, and little or no effect of the poison could be observed. Three hours after the injection it did not seem very well. Next morning it was found dead. On examining it 22 hours after the injection it had begun to undergo decomposition. The abdomen was somewhat inflated, and sulphuretted hydrogen issued from it when opened. The hair came off readily from all parts of the animal's skin. The muscles were soft. There was little ecchymosis at the spot where the injection had been made. The tissues near it were rather watery. The heart was contracted; the lungs somewhat congested.

Action on the Nervous System.

The most prominent symptoms of an affection of the nervous system after the bite of a cobra, or other venomous snake, in animals or man, are depression, faintness, lethargy, and in some cases, somnolence. There is loss of co-ordinating power, and paralysis, sometimes affecting the hind legs first and creeping over the body, sometimes affecting the whole body at once. Death occurs by failure of the respiration, and is preceded by convulsions.

These symptoms clearly point to paralysis either of the nervous centres or of the peripheral nerves. It may be supposed that the mention of the latter alternative is superfluous, and that paralysis of the peripheral nerves cannot produce such symptoms, which must therefore, by exclusion, be

due to an affection of the central ganglia. More especially may the occurrence of convulsions be thought to exclude the possibility of death being due to paralysis of the peripheral terminations of motor nerves; for if their function is abolished here, how, it may be said, can general convulsions, which have their origin in the nervous centres, occur?

The answer to this is, that although the ends of the motor nerves are so far deadened that they no longer transmit to the muscles any ordinary stimulus proceeding from the nerve-centres, their function is not so thoroughly abolished that they cannot transmit those which are stronger than usual. This is shown by the fact that when an animal is slowly poisoned by curare (as for example when that poison is introduced into the stomach after ligature of the renal vessels), convulsions occur just as in death from cobra-poison. Although the motor nerves have their function so much impaired that they no longer transmit to the muscles of respiration the ordinary stimuli from the medulla, which usually keep up the movements of breathing, they can still transmit those stronger impulses which proceed from it when greatly stimulated by the increasing venosity of the blood, and which cause the respiratory as well as the other muscles of the body to participate in the general convulsions. The loss of co-ordination which occurs in poisoning by cobra-venom has also been noticed by Voisin and Liouville in poisoning by curare.

That the peripheral terminations of the motor nerves are actually paralysed by cobra-venom is shown by Experiment XXXVI, in which the animal was able to move the leg which had been protected from the action of the poison for some time after the rest of the body was perfectly motionless, as well as by Experiment XXXVII and those succeeding it. Its occurrence in man is indicated by the symptoms of a case described by Dr. Hilson (*Ind. Med. Gaz.*, October, 1873, p. 254).

But paralysis of motor nerves is not the only effect of cobra-poison on the nervous system. The spinal cord is also paralysed, as is seen from Experiment XLI, where motion ceased in the frog's leg which remained free from poison, although it answered with great readiness to a very weak

stimulus applied to its nerve. In some instances paralysis of the spinal cord appeared to cause death when little or no affection of the motor nerves could be observed (Experiment XLVII, etc.); but in others the peripheral paralysis was strongly marked. In no case was it more obvious, and in few was it so distinct as in Experiment XXXVI, made with the virus itself, which had neither become coagulated nor dried. In experiments made with the coagulated poison, death seemed invariably to be caused by paralysis of the spinal cord, the motor nerves being little affected (Experiment XI); while, in those made with the dried venom, sometimes the action on the cord predominated, and sometimes that on the nerves. In this respect, as well as in some of the symptoms it produces, cobra-poison agrees very closely with conia. This alkaloid, as Crum-Brown and Fraser have shown, often contains a mixture of true conia and methylconia. Conia alone paralyzes the motor nerves without affecting the spinal cord; but when mixed with methylconia, sometimes the one is affected first and sometimes the other. When the dose is small, the motor nerves are usually paralyzed before the reflex function of the cord; but when the dose is large, the cord is paralyzed before the nerves. Methylconia also affects both; but a small dose of it paralyzes the cord before the nerves, while a large one paralyzes them first. The paralysis of the hind legs, often observed in snake-poisoning (Experiments VI and VII), is probably partly due to the local action of the poison in the nerves and muscles of the bitten member, and partly to its action on the cord. This paralysis is noticed in Genesis xlix, 17, where Jacob says, "Dan is an adder in the path, biting the horse-heels, so that the rider falleth backward." In this point cobra-venom, when dried, appears to resemble methylconia rather than its admixture with conia; but it exercises numerous other actions upon the blood, muscles, etc., which neither of these substances has been shown to do. It is doubtful whether the cerebrum is directly affected by cobra-poison, as the intelligence both in man and animals often remains almost unimpaired to the last, and the stupor and drowsiness which are sometimes noticed may be caused indirectly by the action of the venom on the

motor and vaso-motor nerves and on the functions of the cord. The reflex centres, through which irritation of the fifth nerve acts, remain unaffected after the reflex function of the cord is nearly gone; and even then the power of voluntary motion still exists.

The effect of the poison upon the respiratory and vaso-motor nerves will be considered under the heads of respiration and circulation.

Action of Cobra-poison on Motor Nerves.

As the contraction of a muscle, on irritation of the motor nerve supplying it, is the index by which we judge of the irritability of the nerve itself, the paralyzing effect of cobra-poison upon muscle renders the exact determination of its action upon motor nerves much more difficult than in the case of such a poison as curare, which leaves the muscular irritability intact. For the failure of a muscle to contract on irritation of its motor nerve can be due only to paralysis of the motor nerve in the case of curare; but in poisoning by cobra-venom it may be due to enfeeblement of the muscles, as well as paralysis of the nerve. But if we find instances in which the muscles still retain their irritability almost unaltered, and respond readily to direct stimulation after they have ceased to contract on irritation of their motor nerve, we are justified in saying that the nerve is paralysed; and such is the case in Experiment XLI.

In Experiment XXV this action on the ends of motor nerves is all the more evident from the paralysis being most complete in the part where the poison was introduced. At this part, it was brought, in a concentrated state, into contact with the ends of the motor nerves, while the other parts of the body received it after dilution with the blood; and in them the paralysis was much less marked.

The paralysis of the hind legs, so often noticed in experiments, appears to be due, at least in considerable measure, to the local action of the poison on the ends of the motor nerves of the legs, as the injection or bite is often made on the flank or thigh.

The action of the poison on motor nerves is illustrated by the following experiments, performed by Bernard's method of ligaturing one leg of a frog before poisoning it. The poison is thus carried to every part of the body except the ligatured limb, the motions of which indicate the state of the nerve-centres after the other parts of the body have been paralysed.

Experiment XXXVI.

A ligature was placed round the right thigh of a young frog, excluding the sciatic nerve.

2.42. A drop of dark fluid cobra-poison (the first supply) was injected into the dorsal lymph-sac. Immediately after the injection the animal became restless.

3.0. It lies quietly with its eyes shut. It hardly moves when touched; but it struggles when laid upon its back.

3.8. It can still draw up the ligatured leg. The other one can be drawn up, but with a wriggling motion. When laid on its back the animal no longer resists.

3.9.30. It lies quite flat. There is trembling of the leg when either foot is touched; and when it is pinched, either leg can still be drawn up. On suddenly touching the poisoned leg, the frog gave a jerk with both. Respiratory movements have ceased. The exact time when they did so was not noticed.

3.17. The frog has become much lighter in colour, with the exception of the ligatured leg.

3.45. The eyes no longer shut when touched; they remain widely open. Dilute acetic acid of 1 per cent. produces no effect when applied to the sound leg; but when the leg is lifted up, so as to prevent friction against the table, it is drawn in towards the body.

4.9. On applying a strong interrupted current to the eye of the frog the unpoisoned leg jerks feebly, the poisoned one not at all.

4.13. On turning the frog on his back the non-poisoned leg moved.

4.20. Opened abdomen. The heart was beating, but only slowly. Irritated the lumbar nerves on the left side (those of poisoned leg) by an interrupted current. No contraction

occurred in the poisoned leg; but twitching took place in the non-poisoned one. Irritated lumbar nerves of right side. Tetanus occurred in the right (non-poisoned leg). No movement of the poisoned leg. Laid bare the muscles of both legs, and irritated them by a Faradic current directly applied. Those of the poisoned leg were paler than those of the other. The muscles of both legs contracted when irritated directly. Exposed the sciatic nerves of both sides and irritated them by an induced current. No contraction in the gastrocnemius of poisoned leg. Tetanus in the non-poisoned leg.

4.35. The heart is no longer contracting. Electrodes were placed in the medulla, and an interrupted current applied. Contractions occurred in the non-poisoned leg. No contractions in the poisoned one.

The movements which occurred in the non-poisoned leg when the lumbar nerves of the other side were irritated may have been due to reflex action through the spinal cord. If this were the case, it would indicate that the sensory fibres in the lumbar plexus were not paralysed, and that the reflex power of the cord was not quite destroyed; but the nerves were not very carefully isolated, and it is probable that the twitchings were due to direct irritation of the lumbar nerves of the right side by conducted currents, especially as irritation of the left sciatic nerve caused no movement in the right foot.

The continuance of movement in the ligatured leg, after it had ceased in other parts of the body, indicates that the ends of the motor nerves have been paralysed; and this is confirmed by the production of tetanus in the ligatured and absence of movement in the poisoned leg when their motor nerves are stimulated. The slightness of the movements in the ligatured leg when a strong interrupted current was applied to the eye, while the motor nerves of the limb still retained their irritability, indicates that paralysis of the reflex function of the cord had taken place. The motion of the leg on turning the frog on his back afterwards shows that the higher nervous centres, through which the opposition to the change of posture was manifested, retained their power longer than the cord.

Experiment XXXVII.

November 29th, 1872.—The sciatic nerve of the left leg of a frog was exposed; and a double ligature being passed under it round the limb, the whole of the tissues except the bone were then divided and removed between the ligatures. A fraction of a drop of cobra-poison, diluted with $\frac{1}{2}$ -per-cent. salt solution, was injected into the lymph-sac. After about two hours the animal seemed paralysed. On irritating either fore leg by electricity, or by acetic acid, slight movements occurred in the hind feet, and were fully stronger in the poisoned than the ligatured limb. Irritation of the poisoned hind foot also occasioned twitches both in it and the non-poisoned foot. Twitches did not invariably occur. No twitching of the fore paws was noticed on irritation of the hind feet. A ligature was then passed round the poisoned hind leg, and the tissues divided, as in the non-poisoned one, and the animal left a little longer. Irritations again applied had a similar result to the former, but the contractions in the non-poisoned limb were sometimes stronger than in the other. Irritation applied by a strong interrupted current to the spinal cord, by electrodes inserted in it, caused very faint twitches in both hind feet. Irritation of the lumbar nerves in the abdomen caused very faint twitches in the feet. Irritation of the exposed sciatic nerve of the non-poisoned limb by an interrupted current caused strong contractions. Similar irritation of the poisoned sciatic caused much weaker contractions. Direct irritation of the muscles by interrupting a constant current caused contractions of nearly equal strength in both.

The dose of poison in this experiment was small, and it was given in a much diluted form. The fact that an interrupted current applied to the sciatic nerve of the poisoned limb had a much slighter effect than the same current applied to the sciatic nerve of the non-poisoned limb, while the interruptions of a constant current by opening and shutting a key caused the poisoned and unpoisoned muscles to contract with apparently the same force, shows that a small dose of the poison causes a considerable amount of paralysis of the ends of motor nerves, while the muscles are but little affected.

Experiment XXXVIII.

May 14th.—The right leg of a frog was ligatured, with the exception of the sciatic nerve, and the animal poisoned by a rather small dose of dried cobra-poison dissolved in water, and injected into the dorsal lymph-sac at 11.45 A.M.

12.15. The animal paralysed. Acetic acid applied to the left arm caused movements in it; but no movements ensued when the acid was applied to the nose. When applied to both arms and one leg, it caused movements in the arms and the left leg, but none in the right leg.

12.33. Acetic acid applied to the left arm causes movement in it, but in no other part of the body.

12.51. Electrodes were placed in the spine and the cord irritated by a Faradic current. At 15 cm. distance of the secondary from the primary coil there is faint twitch in right arm. At 9, distinct twitch in both arms. At 0, distinct twitch in both arms, none in legs; sciatics exposed and irritated. At 50, right leg contracts distinctly. At 36, right leg becomes tetanised. At 16, left leg contracts very faintly indeed. At 8 left leg contracts slightly.

The muscles were then irritated by single induced shocks:—9.8 cm., right leg faint contraction; 9.8, left (poisoned) leg contraction is equally strong; 10.1, left (poisoned) leg contraction occurs. 10.1, right (ligatured one) does not contract.

In this experiment, the irritability of the poisoned muscle is greater than that of the other, the venom having done less injury to the muscular substance than the deprivation of blood by the ligature, and consequently the paralysing action of the poison on the ends of the motor nerves becomes very evident.

Experiment XXXIX.

May 12th, 1873.—A ligature was passed tightly round the right thigh of a large frog, the sciatic nerve being excluded.

12. Right leg ligatured.

12.12. Injected a considerable dose of a solution of dried cobra-poison in water into dorsal lymph-sac.

12.14. The frog has assumed a most peculiar position. The

left hind leg is drawn up, and the two fore legs are held over head with palms turned forwards.

12.20. Cornea sensible. Left leg is drawn up again if it be forcibly extended.

12.31. Cornea sensible. When the left hind foot is pressed it is drawn up very slowly with a wriggling motion. Pressure on the right foot causes no movement whatever.

12.40. Acetic acid applied to a forearm causes vigorous movement in it and also in left hind leg.

1. Acetic acid to right hind foot causes no movement. Applied to left hind foot it causes vigorous movements in both forearms and left hind leg.

1.12. A ligature was applied to the left thigh in a similar manner to that on the right, so as to cut off the circulation in the left leg also, and thus bring the two legs as much as possible under the same conditions. The general condition of the frog is much the same as before; but the reflex action produced by irritation of the cornea is slighter.

1.24. Acetic acid applied to right forearm. Slight movement occurs in *right* hind leg alone. When applied to left forearm it caused slight movement in that arm alone.

1.35. Acetic acid applied to both feet, both forearms, and to the nose caused no motion anywhere. Both sciatic nerves were now laid bare along a considerable portion of their course. It was found that, although the right sciatic had not been included in the ligature, it had been tightly constricted by the fascia at the place of ligature. Sciatic nerves irritated by an induced current.

Leg.	Distance of secondary from primary coil.	
Left.	0	No contraction of muscles of leg.
Right.	32.0	Distinct contraction. As this might possibly have been due to the left sciatic being injured by the ligature more than the right, both sciatics were exposed further, and irritated quite below the points of ligature and just above the knee.

Leg.	Distance of secondary from primary coil.	
Right.	37.5	Distinct contraction.
Left.	7.0	No distinct contraction. When the muscles were irritated by single induced shocks, applied to them directly, they contracted almost equally.
Single shock.	7.5	

In this experiment, the right sciatic nerve had been injured by the operation of ligaturing; and thus the effect of the poison on the other limb as compared with the right one was less manifest. Notwithstanding this it moved, and the other limbs did not, when the right arm was irritated. The difference between the irritability of the sciatic nerves when the muscles of the legs themselves were almost equally irritable, shows, in a marked manner, the influence of the poison on the motor nerves.

Experiment XL.

May 14th.—Frog ligatured round the middle, excluding lumbar nerves.

10.57. Ligature applied. A considerable quantity of blood was lost.

10.58. A considerable quantity of dried cobra-poison dissolved in water was injected into the dorsal lymph-sac. Immediately after being released the frog jumped about, but became quiet in a minute or so.

11.28. Made some voluntary movements.

11.45. Acetic acid to fore feet causes weak reflex movements in both fore feet; stronger in hind feet, especially in right.

11.55. Acetic acid to right forearm caused vigorous kicks of right hind leg. Acetic acid affected right leg in 10 seconds. No motion in any other part of body. Acetic acid to left forearm caused kicks in both hind legs, but much more vigorous in the right. Also movement of left forearm by itself, but weak.

12.5. Acetic acid to left fore leg caused wriggling motion, first in right hind leg and then in left fore leg in 16 seconds.

Applied to right forearm it caused a weak kick in right hind leg and wriggling in left hind leg, but no motion in any other part.

12.27. Acetic acid applied to forearm. No reflex action anywhere.

12.30. No reflex action anywhere on application of acetic acid.

12.30. Distance of coil 8. Electrodes in the spinal cord. Slight contractions in right hind and left fore legs, and also in the abdominal muscles, though very weak. It was now noticed that the cord with which the frog was attached to the board had been very tightly tied round the left forearm and left there. The circulation was stopped there, as the cord had not been removed.

The paralysing effect of the poison on the motor nerves was here shown by an involuntary experiment. On irritating the cord the ligatured leg responded as we had expected, but we were astonished to see movements in the left arm also. An examination of the limb at once showed the cause of the phenomenon. The cord attaching it to the board had been inadvertently drawn so tight as to obstruct the circulation, and thus prevented the access of the poison to the nerves.

Experiment XLI.

May 15th.—Right thigh of frog ligatured, with exception of the sciatic nerve.

1.2. Ligature applied.

1.4. A considerable dose of dried cobra-poison dissolved in water injected into dorsal lymph-sac.

2.26. Acetic acid applied to a limb causes no movement whatever in 60'.

Interrupted current. Distance 0, electrodes in spine; only weak twitch in muscles of forearms; no movement in hind leg.

2.30. Both sciatics exposed.

Right sciatic. Distance 50, distinct contraction of gastrocnemius.

Left sciatic. Distance 0, no contraction of gastrocnemius. Single shocks. Both gastrocnemii exposed and irritated directly.

Distance 9·5, very faint contraction in both tibial and gastrocnemic muscles. Apparently equal in both legs. Heart quite still and contracted.

On testing the irritability of several of the frogs used in these experiments on the ensuing day, the ligatured leg was found to contract on irritation of the sciatic nerve, or of the muscles directly. The muscles of the poisoned leg did not contract, either when irritated directly or through the nerves.

Experiment XLII.

May 20th, 1873.—In order to test the action of cobra-poison on the ends of the motor nerves, without disturbing the experiment by ligaturing one leg, two frogs were taken of as nearly as possible the same size. Both were very small; but No. 1 was somewhat larger and stronger than No. 2. The sciatic nerve was exposed in one thigh of each frog and placed on the hook electrodes used by Marey for his myograph. By means of a Pohl's commutator, with the cross pieces taken out, an interrupted current could be sent at will through either nerve. The distance of the secondary from the primary coil at which the first faint contraction took place in the muscles of either nerve was noted.

Time (about).	Distance of primary from secondary coil.		
	Frog 1.	Frog 2.	
1.25	17·7	22	
1.40	26·3	12·3	
1.46	26	18	Injected a solution of dried cobra-poison in water into dorsal lymph-sac of frog No. 1.
2.7	31·2	24	
2.27	31	18·5	
2.50	24	17·8	
3.10	17·5	19·2	Frog 1 moved the fore legs when the coil was at such a distance (19 ?) that no movement occurred in leg when nerve was irritated.

Time.	Distance of primary from secondary coil.		
	Frog 1.	Frog 2.	
3.30	12	17.5	
3.40	10.5	15.5	
4	10	33	
4.17	9	37	
4.30	11	18	At 37 voluntary movements occurred in legs of Frog 2.
4.50	8	37	
4.55	The brains of both frogs destroyed.
4.58	7.5	16.5	

May 21st.—The sciatics of the other legs were exposed and irritated.

...	0	11.5	Frog 1, no contraction. Frog 2, slight contraction. The irritability of the muscles was now tested by single induced shocks applied to them.
...	0	7.5	Frog 1, no contraction. Frog 2, slight contraction.

The disturbing effects occasioned in the other experiments by the necessity of comparing a limb acted on by the poison, but retaining its blood-supply, with one in which the circulation had been arrested, is here got rid of by employing two frogs of as nearly as possible the same size. The paralysis of nerves caused by the poison is evident.

Experiment XLIII.

December 4th.—Right leg ligatured, with the exception of the sciatic nerve; a small quantity of alcoholic extract of cobra-poison dissolved in water injected into the dorsal lymph-sac.

Noon. Injection made.

1.30. The frog lies quite helpless. A spark of electricity applied to the side causes reflex contraction of both legs. When the poisoned leg is drawn out, the frog draws it up again with a

wriggling motion. The poisoned leg at once reacts when the toes are pinched; the ligatured one does not.

When the sides of the frog are irritated by an electric spark, all the legs, except the ligatured one, give a twitch.

3.50. On exposing the lumbar nerves in the abdominal cavity and irritating them by an induced current, the poisoned leg contracted, the ligatured one did not.

The effect of the alcoholic extract in causing paralysis is shown by this experiment; but the insensibility of the ligatured leg, which was in all probability due to an injury of the sciatic nerve by the ligature, renders it difficult to say how much of the paralysis was due to the cord, and how much to the nerves. That the nerves were affected, however, seems clear from the fact that the muscles no longer reacted to voluntary stimuli, but did so when an extraordinary stimulus was occasioned by pinching.

Experiment XLIV.

August 27th.—A small dog was chloroformed, and both vagi were exposed.

12.35 P.M. About two grains of dried cobra-poison were injected into the peritoneal cavity.

12.42. Water was thrown over the animal to revive him more completely from the chloroform. Bowels acted. He is very unsteady on his legs. Looks drunk.

12.44. Dog vomits freely.

12.45. Both vagi divided. The vomiting ceased, the breathing became very slow, and the head was thrown up with the nose in the air.

12.53. Has become very quiet. Falls down on his side. The vomiting has not recurred.

12.55. Dead. Artificial respiration commenced.

1.12. On laying bare the skull and trephining, slight reflex movements occurred in the limbs.

1.17. Micturated. On irritating the exposed cerebrum by a Faradic current no contractions occurred in the limbs.

1.47. The spinal cord was exposed and irritated by a Faradic current. No contractions occurred in any of the muscles, except those to which the current was conducted, even when the

strongest was employed. On exposing the sciatic nerves and dividing one of them, and applying a Faradic current, no effect could be perceived when the electrodes were applied to either the central or the distal end of the nerve. The motor nerves were thus seen to be paralysed.

The heart continued to beat vigorously all the time. On laying open the abdominal cavity, the intestines and peritoneum were found in a state of intense congestion. Electrodes applied to the lumbar nerves caused no contraction anywhere.

Thorax opened. The heart was beating vigorously. The lungs were normal. A Faradic current applied to the phrenic nerve caused no contraction of the diaphragm; but when applied to that muscle directly, it caused vigorous contractions.

The left vagus was divided and its peripheral end stimulated by a Faradic current. The pulsations of the heart were at once arrested, but again commenced; and no further irritation of the vagi had any effect on the heart.

2.2 P.M. Stomach removed. Its coats were intensely congested, as though some irritant had been swallowed. It contained much bile. The blood was florid, and formed a firm coagulum.

This experiment clearly shows that cobra-poison produces paralysis of the motor nerves in warm as well as in cold-blooded animals, the sciatics being so completely paralysed that they did not respond to the strongest irritation, although respiration was efficiently kept up and the circulation continued unimpaired. In almost all the other experiments, when the nerve was irritated immediately after death, contractions were produced; but the same is the case when the animal is poisoned with curare, and the contractions are due to the poison not having had sufficient time to exert its full action.

The complete cessation of vomiting after division of the vagi seems to indicate that the poison produces emesis by acting on the peripheral terminations of the vagi, and not on any nerve centre.

Action of Cobra-poison on Secreting Nerves.

A notable symptom of cobra-poison in dogs is great salivation; and this might be supposed at first sight to indicate that the poison acted as an irritant to the secreting nerves of

the salivary gland. Nausea and vomiting being also present, however, it is by no means improbable that the salivation is due to the poison stimulating the secreting nerves of the salivary glands not directly, but by reflex action, through the gastric branches of the vagus. Unfortunately we are unable to say in which of these ways salivation is induced, as we have not noted whether it occurred after division of the vagus or not. So far as memory serves us, we are inclined to think that it was much less in these cases; but on this point we cannot be at all positive.

Whether cobra-poison has any stimulating action on secreting nerves at first or not, it seems finally to paralyse them, or at least greatly to diminish their power.

This is evident from the following experiment.

Experiment XLV.

A dog was etherised and the chorda tympani exposed after its separation from the lingual nerve. A cannula was then placed in the duct of the submaxillary gland. On irritating the chorda by a weak Faradic current, applied at intervals, saliva flowed freely. Some dried cobra-poison dissolved in water was then injected into a vein in the leg. Shortly afterwards the saliva began to flow much less freely than before; and although the current was increased in strength, only a small quantity could be obtained.

Action on Sensory Nerves.

The sensory nerves seem to be little, if at all, affected by cobra-poison. As appears from Experiment XXXVI, they retain their power after the motor nerves are paralysed; and Experiment XLVI shows the comparative effect of the poison and of want of blood both on the sensory and motor nerves. The former were so little affected by the poison that they caused a ready response when those which had been deprived of blood had nearly ceased to act. The motor nerves of the poisoned limb, on the contrary, were quickly paralysed, while those of the ligatured one, although doubtless weakened by the loss of their vascular supply, long retained their irritability. In Experiment LX the optic nerve and the aural and buccal

branches of the fifth nerve retained their irritability after the cord had become nearly paralysed ; and, in several experiments, reflex actions could be induced by irritation of the cornea after voluntary motion and respiration had ceased.

Experiment XLVI.

The right leg of a frog was ligatured, excluding the sciatic nerve, and a concentrated solution of dried cobra-poison injected into the dorsal lymph-sac at 2.3 P.M.

2.5. Already affected. Much less active. Lies very quiet.

2.34. Paralysed. On touching his body he moves the right, but not the left leg.

When acetic acid is applied to the hand, he straightens both the arms and contracts the right, but not the left leg.

Acetic acid applied to left hind leg causes him to straighten both arms and draw up the right leg ; but there is only feeble movement in the left leg.

When acetic acid is applied to the right foot, the foot itself is drawn up ; but there are no movements of any other part of the body.

When acetic acid is applied to left hand, the left arm is powerfully straightened, and there are strong contractions of right hind leg, but none in the left, and little movement in any other part of the body.

Acetic acid applied to left foot causes powerful extension of both legs.

Acetic acid applied to the right foot has no effect. Electrodes were inserted in the spine and the cord irritated by a Faradic current. Distance of the secondary from the primary coil 18 cm. There was movement of left hand.

At 16 cm. movement of left hand and right leg.

At 12 cm. also faint movement of left leg.

At 15 cm. the interrupted current was kept up for some time, and the muscular twitchings were more powerful in the left gastrocnemius than in the right one.

On applying the electrodes to the lumbar nerves, coil at 48 c., the right leg contracts.

Coil at 42 cm. the left leg only twitches.

Action on the Spinal Cord.

The spinal cord has the threefold function of a conductor of sensory impressions, a conductor of motor impressions, and a reflex centre; and in examining into the nature of the action of cobra-poison upon it, we must consider the manner in which each of these functions is affected.

Cobra-poison, as has already been intimated, has a powerful paralyzing action upon the reflex function of the cord; and this is exemplified in Experiment XLVII, etc.

As a conductor of sensory impressions, the cord is able to transmit two kinds, viz., tactile and painful, and these have been stated to pass through different parts of the cord, the former being conveyed by the posterior and lateral white columns, and the latter by the grey matter.

From Experiments XXXVI and LX it would appear that the power to convey tactile impressions is retained, both in warm-blooded animals and frogs, after the transmission of painful impressions has almost, or entirely, ceased. Thus, in Experiment XXXVI the frog's leg moved when the animal was laid upon its back, although an extremely painful stimulus, the application of sparks from a coil to the eye, had caused in it only the feeblest movement. In Experiment LX no response was elicited by striking, pinching, or pricking the paws of the animal, but when the ear was tickled the cat shook its head, or moved its paw to ward off the irritant.

From these cases we think we are justified in concluding that the grey matter of the spinal cord, through which painful impressions are transmitted, is paralysed by cobra-poison; but the white sensory columns are little, if at all, affected. The power of the cord to conduct motor impressions from the encephalic ganglia appears to be little, if at all, affected, until the apparent death of the animal; for in Experiment LX we find that, very shortly before respiration ceased, and when ordinary reflex action from the cord was nearly gone, purposive or voluntary movements were still made. The absence of movements in Experiment L, when the cord was irritated by a needle, as well as the rapid loss of its power to produce movement in the limbs when irritated by a Faradic current, is, we

think, to be attributed to paralysis of its function as an originator, and not as a conductor, of motor impressions.

Experiment XLVII.

May 19th.—The lumbar nerves of a frog were exposed and a ligature tied round the body, excluding these nerves.

12 (noon). Some dried cobra-poison dissolved in water was injected into the dorsal lymph-sac.

1.45. The frog is partially paralysed; mouth gaping; reflex action is still marked in all the limbs, but more in the legs than in the arms.

The heart was exposed when the ligature was applied; it still beats, but feebly and slowly.

1.50. Acetic acid causes reflex movements when applied to either the hind or fore feet.

1.54. Applied to the nose, acetic acid causes movements in all the extremities, and especially in the arms.

1.56. Applied to the right hind foot it causes movements of the arms and of the jaw, which otherwise gapes.

2.2. Applied to the left hind foot it causes no reflex action.

2.14. Heart beating very feebly, 18 pulsations per minute. Reflex movements still occur in all the limbs, and rather more in the legs than in the arms.

2.30. Acetic acid produces no reflex action anywhere. The heart has almost ceased to beat, and only contracts faintly at long intervals.

2.34. All reflex action has ceased.

2.45. Electrodes placed in the spine and the cord irritated by a Faradic current. At 15.5 cm. distance, faint contractions in both arms. At 0 cm. distance, no contraction in legs. Sciatic nerves exposed and irritated. 32.5, slight contraction in left leg; slight contraction in right leg.

2.48. Heart is still acting feebly and slowly; brachial nerves exposed and irritated.

At 46.5 cm., contractions in both arms.

2.49. The heart has now ceased to beat, except a faint pulsation in the auricles.

Muscles of arms and legs exposed and irritated by single induced shocks. 6.5 cm., muscles of both arms contract; muscles of both legs contract, but somewhat more strongly.

In this experiment there is no evidence of paralysis either of the nerves or muscles; death appears due to paralysis of the spinal cord. This is caused by the action of the poison; for the circulation still continued, though feebly, after all reflex action had ceased.

Experiment XLVIII.

A ligature was passed under the right sciatic nerve of a frog and tightly tied round the limb, so as to constrict the whole of the thigh, with the exception of the nerve, and completely arrest the circulation.

At 1.8 half a drop of cobra-poison (first supply), diluted with $\frac{1}{2}$ c.c. of water, was injected into the dorsal lymph-sac.

1.12. The animal is sluggish.

1.15. Crawls about but sluggishly, and keeps the unligatured limb drawn up close to the body.

1.20. The frog is more sluggish.

1.23. The hind limbs seem paralysed; the fore limbs still move, but much less than before.

1.30. Frog almost motionless. Contractions of the fore limbs still occur; but they no longer respond when pinched.

1.57. There is a faint motion in the limbs.

2.18. Frog is dead. Much ecchymosed.

On irritating the lumbar nerves in the abdominal cavity by an induced current, the poisoned leg contracted rather more than the non-poisoned leg.

On irritating the sciatic nerves in the thigh, below the level of the ligature, the contractions of the poisoned leg were much less vigorous than those of the non-poisoned leg.

Electrodes were then placed in the spinal cord, and the cord irritated by an induced current.

2.34. When irritation is applied in this way the fore limbs contract, but not the hind limbs.

When the cord is irritated lower down, the non-poisoned leg responds to the irritation, but the poisoned leg does not.

The muscles of the ligatured leg respond to the direct application of electricity more freely than the other muscles.

In this experiment the poison employed had not been coagulated or dried, and the dose was somewhat small. The failure of reflex action while voluntary motions still continued in the nerves shows that the cord in this instance became paralysed before the motor nerves. It is, indeed, difficult to say whether the motor nerves were paralysed in this case or not, as the muscles themselves were distinctly weakened.

Experiment XLIX.

December 1st, 1872.—The right leg of a frog was ligatured, excluding the sciatic nerve, which was kept covered by a flap of skin to prevent its becoming dry. A ligature was also put round the left leg in a similar manner, but not tightened.

2 P.M. Cobra-poison injected into the abdominal vein.

The effect not being marked, the aorta was exposed.

2.27. Some poison injected into the aorta. It seemed to take effect at once; all motion ceased immediately.

2.30. The ligature was then tightened round the left leg.

2.48. The frog has since moved, but all motion has now ceased.

2.52. Even when irritated by acetic acid there is no movement. The heart is still contracting.

No reflex action occurs when a strong interrupted current is applied to the nose or limbs.

Lumbar nerves exposed and irritated.

Right. Distinct contraction of thigh. Coil at 58.5.

Left. " " " " 58.5.

Right. Distinct contraction of whole leg. Coil 50.

Left. " " " " 50.

Sciatics exposed and irritated.

Right. Contraction. Coil 77.

Left. " " 52.

3.28. Right. Contraction. Coil 50.

Left. " " 43.

The poisoned leg seems to be losing its irritability more quickly than the other. Irritability of spinal cord gone.

3.35. The left still contracts, with the coil at 35. The other, when irritated by a current of the same strength, contracts more strongly.

The loss of power occasioned by the cessation of the circulation in the ligatured limb (which is used as a standard with which to compare the other) was diminished in this experiment by injecting the poison directly into the circulation, so as to enable it to reach the motor nerve-ends at once. As soon as it had taken effect, the poisoned leg was likewise deprived of its circulation, so as to bring the two limbs as nearly as possible into the same conditions. The cause of death in this experiment was paralysis of the cord, all reflex action having been almost immediately abolished by the large dose of the poison injected into the circulation, though the heart continued to beat. The motor nerves were not at first affected, but after a little while paralysis appeared in the poisoned limb. This experiment is especially interesting in reference to the cause of death when a considerable quantity of poison enters the arterial system at once. In warm-blooded animals, as is shown by Experiment LXVIII, the heart is arrested in many instances, and death thus occasioned; but when this is not the case, the appearance of paralysis is probably due to affection of the nerve-centres.

Experiment L.

September 13th.—A ligature was placed round the middle of a frog, excluding the lumbar nerves.

3 P.M. Some dried cobra-poison dissolved in water was injected into the dorsal lymph-sac. Immediately after the injection the animal could move all its limbs quite well.

3.3. Restless; moves all its limbs.

3.17. Can still move vigorously.

3.21. Can kick vigorously with its legs, especially the right. When it moves it seems to overreach itself and turns over, apparently from the hind limbs remaining unaffected and the arms becoming partially paralysed.

3.40. Still moves voluntarily.

3.52. No reflex motion can be produced by touching any of the extremities with acetic acid.

A minute or two afterwards a slight twitch was noticed in one arm, to which acetic acid had been applied, but whether this was greatly delayed reflex action caused by the acid, or whether it was due to something else, is uncertain. A needle was now run down the spinal cord. It produced no effect.

The legs contracted readily when the lumbar nerves were irritated.

The absence of motion in the legs when the cord was irritated by a needle run down the spinal canal shows that the power of the cord to originate motor impulses had been destroyed, as it would usually have caused violent contractions in the extremities. These, having been protected from the action of the poison either on muscle or nerve, would respond readily, as, indeed, they did, to voluntary motor impulses shortly before the death of the animal.

Experiment LI.

May 12th, 1873.—The sacrum of a frog was removed, and a ligature passed round the body, excluding the lumbar nerves. There was a good deal of bleeding.

12.30. Ligature tied.

12.33. A good dose of dried cobra-poison dissolved in water was introduced into dorsal lymph-sac. Immediately afterwards the frog sprang about once or twice.

1.27. Cornea insensible. On pinching the finger of either hand it kicks out vigorously with the right hind leg. On squeezing the toes of right hind foot it kicks out vigorously with it. On squeezing toes of the left hind foot there is no movement whatever. On placing acetic acid on either forearm the frog kicks out strongly with the right hind leg.

2. Interrupted current, distance 7. Acetic acid applied all over the frog no longer causes any movement whatever. Electrodes placed in spinal cord just below occiput. Cord irritated by an interrupted current. Right leg kicks vigorously. No motion in any other part of the body.

Experiment LII.

May 15th.—Frog ligatured round the middle, the lumbar nerves excepted. A moderate amount of bleeding.

12.40. Ligature applied.

12.52. Frog springs actively about when touched. A considerable dose of dried cobra-poison dissolved in water injected into the dorsal lymph-sac.

1.15. Cornea insensible. When either hind foot is pinched, it is drawn up with a wriggling motion when the frog is lying on the table. When the frog is suspended the foot is drawn up at once.

1.20. On applying acetic acid to both fore limbs and nose, the hind legs were vigorously drawn up to the body, but only after a long interval.

1.26. Strong acetic acid applied to both fore limbs and nose. Movements in all four limbs after 8 seconds.

1.36. Weaker acid applied to both fore limbs. Movements in all the limbs in 37 seconds.

2.20. Applied to both fore legs. Movements in both fore limbs in 4 seconds. Worse in hind legs.

2.53. Applied to all the limbs and the nose. No motion anywhere. Divided medulla.

2.58. No reflex at all in 200 seconds after application of acid to all the limbs and the body.

Abdomen opened. Lumbar nerves irritated just below exit from spine.

Leg.	Distance of primary from secondary coil in centims.	
	6.3	Left gastrocnemius contracts very slightly; right not.
	0	Left gastrocnemius contracts slightly; right not. Both sciatics exposed and irritated in the thigh some distance below ligature.
Left	57	Tetanus of leg.
Right	58	Tetanus. Nerve rather more firmly applied to electrodes. Viscera removed and brachial nerves irritated.
Right	47	Contraction of foot.
Left	45	Contraction of foot.

In this experiment the loss of reflex motion was gradual. It is shown to be due to paralysis of the cord, and not to excitation of Setschenow's inhibitory centres, by the division of the medulla having no power to increase the reflex action.

The fact that irritation of the lumbar nerves hardly caused any contraction in the legs, while irritation of the sciatics below the ligature caused them to contract readily, indicates either that the nerves had been injured by the ligature, or that the part of them lying between the spine and the ligature had been paralysed by the poison. The latter is possible; but as the frog moved its arms and not its legs before death, the former is more probable.

Several years ago Setschenow showed that the optic lobes in the frog possess an inhibitory power over the reflex acts originating in the spinal cord. Irritation of the optic lobes greatly lengthens the time required for the performance of any reflex act, and thus produces an effect apparently similar to that of diminished excitability, or paralysis, of the spinal cord. A diminution in reflex action may therefore be due to two very different causes:—(1) Lessened excitability of the cord, and (2) excitement of Setschenow's inhibitory centres. These can, however, be readily distinguished from one another by dividing the cord just below the medulla. It is thus separated from the inhibitory centres; and if the diminution in reflex action is due to excitement in them it will disappear, but will be permanent if it is caused by paralysis of the cord. The following experiment, performed by Türek's method, shows that in cobra-poisoning the diminution of reflex action is due to the latter of these causes.

Experiment LIII.

May 19th, 1873.—The right leg of a frog ligatured, excluding the sciatic nerve.

3.5. A full dose of dried cobra-poison dissolved in water injected into the dorsal lymph-sac.

3.54. The animal appears dead. Both hind legs dipped into dilute acetic acid. Right arm twitched.

3.57. Reflex action in both arms. None in the legs when the left leg is dipped in the acid.

4. No reflex action from ligatured leg.

4.2. No reflex action from left leg in 60 seconds when it is dipped in the acid.

4.10. No reflex action from either leg in 250 seconds.

The medulla was now divided in order to separate the cord from Setschenow's inhibitory centres.

4.35. No reflex action can be observed.

As the operation of dividing the cord somewhat lessens the excitability, in the following experiment the division was performed on the previous day, so that its effects should have passed off before the poison was injected.

The columns headed "left" and "right" indicate the number of seconds which elapsed before the corresponding leg was drawn out of the acid.

Experiment LIV.

May 15th.—About 3 P.M. divided the medulla of the frog.

May 16th.—Suspended the frog by a hook in its jaw.

Time.	Left.	Right.	
11.17	8	8	When touched the frog draws up its legs, and makes wiping movements on its flanks.
11.44	5	6	
11.59	4	5	
12.6	3	7	
12.10	5	3	
12.25			
12.30	8	10	The point of an aneurism needle was drawn across the spine so as to destroy any remnant of medulla. The frog at once passed into a state of opisthotonos, but in a few minutes this passed off.
12.40	12	9	
12.48	12	9	
12.55	10	8	
12.58	10	5	
1	8	5	

Time.	Left.	Right.	
1.2	Injected a drop of concentrated solution of dried cobra-poison under skin of back.
1.5	It draws up legs and wipes back once or twice.
1.9	11	10	
1.16	10	10	
1.18	Another drop.
2.35	300	300	No reflex action in either foot. The heart could not be seen beating till the frog was opened; then it was found beating slowly and languidly, 24 in a minute.
2.45	Half a drop of liquor atropiæ placed on heart. Immediately afterwards its pulsations became more forcible, but were still 24.

Experiment LV.

May 15th.—Divided the medulla of a frog about 3 P.M.

May 16th.—Suspended it by hook through the jaws.

1.3	6	3	
1.6	5	5	
1.11	6	6	
1.16	6	12	
1.18	5	6	
1.19	One drop of slightly diluted, but still concentrated solution of cobra-poison injected under the skin of the back.
2.23	10	14	The foot was twitched up in the acid at these times, but the leg was not drawn up.
3.25	150	150	No reflex action. Strong acetic acid causes none. Thorax opened. Heart quite still.

These experiments show that the time required for the performance of a reflex act went on increasing, or, in other words,

the excitability of the cord went on diminishing, after the injection of the poison; and all communication with the inhibitory centres having been previously cut off by dividing the medulla, this effect could only be due to the action of the poison on the cord.

Experiment LVI.

At 1.16. Half a drop of cobra-poison was injected into the peritoneal cavity of a guinea-pig.

1.17. The animal is restless and twitching; runs about.

1.18. Micturates.

1.24. It is getting weak and sluggish. The hind quarters have assumed a crouching posture. It moves when roused.

1.26. It looks drowsy, is disinclined to move, and is jerking. The hind legs are almost paralysed. When they are retracted it draws them up with difficulty.

1.27. Has defecated. Is convulsed generally, but the convulsions are more marked in the hind quarters.

1.32. Convulsions continue. They are not increased or excited by external stimuli. Cornea insensible.

1.34. Mouth only twitches. Heart acting vigorously.

1.35. The animal is quite dead.

1.36. The spinal cord irritated by an induced current through electrodes inserted in the vertebral column. The irritability of the cord seems perfect. (It was judged of by the contractions of the hind limbs.)

1.40. The heart continues to beat. Thorax laid open. The vagi isolated and one of them irritated. The cardiac action seems to be increased by the irritation of the vagus. The auricles contract very rapidly, the ventricles not so rapidly. The cord is still irritable.

1.50. The irritability of the spinal cord as affecting the lower extremities is almost gone; as affecting the upper limbs it is still retained. Heart still contracts vigorously.

1.54. The lower limbs are no longer affected by electricity applied to the spinal cord. The upper limbs are affected.

1.56. The spinal cord is still slightly irritable. The heart is acting freely.

2. Cord still slightly irritable. Heart acts briskly.

2.2. Heart acts as vigorously as ever. Artificial respiration was tried.

2.15. Artificial respiration has been kept up, but has been of no service. The irritability of the cord is much diminished, though not quite extinct. The strongest current causes a barely perceptible motion. The heart is still acting. There are spots of ecchymosis all over the intestines.

2.40. The irritability of the cord is quite gone. The heart is still acting. The blood collected from the large vessels coagulated firmly.

Experiment LVII.

August 30th.—A cannula was placed in the trachea of a cat, and $1\frac{1}{2}$ decigramme of dried cobra-poison was weighed out and dissolved in a small quantity (about 2 c.c.) of distilled water. The solution was clear and glairy, hanging in threads from the stirring-rod.

2.40. Injected about two-thirds of this solution under the skin of the right hip.

2.50. Respiration is quicker. The cat lies down and does not like to rise. When raised it walks toward a dark corner, dragging the right leg.

2.58. Shivering of right leg and partially of body. No other symptom than paralysis of right leg being noticed, a further injection was made.

4.26. The remainder of the solution injected in the same place. This also seemed to produce little effect.

5.10. Injected 0.02 grain dissolved in a little water, as the cat did not seem about to die.

6.2. Injected $1\frac{1}{2}$ c.c. of a 2-per-cent. solution of cobra-poison in distilled water, partly into a vein in the back of the left hind leg, partly into the peritoneum. The left hind leg seems partially paralysed. The respiration has a peculiar character, the diaphragm seeming to relax with a jerk. The respiratory movements are very deep. Peristaltic action of bowels.

6.20. The fore legs are now becoming paralysed.

6.25. Respiration quick. Entirely diaphragmatic. Cornea quite sensitive. The animal opens its mouth when the tail is pinched, but not when the feet are pinched.

6.37. Sensibility of the cornea seems nearly gone. When the inside of the ear is tickled the animal shakes its head.

6.43. Although respiratory movements still continued, artificial respiration was begun. The animal was laid in an apparatus which kept it warm.

6.45. The cat tries in vain to vomit. The cornea is almost insensible.

About 8.30 the heart-beats ceased. The body of the animal was examined next day at noon. *Rigor mortis* well marked. The body of the animal had a strong odour of decomposition. The lungs were congested, the right side of the heart gorged, the left empty and firmly contracted. The pericardium contained a quantity of dark-red serum. A considerable quantity of dark-red serum was contained in the abdominal cavity. Inside of stomach quite normal. The bladder was firmly contracted and quite empty. Where the injection had been made, the muscles were infiltrated with blood, soft, and decomposed. Those of the left thigh were normal.

Experiment LVIII.

July 14th, 1873.—Some dried cobra-poison dissolved in water was injected into the peritoneum of a cat at 2.15 P.M.

2.20. Vomits.

2.30. Vomits again. The animal can walk perfectly, but it prefers to lie on its side.

2.40. Can walk, but seems slightly giddy.

2.45. Vomiting and defecation.

3.12. Sensibility of the cornea nearly gone. When the ear is irritated the cat shakes its head. When the eye is touched the eyelids do not move; but when the point of a pair of forceps is pressed into it, the fore foot is raised to push the forceps away.

3.20. The animal suddenly got up, walked a few steps, and then fell.

3.22. It seems as if it wanted to vomit, but is too comatose. When the ear is tickled it shakes its head.

3.26. There is distinct reflex action on irritation of the hind feet, but not when the fore paws are pinched.

3.32. Breathing is getting deep and slow, and the head is extended at each inspiration. There is still motion of the head when the ears or mouth are tickled. A minute or two ago it got up, stood for a second or two, and then fell. Respiration gradually ceased. A cannula was placed in the trachea, and artificial respiration kept up. The heart ceased to beat very shortly after. Electrodes were placed in the cord opposite the seventh and twelfth dorsal vertebra. A Faradic current passed through them caused contractions in the adjoining muscles of the back, but none elsewhere. The left sciatic was exposed and irritated. The limb contracted. About an hour afterwards curious and somewhat rhythmical movements took place in the *right* foot. The sciatic had not been exposed in the right leg.

Experiment LIX.

July 25th.—At 3.34 a little cobra-poison was injected into the peritoneum of a guinea-pig. Immediately afterwards the animal became restless and uneasy.

3.38. The animal is quiet. Occasional lifting of head. The fore legs are spreading out laterally. When made to walk it staggers, and has difficulty in maintaining its balance. It rises up and runs when any sound is made. Respirations 68 per minute.

3.44. The left ear is drooping.

3.58. Passed milky urine.

4.4. Convulsive motions occur, but the animal can still run. Almost immediately after, when laid on its side, it could not get up.

4.7. The cornea is now insensible. A cannula placed in the trachea and artificial respiration commenced.

4.15. A needle placed in heart. Pulsations quick. The artificial respiration was discontinued. The pulsations became quicker.

In this experiment the paralysis began in the fore legs. There was distinct loss of co-ordination; but the animal could run up to the last, although it could not walk. This indicates that the higher co-ordinating centre (probably the cerebellum)

was paralysed before the lower ones, just as in the case of a man who is drunk.

Experiment LX.

August 29th, 1873.—A cannula was placed in the trachea of a cat about 5.30 P.M.

5.35. One decigram of dried cobra-poison, dissolved in 2 c.c. of water, was injected into the peritoneal cavity.

5.39. The animal lies on its side breathing very rapidly and wagging its tail. Rises, sits with head erect and mouth widely open.

5.45. The respiratory movements are very rapid and shallow, with occasional deep ones. The animal sits up. Respirations 240 per minute. Pulse 148 per minute.

6.3. The animal was lying down and occasionally rising. Is now lying down. The respiratory movements have an extraordinary vermicular character. Dr. Sanderson ascertained by palpation that this is due to the diaphragm contracting before the thoracic walls expand.

6.7. The respirations are feeble, with occasional deep ones. The cat walks quite well. The bowels act.

6.20. Bowels act again. Tries to vomit several times.

6.37. The cat lay on its side, and stretched itself once or twice in a sort of convulsive manner.

6.41. Lies quietly. When the cornea is touched or poked with a pointed instrument, or when the finger is rubbed over it, the eyelids do not close, nor does the animal give any sign of feeling. When the hind legs are struck, it moves its fore legs very faintly. Respiration is quite regular and apparently normal. The end of the tail gently moves from side to side. When the inside of the ear is tickled the animal shakes its head. It took a deep breath, and moved its head voluntarily. The pupil is much contracted. When the arms are irritated by a sharp stick the animal draws its body slightly together. A minute or two afterwards it moved its tail from side to side several times voluntarily. The animal was lying on its side. Lifted it up and laid it on its belly with its feet under it. It rose up and walked several steps.

6.45. The cat again rises and walks, but staggeringly. It

then falls and lies on its side. The hind legs seem to be weaker than the fore legs.

6.52. Animal lying on its side. When a bright light is brought before its eyes it draws back its head. The cornea is quite insensible. When the paws are irritated by striking, pinching, or pricking there is no response. When the inside of the ear, nose, or mouth is tickled, the cat shakes its head, and sometimes moves its paw to put the irritant away.

7.5. On touching the eyes it sometimes draws back its head, but there is not the slightest motion of the eyelids. It voluntarily moved its paws and head as if to rise, and then sank back as if asleep, and lay still on its side.

7.6. Laid it on its belly. It rose and walked a step or two towards a darker corner and then fell. Immediately afterwards the muscles of the neck gave a sort of shudder. After movement the respiration becomes much quicker, and then rapidly becomes slow. After lying a minute or so its respirations are 27 per minute.

7.25. Moves its paws and tries to get up voluntarily, but cannot do so. Irritated paws and ear by sparks from a Du-Bois coil. No reaction. On irritating the inside of the thigh in a similar manner, it stretched out its fore legs, protruded its claws, and seemed to be trying to grasp me.

7.33. The respiration ceased without convulsions. The cannula in the trachea was immediately connected with an apparatus for artificial respiration, and this was kept up. While some adjustment was being made on the apparatus the animal was observed, and its heart was found to have ceased to pulsate about five or ten minutes after artificial respiration had been begun.

On opening the thorax the lungs were found somewhat congested. The right side of the heart was moderately filled. The left ventricle was quite empty and firmly contracted. The surface of the stomach and intestine was much congested. The interior of the stomach was not congested.

In this experiment, respiration continued for two hours after the injection of the poison. The most remarkable points as regards respiration are its great acceleration, with occasional

deep breaths at first, its vermicular character about the middle of the experiment, and its regularity towards the end. Reflex action seemed entirely abolished, and sensation very much impaired; the mental faculties seemed sluggish; but voluntary power was retained, and the movements of the animal were not indefinite but distinctly purposive.

The motor nerves and muscles were evidently not paralysed; but the grey matter of the cord seemed to have lost its power of inducing reflex actions or of conveying painful impressions. Tactile impressions, such as laying the animal on its belly, still caused reaction. The movements thus induced, as well as those caused by irritating the ears, etc., may all be reasonably ascribed to the action of the brain.

Closure of the eyelids would seem to be a purely reflex act, in which the brain is altogether unconcerned.

Experiment LXI.

October 29th, 1872.—To ascertain if a mixture of strychnia and woorara produced the same effect as cobra-poison, a guinea-pig weighing 1 lb. was experimented upon.

2.36.30. 1 c.c. of a solution of woorara (1 in 1000) was injected under the skin of the side.

2.54. As the first dose seemed to produce little effect, another cubic centimetre was injected in the same way as before.

2.56. A drop or two of *Liquor Strychniæ* (4 grains to 1 fluid ounce) was injected into the side.

2.57. Twitchings motions of the body begin. (They were not exactly like those produced by cobra-poison.)

2.58. The animal has fallen over on its side and is paralysed, but the twitching continues.

3.2. The animal is dead. No convulsions. On opening the animal the heart was found contracting vigorously.

Electrodes were inserted in the spinal column and the cord irritated by an induced current. The limbs contracted when irritation was applied to the cord. The sciatic nerve was exposed and irritated by an induced current. The muscles of the limb contracted.

3.9. Heart still contracts feebly. The lungs are congested.

Action of Cobra-poison on the Stomach and Intestines.

One of the most noticeable symptoms of cobra-poisoning in dogs is vomiting of a violent, repeated, and most distressing kind; and it is also present in cats and guinea-pigs, though to a less degree. Its occurrence in guinea-pigs is somewhat extraordinary, as these animals very rarely vomit, and, according to Schiff, only do so after their vagi have been divided; whereas other animals which vomit under ordinary circumstances are then unable to vomit at all. The nervous centre by which the movements of vomiting are originated is closely connected with the respiratory centre, and it may be set in action by stimuli conveyed to it by the branches of the vagus distributed to the stomach and other intestinal organs, and also through the pharyngeal branches, either of the vagus or, possibly, of the glosso-pharyngeal nerve. The brain can also excite it; but the vomiting it produces is not usually prolonged. The vomiting which occurs in cobra-poisoning is, in all probability, due, in part, to irritation of the gastric or abdominal branches of the vagus—but not altogether; for the attempts to vomit continued in Experiment LXV after that nerve had been divided in the neck; and the failure to bring anything up is to be attributed to the cardiac aperture of the stomach failing to dilate at the proper time—a result which usually occurs after section of the vagus.

In Experiment XLIV there was intense congestion of the mucous membrane of the stomach; but this does not occur in all cases. It could hardly be due to the division of the vagi in this instance, as that operation is usually followed by paleness of the membrane. The intestinal movements are quickened by the poison, since there is purging, which cannot be due to increased intestinal secretion, as the stools consist chiefly of mucus. The movements continue for a considerable time after death.

Effect of Cobra-poison upon Respiration.

The action of cobra-poison upon respiration is perhaps the most important of those which it exerts upon the organism; for it is through this action that death is generally caused.

The respiratory movements, besides being frequently altered in form, are generally quickened after the introduction of the poison; then the number sinks to the normal or even below it; they become weaker and finally cease altogether. The blood, being no longer aerated, becomes more and more venous, and, by irritating either the respiratory centre itself or some nervous centre closely associated with it, occasions general convulsions. These disappear whenever artificial respiration is begun and the blood again aerated; while they reappear when the respiration is discontinued and the blood regains its venous character. This condition is to be observed in Experiment LXII. The dependence of the convulsions on the venosity of the blood is well shown by Experiment VIII of our former communication, where the condition of the blood was indicated by the colour of the fowl's comb, and as this became florid, or livid, the convulsions disappeared or returned. After they have continued a short while the convulsions cease; for the venous blood does not maintain the vitality of the nervous centres sufficiently to keep them in action; but if artificial respiration be recommenced, the first effect of aerating the blood is to renew the convulsions, by increasing the vitality of the nervous centres, and rendering them again susceptible to the action of a stimulus, though the convulsions disappear as soon as the arterialisation has proceeded sufficiently far.

Increased rapidity of the respiratory movements may depend either upon greater excitability of the respiratory centre in the medulla, or upon stimulation of some of the afferent nerves which have the power to accelerate it. The chief of these are the pulmonary branches of the vagus, though there are probably others proceeding from the cerebrum, through which the emotions influence the breathing, and others from the general surface of the body.

In order to ascertain the cause of the acceleration of respiration, several experiments were made. Experiment LXIII shows that it is not due to the action of the poison on the cerebrum; for it occurs after the cerebral lobes have been removed. The ultimate arrest of respiration is probably due, in part, to paralysis of the medulla, and, in part, to paralysis of the motor

nerves distributed to the respiratory muscles. The complete insensibility of the phrenic nerve to the strongest stimuli, while the sciatics and vagus still retained a considerable amount of irritability, in Experiments XLIV and LXVI, is very remarkable. The want of co-ordination between the diaphragm and the thoracic muscles in Experiment LX is not improbably due to paralysis of the phrenic nerve, though it may be attributed to some alteration in the respiratory centre. Brown-Sequard states that the diaphragm contains ganglia which will keep up rhythmical movements in it after the central nervous system has been destroyed; and if this statement is correct, it seems probable that paralysis of the phrenic, by interrupting the connection between the respiratory centres in the medulla and those in the diaphragm, may allow the movements of the thoracic respiratory muscles and of the diaphragm to occur one after the other instead of simultaneously.

It is difficult to say to what extent the stoppage of respiration depends on paralysis of the medulla, or of the motor nerves, in each case. Probably the effect of the one preponderates in some cases, and that of the other in others.

Experiment LXII.

November 29th, 1872.—The vagi of a cat were exposed and some dilute cobra-poison injected subcutaneously. Little effect being produced, the dose was repeated, and then a solution of alcoholic extract of the poison injected subcutaneously and into the peritoneum. After the last injection the animal became feebler. No vomiting. Before death slight convulsions occurred. After they ceased, a cannula was put in the trachea and artificial respiration begun. Slight convulsions again appeared, but ceased as respiration was continued. They recommenced when the respiration was stopped, and disappeared when it was again begun. On once more stopping respiration and allowing the convulsions to cease spontaneously, recommencement of the respiration caused them again to appear.

Experiment LXIII.

July 21st, 1873.—A rabbit was etherised and the cerebral lobes were exposed and carefully removed.

3 P.M. Operation finished.

3.7. Respirations 37 per minute.

3.8. A small quantity of cobra-poison injected into the flank. Active reflex movements occur on pinching the limbs and tail, and respiration also becomes more rapid.

3.12. Respirations 96 per minute. Heart's action feeble.

3.23. Breathing hurried. Reflex force continues active.

Another quantity of cobra-poison injected, the two doses together not making more than a moderate amount.

3.37. Respirations very feeble. The upper part of the spinal cord, on being irritated by a Faradic current, caused movements in the limbs. Reflex movements still present, but much diminished.

3.38. Respirations ceased. Cannula inserted in the trachea, and artificial respiration commenced.

3.40. Sciatic nerve exposed and irritated by a strong current, induced twitchings in the limbs, but occasioned no reflex movement in any other part of the body.

3.45. The animal seems perfectly dead. The strongest current produces no effect either when applied to the cord or to the sciatics.

The colour of the muscles seems changed when compared with those of the other rabbit (Experiment LXIV) which had no poison. They are of a less vivid colour, and altogether have an altered appearance.

In this experiment the respirations became quickened from 37 to 96 per minute after the injection of the poison, although the cerebral lobes had been previously removed. The acceleration, therefore, could not be due to emotion, or to the action of the poison on the cerebrum. A comparison with Experiment LXIV, in which the cerebral lobes were removed without injecting any poison, shows that in the latter no acceleration whatever occurred, and the respirations became gradually slower till they ceased.

Experiment LXIV.

July 21st, 1873.—A rabbit was etherised, the calvaria removed, and the cerebral lobes carefully excised. The bleeding was arrested by cotton-wool steeped in perchloride of iron, and by the actual cautery.

1.18. The operation concluded.

1.23. Respirations 32 per minute. Reflex movements well marked on pinching feet or tail.

1.33. Respirations 16 per minute and much deeper; and each one ended with a jerk, as if of the diaphragm.

1.35. Fore legs extended in a convulsive manner. Respiration ceased almost entirely; but at long intervals of about 15 and 20 seconds, an inspiration occurred.

On pinching the feet the respiratory movements became more perfect, though feeble.

1.43. Heart beats rapidly but feebly. Respiration has ceased. Reflex movements are still well marked.

1.44. Cannula placed in the trachea, and artificial respiration begun. Reflex movements continued for some minutes; but then the heart ceased to beat.

3.55. Sciatics exposed and irritated by a Faradic current. No contractions occurred in the limbs. The muscles contracted when irritated directly.

From these experiments it was evident that the accelerated respiration was not of cerebral origin; and it was therefore probably due to stimulation of the pulmonary branches of the pneumogastric by the poison. If this were so, the acceleration would not appear if the vagi were divided previously to the injection of the poison, as the stimulation of the terminal branches of the nerves in the lungs would no longer be conducted to the medulla. The following experiment shows that our hypothesis is correct, the injection of the poison rendering the respirations, which had already been greatly diminished in rapidity by division of the vagi, still slower.

Experiment LXV.

September 15th.—A dog was chloroformed; both vagi were divided, and a cannula placed in the trachea. On recovering

from the chloroform, the animal became very restless and retched constantly, but was unable to vomit. A little while afterwards he became more quiet, and his respirations were counted.

3.10. Respirations $7\frac{1}{2}$ per minute.

3.13. Respirations 7 per minute.

3.15. About 0.01 grain of dried cobra-poison dissolved in $\frac{1}{2}$ c.c. of water was injected into the vein of dog's leg.

Immediately the animal became very restless, and tried in vain to vomit. Respirations 7 per minute.

3.21. Constant retching, but no vomiting. Respirations 7.

3.23. About 0.02 grain more was injected.

3.27. Constant retching. Respirations 6. The animal now lay down exhausted, and was killed by a blow on the head.

Experiment LXVI.

July 9th.—About 1 grain of dried cobra-poison dissolved in water was injected into the flank of a white cat.

3.38. Injection made.

3.43. Cat seems depressed, sits with head drooping and eyes nearly shut. Licks its lips occasionally. Pupils moderately dilated.

3.48. Rubs its ear with fore paw, and licks fore paw afterwards. Is disinclined to move. Pupils more widely dilated.

4.25. Another dose injected.

4.50. Another dose injected into peritoneum. As yet there is no symptom except depression and languor.

4.51. Vomiting. Lies crouched down.

5.5. Still vomiting.

5.14. Lies on its side. Movements of vomiting. When the cornea is touched the eyes move, but the lids do not close. There is also sometimes a movement of fore foot as if to ward off the irritant.

5.17. Whining. Pupils much contracted. When the inside of the ear is tickled the animal scratches at its shoulder with the hind leg of same side. It cannot stand. It shakes its head sometimes when its ear is tickled.

5.25. Reflex movement of leg much fainter when the ear is irritated.

5.31. Tries to get up voluntarily. Got up, staggered some steps. Convulsive movements. Death. Immediately a cannula was placed in the trachea and artificial respiration begun. Sciatic nerve isolated. Irritated by induced current. Foot twitched when secondary coil was at 57 cm.

About 6.30. Electrodes screwed into cord about 2nd and 5th dorsal vertebræ.

The strongest current of the coil produced contraction of the muscles of the back, but no contraction of the limbs. The sciatic nerve, when irritated directly, caused contraction of foot with the coil at 23.

6.50. The phrenic nerve irritated; no contraction of diaphragm; vagus irritated; heart stopped.

In this experiment the continuance of reflex action on irritation of the ear, and of voluntary movements, after reflex action on irritation of the eye had disappeared, and almost up to the time of death, are remarkable; as is also the paralysis of the phrenic before the sciatic and vagus nerves.

Action of Cobra-poison on the Circulation.

In most cases of death from cobra-poison, the fatal issue is not to be attributed to any failure of the circulatory apparatus; for the heart continues to pulsate vigorously, long after all motions have ceased in the voluntary muscles and the strongest irritation applied to the spinal cord and motor nerves fails to produce the slightest effect. But this only occurs when the dose of poison is not excessive; and when a large quantity of it is introduced at once into the circulation, the heart is not exempted from its action, but is, on the contrary, most seriously affected. This is seen in Experiments LXVIII and XXVIII, where the poison having been either injected into the circulation, or absorbed with extreme rapidity, the action of the heart was at once arrested. But it is to be noted that it is not paralysis, but tetanic contraction of the heart which is produced, the poison, in fact, seeming to act as an excessive stimulus; and this being the case, we feel less surprise on

finding that, in ordinary cases of poisoning, the cardiac action may be maintained by the use of artificial respiration for more than thirty hours, as Mr. Richards has succeeded in doing in India. The cardiac movements cease much sooner in frogs poisoned by cobra-venom than in those paralysed by curare—the pulsations in the latter often continuing for very many hours, or even for one or two days. They are also arrested by the direct application of the poison to the heart, as in Experiment LXXII. Its action seems to be somewhat different in degree, if not in kind, when applied to the outside of the heart, as in Experiment LXX, and to the inside, as in Experiment LXXII; for in the former case the pulsations continued for a considerable time, while in the latter they were instantly arrested, the heart stopping in partial systole and moderately contracted.

The action of cobra-poison being exerted on the heart of the frog after its excision shows that it acts on the heart itself; and its effect being very much the same without the body as within it renders it probable that the central nervous system is little concerned in the arrest of circulation by the poison, at least in the frog.

The stoppage of the excised heart may be due (1) to irritation of the inhibitory centres contained within it, or (2) to paralysis of its motor ganglia, or (3) to excessive stimulation of them producing tetanus, or (4) to the action of the poison on the muscular fibre of the organ. It is not due to the first of these causes; for atropia, which paralyses the inhibitory ganglia, does not restore the movements. The second is improbable, as the heart does not stop in diastole but in systole, and resists distention by fluid within it. The third seems the most probable cause, as one does not see why the poison should arrest the cardiac pulsations at once when applied to the interior of the organ, and not do so when placed on the outside, if it acted on the muscular fibre, whereas it may readily be supposed that the poison may reach the ganglia more readily from the inner side of the heart—though we do not venture to assert that this is the true explanation of the facts we have observed.

The inhibitory branches of the vagus are not always paralysed (Experiment LXVI); but sometimes the cobra-poison appears to affect them as well as the motor nerves; and in this it resembles curare, which in small doses does not impair the inhibitory action of the vagus, but in large doses completely destroys it. In Experiment LVI irritation of the vagus quickened, instead of retarding, the cardiac pulsations—a circumstance which indicates that the inhibitory fibres of the vagus were paralysed by the poison, but not the accelerating ones.

The capillary circulation is not unaffected by the poison. In Experiment IV of our former paper, the rhythmical contractions and dilatations, altogether independent of the cardiac pulsations, which Schiff first observed in the rabbit's ear, and which were noticed by Ludwig and Brunton in the vessels of many parts of the body, were greatly increased by the injection of the poison.

In Experiments LXXIV and LXXV the blood-pressure remained high after the heart had ceased to beat. This shows that the arterioles, or capillaries, must have been much contracted, thus opposing a barrier to the exit of blood from the arteries into the veins.

Experiment LXVII.

May 21st.—A cannula was placed in the trachea of a large black rabbit; and some dried cobra-poison dissolved in water was injected into the hip at 1.25 P.M.

1.50. The animal shows symptoms of poisoning. Limbs becoming weak. There is trembling, and the body sinks down. There is starting. The respiration is hurried.

2. Reflex action is well marked when the animal is touched. The limbs seem almost paralysed; but the animal moves the head and neck freely. It makes efforts to rise, but is unable to do so. The head falls over; the respiration is getting feeble. The animal seems quite conscious, and starts if touched.

2.4. It is now quite feeble. When the cornea is touched the reflex action is less than before.

2.5. No convulsions. Artificial respiration commenced. The

rabbit, wrapped in cotton, was placed in a double tin bath filled with warm water. Temperature in rectum $98^{\circ}8$.

2.11. Respiration discontinued for a space.

2.12. Convulsive twitchings of legs begin. Natural respiration has ceased.

Artificial respiration resumed. Pupils contracted. Reflex action on irritation of the cornea has ceased.

2.16. Since the artificial respiration has been resumed there have been no more convulsive twitchings.

2.55. The heart beats rapidly but vigorously.

Temperature 101° . The bath being rather hot, its temperature was lowered by a little cold water added to it.

2.57. The animal passed a quantity of urine tinged with blood.

3.5. Heart beats vigorously.

3.15. The eyeballs are very prominent; pupils normal.

3.45. Heart beating well, but apparently not so vigorously as before. Temperature $100^{\circ}5$.

3.55. The bath getting cold; a little hot water added to it. The heart beating more vigorously than at 3.30.

4.20. Heart beating well—if anything more vigorously than before.

4.40. Heart beats steadily, but apparently with less vigour. Temperature $100^{\circ}2$.

5. Heart sometimes beats steadily 130–140 times per minute. Then it gets feeble and intermits, and again beats steadily.

5.5. Heart beats more freely. Added more warm water to the bath.

5.25. Heart beats rapidly but more feebly.

5.35. The same.

6. Heart beating rapidly, perhaps rather more feebly. Temperature maintained at $100^{\circ}5$.

6.10. Heart beating well and more vigorously.

6.30. Heart beating well, rapidly but steadily.

The attendant, being left alone, discontinued artificial respiration, and the animal died. The fluctuations in the activity of the pulsations were, in all probability, due to the more or less perfect maintenance of the artificial respiration.

Experiment LXVIII.

A small rabbit had two drops of diluted cobra-poison injected into the jugular vein. In 30 seconds he was in convulsions, and in 60 seconds was dead.

The thorax was opened immediately; the heart had ceased to beat, and was firmly contracted.

A large vein entering the auricle on the left side was pulsating vigorously and rhythmically, though no part of the heart itself showed the least trace of motion.

Experiment LXIX.

June 26th, 1872.—Half a drop of cobra-poison diluted with $\frac{1}{2}$ c.c. of water was injected under the skin of a guinea-pig, weighing about 450 grammes (1 lb.).

At 12.13.15 the injection was made. Immediately the animal became restless and cried constantly.

At 12.15 twitching movements began in the limbs.

At 12.16 the animal was quiet, and would not move when touched. It then became restless again, and remained so till 12.44.

12.44. The jugular vein was exposed, and $\frac{1}{2}$ c.c. of the diluted poison was injected into it (= $\frac{1}{2}$ drop of poison).

In less than 30 seconds the animal appeared to be dead.

The thorax was opened, and the heart found to be motionless and the walls of all its cavities firmly contracted. The lungs were ecchymosed.

12.55. Electrodes were inserted into the spinal cord, and an interrupted current passed through it. Whenever the current passed, the legs of the animal jerked vigorously.

The blood which was collected from the large thoracic vessels formed a firm coagulum.

1.22. The cord was still irritable when excited by the induced current.

Experiment LXX.

January 14th, 1873.—The heart of a frog was excised. It beat 20 times in 1 minute. Several drops of cobra-poison were

then placed upon it, and it beat 24 times in 1 minute. When seized with forceps and placed in cobra-poison it stopped in systole; but this might be due to the effect of the compression by the forceps.

Experiment LXXI.

Frog's heart excised. Beats, 30 in the first minute, 34 in the second.

Cobra-poison applied to it. It immediately stopped, and then began again, but slowly and feebly. Then it beat 26 times per minute, less strongly than before. It gradually recovered and seemed little affected, but stopped about 10 or 15 minutes afterwards.

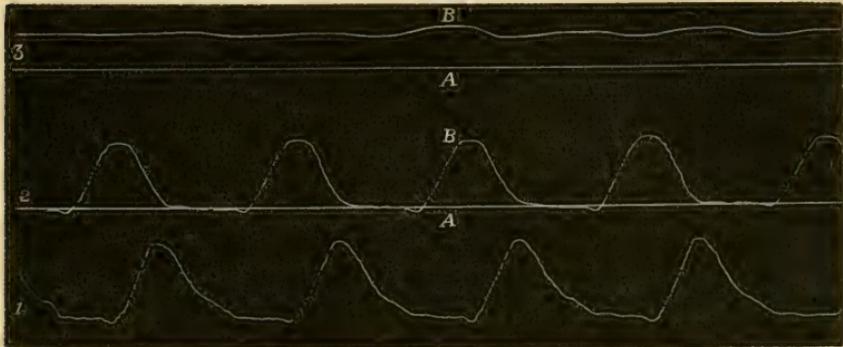
Experiment LXXII.

A cannula was placed in the aorta, and another in the vena cava of a frog. All branches were tied, the heart excised, and placed in connection with H. P. Bowditch's apparatus for keeping a stream of serum circulating through the heart and recording its pulsation by means of a manometer on a revolving cylinder. When fed with pure serum, the heart's contractions were regular and strong; but whenever serum containing dried cobra-poison in solution (in the proportion of about 2 grains in 3 fluid drachms) was introduced into the apparatus the heart stopped almost immediately. As will be seen from the accompanying tracing, it became partially contracted and gave one or two feeble beats, but did not dilate, and then remained still, the contraction, however, very slowly and gradually increasing.

Experiment LXXIII.

A cat was deprived of consciousness by a severe blow on the head; and a cannula being placed in the trachea, artificial respiration was begun. The thorax was then opened and the heart exposed. A solution of dried cobra-poison in water was then injected into the jugular vein. At first the cardiac pulsations became much quicker, but they were also strong. They next became very small and rapid. Lastly, the right ventricle became much distended, and the heart stopped. The lungs became contracted; and when force was used to distend them

they did not expand equally, but became emphysematous in spots, so that the exterior of the lung assumed a nodulated appearance. When the right ventricle was punctured it contracted firmly. No further contraction took place when it was irritated by the direct application of a Faradic current. The blood coagulated.



These tracings were obtained from a frog's heart by means of a small mercurial manometer connected with the aorta. The tracings all read from right to left.

1. Tracing obtained from the heart supplied with pure serum by means of a tube in the vena cava.

2. Tracing of the same kind, with the addition of the line A, which indicates the zero of the mercury. The tracing B, given by the heart, sinks down to zero during each diastole.

3. Tracing given by the heart after it had been supplied with serum containing a small quantity of cobra-poison in solution. The heart makes a few ineffectual attempts, but can neither contract nor relax, and remains still, in a condition midway between complete systole and complete diastole. The line A is the zero to which B would sink if the heart relaxed completely during diastole.

Experiment LXXIV.

A cannula was placed in the carotid of a dog and connected with a kymographion.

Time.	Mean blood-pressure. millims.	Pulse per minute.	
1.36	150	144	Injected some cobra-poison dissolved in water into the sciatic vein. The pressure rose to 165, and then sank in 7 seconds to 135.
	165		
	135		
1.45	50		

	Time.	Mean blood- pressure. millims.	Pulse per minute.	
	1.48	57	...	Fæces passed. A clot formed in the cannula and had to be removed.
	1.55	70		
About	1.58	80	...	Injected some more poison.
	1.58 $\frac{1}{2}$	20		
	1.59	55		
	1.59 $\frac{1}{2}$	70	...	Clot again formed.
	2.2	75		
	2.7	85		
	2.10	85		
	2.16	80	...	Legs loosened, but the animal did not move. Convulsive movements occurred almost immediately afterwards.
	2.17 $\frac{1}{2}$	Cornea still sensible.
	2.18	85	...	Convulsive movements.
	2.19 $\frac{3}{4}$	90	...	Convulsions.
	2.20 $\frac{1}{2}$	80	80	No movement.
	2.20 $\frac{3}{4}$	90	64	The pulse here suddenly changed from 80 to 64, and at the end of every third beat the pressure sank 25 millims., while at each of the others it only sank 5 millims.
	2.21 $\frac{1}{4}$	98	...	Height of each single pulse-wave is now 10 millims. instead of 5, and every now and then it sinks 30; but the number of beats after which it sinks is not now so regular.
	2.21 $\frac{3}{4}$	100	64	Convulsions.
	2.22 $\frac{1}{4}$	105	...	There were now 8 pulsations, and then an interval of 6 seconds, during which the pressure went down to 43

Time.	Mean blood-pressure. millims.	Pulse per minute.	
			millims. Five beats more raised it to 120. Height of each pulse-wave about 15 millims.
2.29	30	...	The pulse has been getting smaller and smaller, and the intervals longer and longer; it is now imperceptible.
2.30	30	...	The pressure still seems at 30, notwithstanding the imperceptibility of the pulse.
2.45	The heart was cut out. It still contracted when irritated.

The injection of cobra-poison here caused a diminution of the blood-pressure at first; but a further injection again raised it. In the latter part of the experiment there is not the slightest trace of failure of the heart's action, but, on the contrary, every evidence of powerful action. When the respirations failed, the heart became slow from irritation of the roots of the vagus by venous blood; and the pulsations were gradually weakened by the same condition. The fact that the blood-pressure sank slowly and did not fall below 30, even after the heart had almost entirely ceased, shows that the arterioles were much contracted.

Experiment LXXV.

A cannula was placed in the carotid artery of a rabbit and connected with a kymographion.

The blood-pressure was 75 mm. of mercury. One cubic centimetre of a 2-per-cent. solution of cobra-poison was injected into the jugular vein. Almost immediately the animal began to struggle, and the pressure rose to 95. It remained at this for a minute and then fell. The float unfortunately stuck, and the curve it should have described in falling was consequently lost. On again getting the instrument to work, the pressure

was found to be 25; and this continued, although the heart had ceased to beat and the thorax was opened. On cutting across the aorta, the pressure fell to zero, showing that it had not been due to any clot in the vessel.

In this experiment the poison seems to have caused tetanic contraction of the heart, and also of the arterioles. The permanence of the pressure at 25, notwithstanding the stoppage of the heart's action, can only be ascribed to contraction of the arterioles preventing the escape of blood from the arterial into the venous system.

Excretion of Snake-poison.

We have made only one or two experiments, ourselves, on the excretion of cobra-venom; but, from the data afforded by the experiments and observations of others, we consider that it is excreted by the kidneys and mammary glands, and probably also by the salivary glands and mucous membrane of the stomach. A case reported by Mr. Shircore, of Calcutta, in which an infant, suckled by its mother after she had been bitten by a snake (species unknown), died in two hours after it had partaken of the milk, shows that the poison is excreted by the mammary glands, and with considerable rapidity; for the child took the breast before any marked symptoms had occurred in the mother.* Its excretion by the kidneys appears from an experiment of Mr. Richards, of Balasore, who found that some urine from a dog poisoned by the bite of a sea-snake (*Enhydrina bengalensis*) killed a pigeon in 22 hours after being hypodermically injected.† Some saliva, which we obtained from the submaxillary gland of a dog poisoned by cobra-venom, had no effect when injected under the skin of the thigh of a lark; but Mr. Richards found that 1 drachm of the greenish liquid which flowed from the mouth of a dog poisoned by cobra-venom killed a pigeon in two hours. As this fluid flowed constantly from the mouth, and the animal was paralysed and motionless, it seems probable that, notwithstanding its colour, it was saliva and not bile.

* *Thanatophidia*, p. 43.

† *Indian Medical Gazette*, May 1, 1873, p. 19.

As the poison-glands of the snake are modified parotid glands, we should naturally expect the poison to be excreted by the salivary glands; and we think it possible that the immunity which poisonous snakes enjoy from the effects of their own poison or that of another species (an immunity which is not shared by innocuous serpents, nor even by small individuals of a venomous species poisoned by a large dose of venom) may be due, at least in some measure, to their power of excreting the inoculated venom through their own poison-glands. We have, however, had no opportunities of trying whether venomous serpents, after extirpation of their poison-gland, succumb to the bite of others in the same way as innocuous ones.

On the Means of preventing Death from the Bites of Venomous Snakes.

In the case of all poisons, snake-venom included, there is a dose which is insufficient to kill; and animals may recover from it even after the characteristic symptoms of the poison have been distinctly manifested.

It has been clearly shown by Hermann that the real dose of any poison, or, in other words, the quantity which is actually circulating in the fluids and operating on the tissues of the body, depends on two factors, viz., the rapidity with which it is absorbed and the rapidity with which it is excreted. If absorption goes on more rapidly than excretion, the poison accumulates in the blood and exercises its lethal action; while the quantity in actual circulation may be reduced to an infinitesimal amount and deprived of all power for evil, if the excretion can keep pace with, or go on more rapidly than, the absorption. Thus it is that curare kills an animal when introduced into a wound; for the poison is absorbed from the wound more rapidly than it can be excreted by the kidneys. If placed in the stomach, curare has usually no apparent action whatever; for it is excreted in the urine as quickly as it is absorbed by the gastric walls. But if absorption be quickened by increasing the quantity administered and giving it on an empty stomach, curare will have the same effect as when it is placed in a wound

or injected into the circulation. A like result is obtained by arresting its excretion, either by ligaturing the renal vessels or extirpating the kidneys. Snake-venom is also poisonous when absorbed by the mucous membrane of the stomach.

On the other hand, when we wish to prevent the accumulation of a poison in the blood and thus to arrest its action, we must either lessen its absorption, quicken its excretion, or combine the two means.

In the case of curare the former of these is sufficient ; and all the bad effects of the introduction of this poison into a wound may be prevented by applying a ligature between the wound and the heart, and only loosening the bandage occasionally, for an instant or two at a time. The same obtains in snake-poisoning. In this way only a little of the poison is absorbed each time the ligature is slackened, and this is excreted by the kidneys before another quantity is absorbed. If the poison can be removed from the wound itself by other means, instead of making the whole of it pass through the circulation, the danger it causes will, of course, be sooner over. Our power to quicken excretion is, in most cases, much less than that to retard absorption ; and it is therefore on the latter that we mainly rely in cases of poisoning in general, as well as snake-bites in particular.

The various methods of mechanically arresting the introduction of the virus, by excision, cauterly, and chemical agency, have been fully discussed in the *Thanatophidia of India* ; and we purpose now to consider its excretion or removal from the organism.

Before doing so, however, we must inquire whether its removal is likely to be of any service or not ; for, as we have already pointed out in our previous communication, the action of the poison may be of two kinds :—1st. It may resemble curare in destroying the power of the nervous system so long as it is present in the blood, but leaving it in a condition to resume its functions as soon as the poison has been removed. 2nd. Its action may be identical with, or similar to, that of a ferment, decomposing or altering the nervous and muscular tissues *in situ* (in somewhat the same way as the pancreatic or gastric

ferments would decompose them if they had been placed in the intestinal canal), and thus rendering them utterly incapable of ever again performing their functions.

If the action of the poison is of the latter kind, no treatment can be expected to be of any avail if the dose has been large ; but if it is of the former, we may still entertain a reasonable hope of averting a fatal result, even when the dose of venom has been large.

We have shown in our previous communication, that, by means of artificial respiration, life may be prolonged for many hours, and time thus afforded for the excretion of some of the poison ; but the means at our disposal have not enabled us to maintain respiration sufficiently long to show us whether the nervous and muscular systems regain their function after the excretion of the poison has proceeded far enough. The experiments of Mr. Vincent Richards, and of a committee appointed by the Government of India in Calcutta, at our suggestion, to investigate the use of artificial respiration in death by snake-bite, being performed under more favourable auspices, have afforded us the data which we were unable to obtain from our own. In one instance, a dog was bitten by a sea snake (*Enhydryna bengalensis*), and, two hours afterwards, died in convulsions. Artificial respiration was commenced ; but, four hours afterwards, the application of a galvanic current caused no muscular contractions ; the eyes were dry and glazed, and the body was cold. Next morning, about sixteen hours after the apparent death of the animal, reaction commenced ; the application of a galvanic current again caused movements of the body and expulsion of urine, and the bowels acted spontaneously. In five hours more reaction seemed established and went on increasing ; the animal appeared as if it would recover ; the eyes lost their glazed appearance, tears were secreted, and a greenish-looking fluid flowed from the mouth ; reflex action became re-established, the eyelids closing when the cornea was touched or when water was poured into the eye. Attempts to swallow were made when water was poured into the mouth ; and the application of a pan of hot charcoal to the chest caused convulsive movements all over the body ;

and these also occurred spontaneously. The animal also became more or less sensible, and the eyelids twitched when the finger was merely brought near the eye.

These phenomena show that the muscles, the motor nerves, the secreting nerves, the spinal cord, and the cerebrum had all recovered their functions to a certain degree, after it had been completely abolished for sixteen hours. This, we think, would not have been the case had the poison acted by decomposing the tissues in the manner of a ferment; and we are therefore inclined to hope that, like curare, it acts only while present in the system, and that its injurious effects may be arrested by its removal.

Notwithstanding the fair promise of recovery which the use of artificial respiration gave in this instance, the heart became weaker, and the animal died 24 hours and 35 minutes after its first apparent decease. Nor has the Committee been more successful in its further experiments, although life has been prolonged for even 30 hours. This result shows that, although artificial respiration may still prove useful in sustaining life and affording time for the use of other measures, it alone is not likely to be of much service in preventing death from snake-bite, except in those cases where the quantity of poison is just enough to kill and no more.

It is evident from the length of time during which life may be maintained without the animal ultimately recovering, that the excretion of the poison is very slow; but we at one time thought to quicken it by the employment of diuretics and sialogogues, and to prevent reabsorption by draining off the urine and saliva constantly. We also proposed to wash out the stomach from time to time, in order to remove any poison which might be excreted through the gastric walls, keeping it partially filled with milk or other nutrient fluid during the intervals, in order to sustain the strength of the animal.

We are by no means certain that some of these methods may not prove useful adjuncts; but as our hope of stimulating excretion, by the salivary glands at least, has been much lessened by our discovery that the poison paralyses the nerves of secretion, we are inclined to think that, perhaps, the readiest

method of removing the poison from the body may be to allow it to flow out along with the blood in which it is circulating, and supply the place of the poisoned blood thus withdrawn by means of transfusion.

The greater part of the poison present in the system is probably contained in the blood, and only a small proportion in the tissues; for one of us (Dr. Fayrer) has found that a few drops of the blood of a dog killed by the bite of a cobra or *Daboia* caused death in 75 minutes, when injected into the thigh of a fowl (*Thanatophidia*, pp. 80, 83, 119, 120). By removing as much blood as could be taken without endangering the life of the animal, a great part of the poison would be withdrawn from the system; and, probably, any harm from the copious bleeding would be prevented by transfusing fresh blood immediately afterwards.

We have tried one or two experiments with transfusion; but they have hitherto been unsuccessful.

We are therefore by no means confident that death may be prevented by the combined use of artificial respiration and transfusion; but we think that they present some chance of success, and that, at all events, the suggestion is justifiable on scientific and rational grounds.

The treatment of animals poisoned by cobra-virus by the hypodermic injection of liquor ammoniæ has been frequently tried in India by one of us (Dr. Fayrer) (*vide Thanat.*, pp. 89 *et seq.*), and also by Mr. Richards, of Balasore, and by ourselves again in London, on several occasions.

The alkali has been administered internally, injected into the areolar tissue, and also into the veins, over and over again; but no benefit has resulted. The objection has been made that experiments of this nature, made on animals, are not conclusive in reference to the probable action of the agent experimented with on human beings; but this objection can hardly be considered valid in a physiological point of view.

At any rate the trials that have been made of this mode of averting the lethal effects of the poison, in India by Dr. Hilson, Civil Surgeon of Moradabad, do not afford any indication that the intravenous injection of liquor ammoniæ was followed by

any diminution of the effect of the poisons, the man in both cases having died* (*vide Indian Medical Gazette*, October, 1873).

The same may be said of other reputed antidotes, such as :— Tanjore pill and other preparations of arsenic ; the hypodermic injection of liquor potassæ, quinine, ipecacuanha, *Aristolochia indica*, and a variety of other drugs, generally of a vegetable nature, and enjoying a large amount of popular confidence : all, when brought to the test of carefully conducted experiment, failed, as might have been expected, to give any favourable result.

It seems almost unnecessary to allude to the so-called snake-stones ; they are powerless for good or evil. They have also enjoyed much confidence ; but when submitted to the test of impartial experiment and observation, their virtues prove as unreal as those of the antidotes above mentioned.

With reference to the mechanical methods of preventing the entry of the poison into the circulation after a bite, we think that the speedy application of an elastic cord (such as is used in bloodless operations) round the limb, combined with the application of cups attached to an exhausting-syringe or pump, † might be of advantage, and that it might be made of general application in India.

* It is unnecessary to occupy time by describing in detail the various substances (animal, vegetable, and mineral) that have been administered as antidotes. Particulars may be found in the *Thanatophidia*, where the details of experiments conducted for the investigation of their actions are recorded.

† Such an apparatus has now been constructed.

ON THE NATURE AND PHYSIOLOGICAL
ACTION OF THE *CROTALUS*-POISON AS
COMPARED WITH THAT OF *NAJA*
TRIPUDIANS AND OTHER INDIAN
VENOMOUS SNAKES ;

ALSO

INVESTIGATIONS INTO THE NATURE OF THE INFLUENCE
OF *NAJA*- AND *CROTALUS*-POISON ON CILIARY AND
AMŒBOID ACTION AND ON *VALLISNERIA*, AND ON
THE INFLUENCE OF INSPIRATION OF PURE OXYGEN
ON POISONED ANIMALS.

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(Reprinted from the *Proceedings of the Royal Society*, No. 159, 1875.)

IN our former papers we described the general phenomena accompanying the physiological action of cobra- and *Daboia*-poisons on warm-blooded animals, reptiles, fishes, and invertebrata. We propose in this paper to compare with these the action of the *Crotalus*-virus in its general effects on life, on the functions, organs, and tissues, and especially as it affects the blood and vessels as regards a marked influence in causing hæmorrhages and extravasations of blood generally and locally ; and, further, to examine the action of snake-poison generally on ciliary and amœboid movements—or that which represents its action on contractility, apart from that which is caused through the medium of the nerve-centres and nerve-distribution.

It appears that there is little difference between the physiological effects of the crotaline or vipurine and the colubrine virus. The mode in which death is brought about is essentially the same in all ; though there are evidences, even when allowing for individual peculiarities, that the action is marked by some

points of difference sufficiently characteristic to require notice in detail.

We have already expressed our belief that death is caused by the cobra-, *Daboia*-, and *Hydrophis*-poison, 1st, through its action on the cerebro-spinal nerve-centres, especially on the medulla, inducing paralysis of respiration ; or, 2nd, in some cases (where the poison has entered the circulation in large quantities and has been conveyed more directly to the heart) by arrest, tetanically in systole, of cardiac action, probably owing to some action on the cardiac ganglia ; 3rd, by a combination of the two previous causes ; 4th, by a septic condition of a secondary nature, and which, being more essentially pathological in its bearings, the details were not considered suitable for discussion here.

There is reason to believe that death is caused in the same way by the *Crotalus*-poison also ; and it appears, from the experiments recently performed in Calcutta, by Dr. Ewart and the members of the Committee appointed by Government, upon *Pseudechis porphyriacus*, or the black snake, and *Hoplocephalus curtus*, or the tiger-snake of Australia, that their virus causes death in the same manner. These reptiles had been sent from Melbourne to Calcutta for the purpose of investigation and comparison. (*Vide* Committee's Report, pp. 58 *et seq.*, Appendix.)

But though the actual cause of death is essentially the same, the phenomena which precede and accompany it differ in some degree according to the nature of the poison, the quantity and site of the inoculations, and the individual peculiarities of the creature inoculated, as may be seen in the experiments herewith recorded.

The condition of an animal poisoned by the rattlesnake-venom, then, essentially resembles that of one subjected to the influence of the colubrine or viperine poison of Indian snakes :—

Depression, hurried respiration, exhaustion, lethargy, unconsciousness, nausea, retching, and vomiting (*vide* experiment on cat, Experiment IX).

Muscular twitchings, ataxy, paralysis, and convulsions (the latter probably chiefly, though not entirely, due to circulation

of imperfectly oxygenated blood, the result of impeded respiration), and, finally, death.

Hæmorrhages or hæmorrhagic extravasations and effusions, both local and general, occur in all varieties of snake-poisoning.

But we observe (and in this our observations are in accord with those of Weir Mitchell) that there is a greater tendency to both local and general hæmorrhage and extravasation of blood and of the colouring-matter of the blood, especially as observed in the peritoneum, intestines, and mesentery, and also probably to a more direct action on the cord (*vide* Experiments I, III, V, VI, VII, IX, XI, XIV, XV), than in poisoning by either cobra or viper (*vide* Experiments IV, VII, XIII, XVI, XVII, XX).

The viscera and other tissues, after death, are found congested and ecchymosed, and in some cases to a great extent, seeming to show that either a preternatural fluidity of blood or some important change in the vessels, favouring its exudation, has occurred.

But with regard to the blood itself, we have observed that it does form a coagulum after death, generally, if not invariably; as we have noted to be the case, though not to the same extent, in the blood of animals that have succumbed to the *Daboia-virus*.*

With reference to the coagulation or non-coagulation of the blood in cases of snake-poisoning, we observe that the following conclusions have been arrived at by Mr. Richards and the Calcutta Committee (*vide* p. 45 of their Report).

“ We now propose to deal with the physical changes produced by snake-poisoning on the blood. From observations which have been made by Mr. Richards and ourselves, we have arrived at the following conclusions:—

“ *The blood appears to remain fluid after death under the circumstances noted below:*

“ 1st. When a large quantity of the cobra-poison has been directly injected into the circulation, as, for example, into an artery or a vein.†

* In Dr. Fayrer's Indian experiments the blood of animals dead from *Daboia*-poison nearly always remained fluid after death.

† This is not always so.—J. Fayrer.

“2nd. In cases where animals or men have been poisoned by the bite of vipers, such as the Russell’s viper.

“3rd. In all cases of snake-bite, whether from the poisonous colubrine or viperine genera, in the human subject.*

“*The blood undergoes either partial or complete coagulation under the following conditions:—*

“1st. When a small quantity only of the cobra-poison has been injected into a vein or an artery.

“2nd. In cases where the lower animals have been bitten by the cobra.

“Why the admixture of a large and quickly fatal injection of the cobra-virus into the circulation of animals should produce comparatively permanent fluidity of the blood or interfere with its ordinary coagulability soon after removal from the body or after death, and why the injection of a smaller and more slowly fatal quantity should interpose no obstacle to its speedy coagulation, are questions extremely difficult to account for or explain. We can only state the fact that, in the one case, coagulation occurs speedily, and in the other this coagulation is retarded or altogether prevented by some cause at present unknown.”

The following experiments were made on the physiological action of the virus of the rattlesnake, with the view of comparison with that of the cobra and *Daboia*.

We are indebted to Dr. Weir Mitchell, of Philadelphia, for a supply of the virus. He was good enough to send about six grains of the dried poison of *Crotalus*—the species not named, but it is believed to be of *Crotalus durissus*.

The dried poison supplied is said to be about 6½ years old, and was dried in July or August at the natural temperature, and has since then been preserved in a phial. It was tried by Dr. Mitchell, and found active three years ago.

It has the appearance of fractured fragments of dried gum-arabic, of rather a darker yellow colour, but otherwise resembling the dried cobra-virus sent from Bengal.

* Not always so.—J. Fayrer.

Experiment I.

June 9th, 1874.—0.015 gramme of the dried *Crotalus*-poison diluted with 1 c.c. of distilled water was hypodermically injected into the thigh of a full-grown guinea-pig at 11.30 A.M.

Restlessness and muscular twitchings of the body generally soon commenced; these passed away, but the animal became sluggish, in which condition it remained all night, and died at about 9 A.M. the next morning.

The injected limb became much swollen, infiltrated, and discoloured with sanguineo-serous effusion.

The intestines were not ecchymosed; there was much sanguinolent fluid and also blood effused into the abdominal areolar tissue.

No convulsions were observed; but as the animal was not seen during a short time previous to death, they cannot be said positively not to have occurred; nor is it known if the heart ceased to beat at the moment when apparent death took place.

Experiment II.

A few drops of watery solution of *Crotalus*-poison, of same strength, were injected under the skin of a guinea-pig's thigh at 12.16 noon.

12.17. Marked twitchings of head and hind legs, very similar to those produced in some of the cases of cobra-poisoning.

12.18. Hind leg (poisoned one) weak.

12.20. Twitchings much increased, now mainly in head and neck, not so much in hind legs.

12.28. Guinea-pig quiet, but with occasional twitchings; sluggish and disinclined to move.

1.30. Sluggish in moving; can still move about, though disinclined to do so. The punctured thigh is very blue.

The rest of the notes of this experiment were lost.

The animal died.

Experiment III.

June 10th, 1874.— $\frac{1}{4}$ of a grain of *Crotalus*- and $\frac{1}{4}$ of a grain of cobra-poison were carefully weighed and diluted, each with

10 drops of distilled water. Two full-grown guinea-pigs of equal weight were then selected.

The solution of *Crotalus*-poison was injected into the peritoneal cavity of guinea-pig No. 1 at 1.52 P.M.

1.55. Muscular twitchings of head and neck.

2 P.M. Startings and twitchings continue.

It gives faint squeaks occasionally, as though the sudden startings, which occur at intervals of 5 or 6 seconds, cause pain.

2.5. Twitchings continue.

2.8. Very restless; twitchings going on, but no paralysis yet.

2.17. The same.

2.25. Restless and weaker, but still moves freely on being roused.

2.42. Sluggish; drags the hind legs.

2.58. Weaker; rolls partially over on one side, but can run when roused.

3.3. Lying on side, but can be roused; is partially paralysed in hind legs. Respiration abdominal and hurried.

3.5. Nearly quite paralysed; is roused with difficulty.

3.7. Can still be roused. Abdomen distended and painful; cries out when it is touched, as though peritonitis were setting in.

3.12. Can be roused with difficulty; respiration hurried; convulsive movements of fore legs and neck. Can still stagger for a few paces, but co-ordination of muscular power much diminished.

3.30. In violent convulsions.

3.38. Convulsions continue.

3.45. Quiet. Paralysed; but reflex action still continues.

3.55. Dead in 2 hours and 3 minutes.

3.56. Electrodes in cord cause twitching of muscles of the back, and very slightly in those of the legs; the cord was evidently all but paralysed. Muscular fibre contracts freely to direct stimulus of current. The intestines were ecchymosed and congested. There were effusions of red serum into the peritoneal cavity, and much ecchymosis of peritoneum and subperitoneal and intra-muscular areolar tissue. Peristaltic action continued faintly.

4 P.M. The heart has ceased to contract 4 minutes after apparent death; it continued to contract, especially the auricles, for part (not the whole) of the time.

The blood removed from the heart-cavities and vena cava rapidly formed a firm coagulum in a glass receiver.

The electrodes applied to the sciatic showed that the nerve-trunk, as well as the spinal cord, was paralysed.

Experiment IV.

Guinea-pig No. 2, an albino, had the $\frac{1}{4}$ -grain cobra-virus solution injected into its peritoneal cavity at 1.56 P.M.

It immediately became much excited.

1.57. Is now quite tranquil.

2. Sluggish. Does not twitch as guinea-pig No. 1 did.

2.4. Started and squeaked slightly, as though in pain, but no twitching.

2.5. Slight twitching generally. Paralysis and ataxy commencing; drags its legs with difficulty.

2.9. Sharp twitchings of head and neck.

2.12. Subsided on to the belly; head fallen over; crawls with difficulty; is very feeble, almost paralysed. The albino eyes have a heavy dull look; lost their bright pink.

2.14. Convulsed.

2.15. Reflex action ceased. Apparently dead, but heart can still be felt beating. Occasional convulsive twitchings of lower lip.

2.16. Dead in 21 minutes.

2.17. All movements have ceased. Heart had ceased to contract, except slight flickering movements of auricles.

2.20. Electrodes in cord. Spinal cord and nerves paralysed; muscles contract freely to direct stimulus of current. Heart distended with blood. Blood, when removed, formed rapidly a firm coagulum. Intestines, peritoneum, and subperitoneal areolar tissue congested and ecchymosed. Sanguinolent effusions into peritoneum, but not so well marked as in the *Crotalus*-poisoning. Peristaltic action of bowels ceased rapidly.

The results of these two experiments show, so far, that the action of the cobra-poison is more energetic than that of the

rattlesnake. Both were watery solutions of exactly the same quantity of the dried virus; but it is to be borne in mind that that of the rattlesnake was $6\frac{1}{2}$ years old, while that of the cobra was only 1 year old.

The guinea-pigs were both full-grown and of the same size, yet one succumbed in 20 minutes to the cobra-poison, while the other survived the inoculation of the rattlesnake-poison for 2 hours and 3 minutes.

There were no very marked differences in the action of the poison in these two cases, except in the energy with which the cobra exceeded the *Crotalus*.

Crotalus.

Twitchings; restless; squeaks; sluggish; ataxy; paralysis. Hurried respiration. Peritonitis. Convulsions. Death in 2 hours 3 minutes. Coagulated blood. Ecchymosis and extravasation of serous effusion well marked. Cord paralysed. Muscles retain irritability.

Cobra.

Twitchings; excitement; squeaks; sluggish; ataxy; weakness; paralysis. Convulsions. Death in 20 minutes. Spinal cord and nerves paralysed. Muscles irritable. Heart distended. Blood coagulated. Ecchymosis. Congestion less than in *Crotalus*.

Experiment V.

June 10th.—A grain of *Crotalus*-poison diluted with water was injected into the peritoneum of a full-grown guinea-pig at 2.40 P.M. Twitchings began almost immediately.

3.3. Restless; startings; staggers on hind legs.

3.20. Very weak, especially in hind quarters. General paralysis setting in. Abdomen distended and very tender.

3.30. In convulsions. Still feels when the abdomen is touched.

3.37. Paralysed, but feels the touch. Reflex well marked.

3.45. Apparently dead in 65 minutes.

3.48. Cavities opened. Auricles flickering. Blood from heart and great vessels coagulated firmly. Abdominal cavity and areolar tissue and subperitoneal tissue infiltrated with bloody

serum. Much ecchymosis of peritoneum and intestines, but not of lungs. Cord and nerves paralysed. Muscles contract vigorously to induced current.

Action of Crotalus-poison on Rabbit.

Experiment VI.

$\frac{1}{4}$ of a grain (0.015 gramme) of the same *Crotalus*-poison, dissolved in 1 c.c. of water.

The jugular vein of a large white rabbit was exposed and the above solution was injected into it at 1.50 P.M.

At 1.51 violent convulsions, with opisthotonos.

At 1.53 apparently quite dead. Artificial respiration commenced immediately. Heart acting still, though feebly and with irregular flickering contractions. Spinal cord exposed. Electrodes applied; no reaction.

2.12. Heart still contracting feebly.

2.15. Faint contractions of heart still observable. Ventricles punctured, and blood withdrawn. Peristaltic action has ceased.

2.20. Feeble cardiac movements continue.

2.21. Heart has now ceased. Muscles react to direct current. Death caused by rapid paralysis of medulla and cord. The blood taken from the heart and great vessels did not coagulate. At 4 P.M. it was still fluid, though very florid in colour.

Examined under the microscope nearly two hours after apparent death, the white corpuscles appeared natural; the red corpuscles not in rouleaux, and very much crenated, though a few retained their natural contour.

The blood was neutral to test-paper.

Experiment VII.

June 17th.— $\frac{1}{4}$ of a grain (0.015 gramme) of dried cobra-poison, dissolved in 1 c.c. of water, was injected into the jugular vein of a large white rabbit, of the same size as in the previous experiment, at 2.55 P.M.

The rabbit passed at once into violent convulsions, and was apparently dead before it could be removed from the board, within one minute. The cord was immediately exposed,

artificial respiration having also been begun. Electrodes applied, with strong current; no reaction; the cord was perfectly paralysed.

Thorax examined at 2.59. Heart had ceased to contract. Ventricles moderately contracted. Auricles distended with blood. Phrenic irritated, quite paralysed. Diaphragm, when directly irritated by current, contracts very faintly, whilst the neighbouring muscles contract vigorously. Peristaltic action goes on. Electrodes applied to vagus appear to accelerate peristaltic action; applied to splanchnic, they diminish it.

3.7. Ventricles of heart have now contracted firmly.

3.15. Blood taken from heart and great vessels has coagulated, but not firmly. The clot is small, and the serum very red.

3.15. Electrodes to sciatic; no reaction. Blood examined under microscope; no aggregation in rouleaux, no crenation of corpuscles. Blood neutral to test-paper.

We have in former papers remarked that when the cobra-poison was injected into the jugular vein directly and caused almost immediate death, that the fatal result was due to cessation of the heart's action by arrest in systole, and such was partially the case in the last experiment (VII), made for the purpose of comparison with *Crotalus*; but in Experiment VI death was not so caused, for the heart continued to contract for about 28 minutes after apparent death, which was probably due to the sudden and total annihilation of the functions of the medulla and cord, no reaction to a strong current occurring when the electrodes were applied immediately after apparent death.

In this instance of *Crotalus*-poisoning it is also to be remarked that the coagulability of the blood was destroyed, whilst in that by cobra-virus it was only partially so.

It appears from the results of this experiment that the direct inoculation of large doses of the virus, whether viperine or colubrine, into the circulation have the power in some cases of annihilating almost instantaneously the irritability of the cord and medulla, as in others they have of arresting the heart's action.

Experiment VIII.

June 17th.—Ten drops of the blood of the rabbit described in the last experiment, poisoned by *Crotalus*-virus, were injected into a guinea-pig's thigh at 3.40 P.M.

The guinea-pig was not apparently affected constitutionally by the poisoned blood. It was alive the next morning; but the leg was swollen and discoloured. It ultimately recovered.

Experiment IX.

June 24th, 1874.—A full-grown cat was chloralised at 1.20 P.M. $\frac{1}{4}$ of a grain of *Crotalus*-poison, diluted with 1 c.c. of water, was injected into the jugular vein. The respirations were immediately quickened.

1.21. Twitching of muscles generally.

1.22. Efforts to vomit. Forcible extension of limbs.

1.24. Hurried respiration and retching. Reflex action perfect.

1.30. Muscular twitching and tetanic stretching of limbs. Efforts to vomit continue. Micturition. Rolls over on the ground.

1.34. Ataxy. Staggers when walking, which it can only do for a few paces. Peculiar twitching of diaphragm; not synchronous with respiratory movements. Rolls over on its side.

2 P.M. In the same state.

2.8. Injected $\frac{1}{8}$ of a grain more of the poison into the same jugular vein. The animal immediately got up and walked, comparatively steadily, for several paces, as though it had been stimulated, and then rolled over.

2.16. Twitching of diaphragm continues at the rate of 150 per minute.

2.18. Again got up and walked for a few paces: but it is gradually becoming more paralysed.

2.44. Violent tetanic spasms of limbs. Reflex action diminished.

2.46. Reflex action gone from eyes. Deep sighing respiration.

2.47. Convulsions. Death. Body opened immediately. Lungs deeply congested and much ecchymosed. Deep red

gelatinous effusion all about the roots of the lungs. Heart contracting. Electrodes applied to phrenic caused vigorous contraction of diaphragm.

2.50. Heart ceased to contract three minutes after respiration had ceased.

2.52. Electrodes in cord; do not cause contraction of limbs.

2.54. The sciatic nerve, when irritated, conveys impressions; muscles of legs contract. Blood from the heart and great vessels did not form a coagulum, and remained permanently fluid. Red corpuscles of blood were much crenated.

Death in this case appeared to be caused through the medulla.

Experiment X.

June 15th, 1874.—Action of *Crotalus*-poison on the frog.

A frog's hind leg was ligatured, excluding the sciatic nerve.

A solution of *Crotalus*-poison was injected into the lymph-sac at 12.32 P.M.

2.30. Sluggish, but not otherwise affected.

3.15. In the same condition.

June 16th.—12.3, noon. Sluggish, but can still move.

June 17th.—Found dead this morning early; pupils contracted.

Electrodes applied; no reaction in either cord or nerves on either side to the strongest current.

The frog may have been dead some hours.

Experiment XI.

June 15th.—At 3 P.M. same day a solution of *Crotalus*-venom was injected into the dorsal lymph-sac of a frog, the aorta having been previously ligatured, so as to prevent the poison from affecting the trunks or peripheral extremities of the sciatic nerves.

3.40. The frog seems quite unaffected.

June 16th.—12.30, noon. Frog dead; not rigid; mouth open.

Irritation of cord with strongest current does not cause contraction of legs. Irritation of sciatic with coil at 24 causes twitchings of gastrocnemius.

Neither of these two experiments give any definite results, as the period intervening between death and examination of the condition of the nerve-centres was not determined exactly.

The results of the following experiments show that the local as well as the general effect of the cobra- and *Crotalus*-poisons, *i.e.* colubrine and viperine, is to cause hæmorrhage, ecchymosis, and sanguinolent effusions into the areolar tissue, not only at the seat of inoculation and its neighbourhood, but also in the mucous membranes and other vascular parts. It is obvious also that the *Crotalus*-poison acts more energetically in this respect than the cobra-poison, and that this is perhaps one of the most marked distinctions between them.

Experiment XII.

August 6th, 1874.—A cat was chloralised, and part of the mesentery placed under the microscope on the warm stage. *Crotalus*-poison, diluted with water, was then applied to the mesentery, and its effects watched. The white corpuscles were observed to cling in quantities to the walls of the vessels, and as the current of blood hurried through them, some masses of pale matter like aggregation of white corpuscles were observed to pass with the stream; very soon, marked extravasation of red corpuscles took place, and to the naked eye the mesentery became discoloured by patches of ecchymosis in the course of the small blood-vessels, like the foliage on the branches of a tree.

There could be no doubt that the local action of the poison had a marked effect in producing extravasation of blood.

Experiment XIII.

A similar experiment was repeated on another part of the mesentery of the same cat with cobra-poison, exactly as the *Crotalus*-poison had been applied in the previous experiment. This was carefully watched, but no extravasation took place; there was a marked difference in the result of the application of the two poisons, at all events as far as these two experiments were concerned.

Experiment XIV.

August 12th, 1874.—A cat was chloralised at 2.30 P.M. Mesentery exposed and placed under microscope on warm stage.

Crotalus-poison applied to mesentery; circulation soon diminished in some vessels but continued vigorously in others. Isolated extravasated patches soon made their appearance, of a triangular form; others followed and coalesced with these until a network was formed in the course of the vessels all over the field. The extravasation soon became general, the circulation still continuing slowly.

Experiment XV.

A fresh portion of mesentery of same cat exposed. Intestines becoming cold and circulation now very languid.

Cobra-poison applied.

No apparent effect produced, but the circulation is very languid, indeed has almost ceased, so that the results of this experiment are not conclusive.

Experiment XVI.

August 14th, 1874.—A cat was chloralised, part of mesentery withdrawn, and placed under microscope on warm stage.

Dried cobra-poison dissolved in a salt solution, 0.75 per cent., applied to the mesentery at 4.10 P.M.

4.14. Circulation is languid, almost ceased in some vessels.

4.18. Slight extravasation taking place where the poison has been in contact.

4.20. Extravasation rather more obvious.

4.35. Exposed another part of the mesentery; examined the state of the circulation before applying the poison. Blood flowing languidly.

Poison applied at 4.37; at first it seemed rather to accelerate the movement of the blood.

4.38. Circulation continues at same rate.

4.42. Same rate.

4.45. It becomes more languid.

4.48. Circulation has ceased, but yet there is no marked extravasation.

Experiment XVII.

Another portion of the same mesentery had cobra-poison applied, but after half an hour there was no sign of extravasation.

Experiment XVIII.

A fresh piece of mesentery exposed of same cat, and diluted *Crotalus*-poison applied at 4.52 P.M.

The circulation was rather languid at the time, and apparently became more languid.

At 4.58 no extravasation had taken place, the blood flowing very languidly.

5.15. Circulation still going on, but very slowly; no extravasation: it soon after ceased.

Experiment XIX.

At 5.20 P.M. a fresh portion of the mesentery was exposed; to one part cobra- and to the other *Crotalus*-poison was applied, and the effect was watched with the naked eye.

5.45. No extravasation visible.

At 6.15 P.M. slight extravasation equally visible on both.

Experiment XX.

August 25th, 1874.—At 2 P.M. a young cat was chloralised. The mesentery was drawn out and a part treated with cobra-poison, another part with *Crotalus*-poison.

At 5 P.M. On examination, that under the influence of the *Crotalus*-poison was found deeply congested and reddened with blood, extravasated in the course of the small vessels, forming a well-marked redness to the naked eye. Under the microscope the red corpuscles were seen in numbers outside the vessels. Circulation still going on vigorously. That part treated with cobra-poison was barely altered, but on close examination slight patches of extravasation were seen in the course of the vessels.

The difference was well marked between the two—the

extravasation produced by *Crotalus*-venom being well marked, that by cobra-venom scarcely perceptible. In both cases the microscope showed red corpuscles outside the vessels.

These experiments show that *Crotalus*-poison causes hæmorrhage and hæmorrhagic effusions more than the cobra-poison does.

The following experiments were made, at the suggestion of Mr. Darwin, with the object of testing the influence of snake-poison on ciliary action, especially in reference to its comparative action on vegetable protoplasm, as will be seen by his remarks.

Experiment XXI.

Influence of Cobra-poison on Ciliary Action.

June 29th, 1874.—Ciliated epithelium from the frog's mouth was treated with a solution of cobra-poison and examined under the microscope.

At 1.35 P.M., when examined, the action of the cilia was vigorous.

At 1.45 it was much diminished.

At 1.55 it had entirely ceased.

Experiment XXII.

Ciliated epithelium placed under microscope; one part was treated with water, the other with the poisoned solution.

At 2.10 P.M. ciliary motion vigorous in both, perhaps more so in that subjected to the poisoned solution.

2.18. Non-poisoned cilia active. Poisoned cilia very feeble.

2.20. Non-poisoned cilia still active. Poisoned cilia very feeble.

2.24. Non-poisoned cilia active. Poisoned cilia very languid.

2.30 Non-poisoned cilia still active. Poisoned cilia have entirely ceased to act.

It is evident from this that the poison first stimulates and then destroys the activity of the ciliary action.

Experiment XXIII.

August 14th.—Frog's blood placed in salt solution, 0.75 per cent., at 1.25 P.M. on warm stage, and then subjected to the action of cobra-poison.

At first the amoeboid movements of white corpuscles went on vigorously. At 2 P.M. they had ceased, or very nearly so, in all that appeared in the field.

2.30. All movement had entirely ceased. The red corpuscles seemed more flattened, the nucleus more visible, and the edges better defined, assuming a pointed and more oval form than usual.

Experiment XXIV.

August 25th, 1874.—Newts' blood examined under $\frac{1}{8}$ object-glass on hot stage, white corpuscles moving slowly. Cobra-poison applied, but no perceptible change observed.

The following communications were received from Mr. C. Darwin on the action of some of the same cobra-poison on vegetable protoplasm:—

“ You will perhaps like to hear how it acted on *Drosera*. I made a solution of $\frac{1}{4}$ gr. to 5ij. of water. A minute drop on a small pin's head acted powerfully on several glands, more powerfully than the fresh poison from an adder's fang.

“ I also immersed three leaves in 90 minims of the solution; the tentacles soon became inflated and the glands quite white, as if they had been placed in boiling water. I felt sure that the leaves were killed; but after eight hours' immersion they were placed in water, and after about 48 hours re-expanded, showing that they were by no means killed. The most surprising circumstance is that, after an immersion of 48 hours, the protoplasm in the cells was in unusually active movement. Now, can you inform me whether this poison, if diluted, arrests the movement of vibratile cilia? ”

“ I dissolved $\frac{1}{2}$ gr. [of cobra-poison] in 5j of water, so that I was able to immerse two leaves. It acted as before, but more energetically; and I observed more clearly this time that the solution makes the secretion round the glands cloudy, which I have never before observed. But here comes the remarkable

point: after an immersion of 48 hours, the protoplasm within the cells incessantly changes form, and I never saw it on any other occasion so active. Hence I cannot doubt that this poison is a stimulant to the protoplasm; and I shall be very curious to find out in your papers whether you have tried its action on the cilia and on the colourless corpuscles of the blood. If the poison does arrest their movement, it will show that there is a profound difference between the protoplasm of animals and of this plant. Therefore if you try any further experiments I hope that you will be so kind as to inform me of the results. I may add that I tried at first 1 gr. to the ζ j, as that is my standard strength for all substances.

“It is certainly very remarkable that the poison should act so differently on the cilia and on the protoplasm of *Drosera*. After the 48 hours’ immersion, I placed the two leaves in water and they partially re-expanded. I thought that the whitened glands were perhaps killed; but those of one leaf which I tried with carbonate of ammonia absorbed it, and the protoplasm was affected in the usual manner. I am very much surprised at the action of the poison on the viscid secretion from the glands, which it coagulates into threads and bits of membrane, with much granular matter. Have you observed whether the poison affects in any marked manner mucus or other such secretions?”

Experiment XXV.

Action of Cobra-poison on Muscle.

June 29th, 1874.—A standard solution of cobra-poison, 0.03 gramme to 4.6 c.c. of water, was prepared.

1.25 P.M. The gastrocnemius of a frog was separated and immersed in this solution in a watch-glass; it immediately contracted considerably.

1.30. The muscle contracts with current at 11.

1.45. The muscle has lost its irritability; does not respond to the strongest current.

Experiment XXVI.

At the same time (1.25 P.M.) the gastrocnemius from the other leg of the same frog immersed in water. Did not

immediately contract like that placed in the poisoned solution.

1.30. Contracts strongly to current at 15 cm. of Du Bois Reymond's coil, more than the poisoned muscle at 11, at the same moment.

1.45. Contracts distinctly at 11, whilst the poisoned muscle has lost all irritability.

From this it is evident that the poison first stimulates the muscular fibre to contract, but rapidly afterwards destroys its irritability.

Experiment XXVII.

The gastrocnemii of a frog were again treated in the same way as in the previous experiment, with precisely the same results.

June 28th.—Made several experiments with cobra-poison on ciliated epithelium of frog's mouth, and found that it at first accelerated, then destroyed, the action of the cilia.

Experiment XXVIII.

To Test the Effects of Cobra-poison, when swallowed, on the Frog.

June 24th, 1874.—At 2.25 P.M. about $\frac{1}{8}$ of a grain of dried cobra-poison was passed down a frog's throat.

2.30. Frog making violent efforts to vomit. Gaping. Head thrown back tetanically.

2.34. Bloody mucus vomited with violent efforts.*

2.50. Moves with difficulty; is becoming paralysed. Efforts to vomit continue.

3. Much the same.

3.5. Very weak; still tries to vomit.

3.10. Reflex action still well marked.

3.15. Motor nerves apparently quite paralysed.

3.20. Apparent death.

Artificial Respiration with Pure Oxygen.

As life had been prolonged for many hours in snake-poisoning by artificial respiration with atmospheric air, it was thought

* This experiment is especially interesting, as showing that frogs do occasionally vomit, a fact which has been denied by some physiologists.

expedient to ascertain if the more complete oxygenation by the undiluted gas would be more efficacious, as it seemed might be possible; accordingly the following experiment was made on the 24th April, 1874.

Experiment XXIX.

$\frac{1}{4}$ of a grain of dried cobra-poison dissolved in distilled water was injected into a rabbit with the hypodermic syringe.

Symptoms of poisoning were rapidly manifested. A tube had been previously introduced into the trachea, and respiration was commenced as soon as poisoning was manifest.

Artificial respiration, with oxygen contained in a large bag, was steadily continued for 2 hours, but with no better effect than in other similar cases where atmospheric air was used for the same purpose. At the expiration of 2 hours, apparent death had occurred; the heart continued to beat for about 2 minutes after the respiration ceased.

Beyond a very florid condition of the blood, there was no obvious difference between the effect of oxygen and that of common air. It did not indeed appear that, as far as the effects produced by the poison were concerned, it differed in its action from common air.

Experiment XXX.

November, 1874.—A little cobra-poison, dissolved in water, was added to water containing some cells scraped from the mantle of a freshwater mussel. Among these was a large ciliated cell, which, before the addition of the poison, had been moving slowly, although its cilia were moving actively. Immediately after the addition of the poison the cell began to spin round on its own axis with extraordinary rapidity. In about three or four minutes its motions began to be languid, the ciliary motion ceased, the cell itself elongated, contracted, and then slowly resumed its former shape and became perfectly motionless.

Experiment XXXI.

Water from the interior of a freshwater mussel, and

containing two specimens of *Paramæcium* in active motion, was examined. They were rotating with great rapidity. A little cobra-poison diluted with water was added. Three minutes after the addition one was discovered with both the cilia and cell-body perfectly still. The cilia of the other were still, but the cell-body was contracted. In about half a minute more it expanded to its normal size and then remained perfectly still.

Experiment XXXII.

A piece taken from the mantle of a freshwater mussel was placed on the slide and examined at the end of about half an hour. Active ciliary motion could be observed in the fringe of the mantle itself and in several specimens of *Paramæcium*. A little dilute poison was added. At first the ciliary motion seemed increased, but in about 2 minutes it became slower, and in 6 had become very languid, and in 10 minutes stopped altogether in the specimens of *Paramæcium*, but still continued in some of the cilia of the mantle.

Experiment XXXIII.

A little dilute cobra-poison was added to a piece of the mantle of a freshwater mussel. The cilia began immediately to move much more rapidly. This was watched for some time. Ciliary motion not affected, or at all events not arrested, after more than half an hour.

Experiment XXXIV.

December 10th, 1874.—A piece of the gills of a freshwater mussel placed under the microscope and a little cobra-poison added at 10.40 P.M. The cilia were extremely active.

At 10.55 still active.

11.5. Several ciliated amœboid masses are now quiet instead of rolling over and over as they did, but the cilia on their surface are still moving.

11.15. The cilia on these Infusoria have now nearly all stopped. A few are moving slowly, whilst those on the gills are but little affected.

11.55. Cilia on the gills are still quite active. Those on the ciliated bodies still moving, rather more actively than before.

1.30. Cilia on gills have become much more sharply outlined. Many are standing still, though many still move briskly.

Experiment XXXV.

To another specimen a strong solution of cobra-poison was added at 10.50.

1.30. Cilia still moving.

Experiment XXXVI.

A third specimen was laid in an almost syrupy solution of dried cobra-poison at 11.28.

At 11.40 no effect observable.

1.30. Some have stopped, but numbers are still moving quite briskly.

In this case the poison seemed not to have any action on the ciliary motion.

Experiment XXXVII.

January 6th, 1875.—At 3.40 some diluted cobra-poison added to *Vallisneria*. Circulation going on vigorously. About $\frac{1}{10}$ grain in 3 drops of water.

3.58. The movements are unchanged.

5 P.M. Movements going on as before.

Experiment XXXVIII.

Added some solution of cobra-poison at 4 P.M. to another specimen of *Vallisneria*.

4.10. No change.

4.45. Circulation goes on vigorously.

4.55. Perhaps rather less brisk in their movements.

The results of these experiments show that cobra-virus must be regarded as, to a certain extent, a poison to protoplasm, seeing that it arrested with rapidity the movements in Infusoria* (*vide* Experiments XXX, XXXI, and following).

* Is this accounted for by the existence of a rudimentary nervous system diffused throughout these two forms of life, and on which the poison could act?

Still it cannot be regarded certainly as a very powerful one, for the cilia of the freshwater mussel continued to move for many hours in a strong solution of cobra-poison; though in other experiments the action was apparently arrested even in weaker solutions of the poison. In the case of cilia from the frog's mouth, the results were more definite, but action was not invariably destroyed. The results of the action of the poison on the amœboid movements of the blood-corpuscles are not very definite. In the case of *Vallisneria*, the circulation in the cells went on with undiminished vigour after the application of the poison for 2 hours.

NOTE ON INDEPENDENT PULSATION OF THE PULMONARY VEINS AND VENA CAVA.

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IN a former communication* we incidentally mentioned that in a rabbit killed by the injection of cobra-poison into the jugular vein we had observed the pulmonary vein pulsating after all motion had ceased in the cavities of the heart. We have since observed the same phenomenon three or four times under conditions which show that this pulsation is not due to the action of the cobra-poison with which the animal in which we first observed it had been killed. The following example will show the changes in rhythm observed in these pulsations.

A cat was chloroformed, and the vagi exposed and irritated by an interrupted current. Artificial respiration was kept up by air containing chloroform vapour, and the thorax was then opened, and a solution of atropia injected directly into the heart by means of a Wood's syringe. The vagi were again irritated, but without any effect being produced on the heart, the inhibitory apparatus in it being evidently paralysed by the atropia. A solution of glycerine extract of physostigma was now injected into the heart in a similar way. The vagi were now irritated again, and the heart stood still, the effect of the atropia having been counteracted by the physostigma. After the irritation ceased the heart again commenced to pulsate.

Artificial respiration was now discontinued, but all the cavities of the heart continued to beat for a considerable time. The

* *Proceedings of the Royal Society*, 1874, vol. xxii, p. 125.

ventricles then stopped, but the auricles continued to beat. It was then noticed that the pulmonary veins in the right lung, which was exposed to view, were pulsating. The veins, as well as both auricles, pulsated at the rate of 119 per minute, but the contractions of the veins were not synchronous with those of the auricles. Both auricles next ceased to beat, but the pulmonary veins in both lungs continued to pulsate. The ventricles now began to beat again, while the auricles remained still. The ventricles pulsated at the rate of 8 per minute, while the pulmonary veins pulsated at the rate of 46 per minute; and no motion was perceptible in any part of the auricles.

One hour and twenty minutes after the thorax had been opened, and about an hour and ten minutes after artificial respiration had been discontinued, the ventricle was still pulsating. Its rhythm was very irregular. After one beat a pause of half a minute followed, and then 37 pulsations all together. One hour and forty minutes after opening the thorax the inferior vena cava was noticed to be pulsating close to its entrance into the auricle. A contraction spread like a wave from the vena cava over the right auricle, and the appendix contracted after the auricle itself. The superior vena cava also pulsated close to the heart. The left auricle had ceased to pulsate a considerable time previously, and the ventricles had also stopped. After the auricles had pulsated for a while the ventricles again began. At one hour and fifty minutes after opening the thorax the inferior vena cava was still pulsating. In ten minutes more all movement had nearly ceased, and the observation was discontinued.

At one hour and fifty minutes after opening the thorax slight contractions of the diaphragm were noticed.

The striking points in this experiment are the contractions of the pulmonary veins and the vena cava independently of the heart, the long time during which they retained their irritability, and the continuance of their pulsations after the other parts of the heart had ceased. The pulsation of the pulmonary veins and of the ventricles at the same time, while the auricles were motionless, is also deserving of attention.

In another experiment we found the pulmonary veins

pulsating in a cat killed by a blow on the head. We have also seen pulsation in animals killed in other ways; but the proportion of cases in which we have seen it to those in which we have not seen it is very small. On looking through several modern text-books of physiology, we have failed to find any mention of the rhythmical contractile power of the pulmonary veins and vena cava; but the earlier anatomists were well acquainted with it, and Haller* states that he has seen the pulmonary veins continue to pulsate for two hours, and that others had seen the vena cava pulsate for three hours while all motion in the other cavities of the heart had already ceased. Johannes Müller† has also observed contractions of the vena cava and pulmonary veins; and in young animals the contractions of the pulmonary veins extend as far as they can be followed into the lungs.

The importance of contraction of the vena cava and pulmonary veins in preventing reflux of blood into them during the contraction of the auricle, under circumstances when any hindrance is opposed to the free flow of its contents into the ventricle, is self-evident. Indeed, Haller‡ says that it was supposed to exist by Senac, although he had not seen it. Especially in cases of valvular disease of the heart is it likely to be of great service; and we think it advisable to bring again before the notice of physiologists and physicians this power of the veins, which, although so long known, appears of late years to have been overlooked.

* *Elementa Physiologia*, 1757, tom. i, pp. 410 and 399; and *Mémoires sur la Nature sensible et irritable des parties du corps animal*, 1756, tom. iv, p. 4.

† Müller's *Physiology*, translated by Baly, 2nd edit., vol. i, p. 182.

‡ *Op. cit.*, p. 410.

NOTE ON THE EFFECT OF VARIOUS SUBSTANCES IN DESTROYING THE ACTIVITY OF COBRA-POISON.

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IN a paper read some time ago before this Society by Mr. Pedler, he mentioned his discovery of the fact that the activity of cobra-poison was completely destroyed by admixture with perchloride of platinum. This substance, however, could only be regarded as a chemical and not as a physiological antidote to the poison, inasmuch as it had no power to modify or prevent the action of the venom after its absorption into the blood. Mr. Pedler expressed his opinion that the proper method of pursuing the investigation was to investigate separately the action of platinum salts and of cobra-poison upon the animal body. In the discussion which followed we stated that the method proposed by Mr. Pedler was, in the present instance, not likely to lead to any results, and that, as the action of the substance employed by him was in all probability due to its simply forming an insoluble compound with the cobra-poison and not to any action of the platinum *per se*, certain other metallic salts would have a similar action to the perchloride of platinum. Experiments have confirmed the opinion we then expressed,* and we find the action of chloride of gold is precisely similar to that of perchloride of platinum, the cobra-venom being rendered entirely inert by admixture with the gold salt before its injection into the body. Chloride of gold, however, like perchloride of platinum, is merely a chemical antidote, and does not modify the action of the venom after its absorption into

* A. W. Blyth, M.R.C.S., "The Poison of the Cobra," *The Analyst*, February 28th, 1877, p. 204.

the circulation. Permanganate of potash, which has been recommended as an antidote, also destroys its activity completely. Chloride of zinc, chloride of mercury, nitrate of silver, and carbolic acid all diminish the activity of the poison, and prolong life when mixed with it before its injection; but they do not prevent death, nor do they prolong life to any great extent. Perchloride of iron has very much less action upon the poison than one would expect, and it prolongs life to a very slight extent. Liquor potassæ impairs the activity of the poison very considerably, and prolongs life for several hours. When a large dose of cobra-poison is injected, none of these substances prevent death, even when applied immediately to the wound. The reason of this probably is that they do not come into such perfect contact with the poison as to destroy the whole of it, and the portion which escapes destruction is sufficient to kill. It is possible, however, that when minimum doses only are injected, the local application of one or other substance may turn the balance between life and death, but this point we must reserve for a future paper.

Our first experiment was made in order to compare the action of chloride of platinum alone with that of cobra-poison alone, and of chloride of platinum injected after cobra-poison.

Experiment I.

February 25th, 1878.—A cat weighing 4 lbs. had about 1 c.c. of the chloride of platinum solution of the British Pharmacopœia injected into its flank.

3.44 P.M. Injection completed.

3.55 „ No apparent effect. The cat well and playful.

No symptoms whatever were observed, but after some days a slough formed at the point of injection. Chloride of platinum thus appears to have no physiological action whatever when injected subcutaneously, beyond its effect as a local irritant.

In Experiments II and III similar doses of cobra-poison were subcutaneously injected into two cats; but in Experiment III the injection of the poison was followed immediately by the injection of a solution of chloride of platinum into the same spot, so as, if possible, to destroy the venom which had

not yet been absorbed. In this case death was delayed, but not to a very great extent, as it occurred in an hour and fifty minutes after the injection of the venom and chloride of platinum, and in an hour and two minutes in the animal which received the poison alone.

Experiment II.

Black cat, weight 5 lbs.

25 milligrammes of cobra-poison dissolved in 1 c.c. of distilled water injected into skin of flank at 3.26 P.M. of February 25th.

3.28 P.M. Vomiting. It had taken chloroform to keep it quiet whilst being weighed, and was recovering from the chloroform. Micturated. Drooping head on one side.

3.32 P.M. Vomiting again. Looks much depressed. *Defecated.*

3.40 „ Breathing slow. *Shallow.*

3.41 „ Vomiting again.

3.45 „ Twitching of muscles.

3.52 „ The same state.

3.58 „ Defecating. Micturating.

3.59 „ Retching. Vomiting. Moves about in a restless manner.

4.6 „ Moving *backwards* with staggering gait.

4.12 „ Staggers, and head droops.

4.13 „ Falls over on its side. The respiration is slow. Reflex from eye and ear almost gone.

4.14 P.M. Reflex from head and legs when irritated. None from tail.

4.15 P.M. Attempts to rise.

4.18 „ Got up, but fell over again. Tried to walk. No reflex from the head.

4.20 P.M. Head raised and fell over again. Touching the eye seems to rouse the cat, but no reflex of lids. Tries to get up, but cannot. Fell over on the opposite side.

4.24 P.M. Again a struggle to rise.

4.27 „ Touching the eye produces no reflex. Breathing very slow. Convulsive twitching of limbs.

4.28 P.M. Apparently dead. Heart still beating one hour and two minutes after injection of poison.

The blood, after death, formed a *firm* coagulum.

Intestines much congested. Patch of congestion in stomach. Red serum effused into the peritoneal cavity.

No local symptoms or changes.

A good deal of food in the stomach, notwithstanding the vomiting. Digestion was in full action.

In these and other experiments the dose of cobra-poison was regulated according to the weight of the animal, the same proportion per pound weight being given in each case.

Experiment III.

A grey cat, 4 lbs. weight, had 20 milligrammes of cobra-poison, dissolved in 1 c.c. of distilled water, injected under skin of flank at 3.39 P.M. of February 25th.

At 3.40 P.M. a solution of chloride of platinum injected at the same spot.

3.42 P.M. Very restless.

3.43 „ Drinks water.

3.52 „ Vomiting.

3.55 „ Dull and depressed.

4.10 „ Same condition.

4.20 „ Sluggish.

4.30 „ Restless. Moving about.

4.45 „ Staggers. Getting very sluggish. Walks with difficulty. Head drooping.

4.54 P.M. Shivering. Head fallen over.

5 P.M. Fallen over. Slow paralysis creeping over limbs. Respiration slow. Gets up, rolls over again. On touching the eye the eyelid moves. Reflex not gone from the ear.

5.6 P.M. Fallen over. Paralysed. Reflex nearly gone, still slight from ear. Pupils dilated.

5.9 P.M. Convulsions. Pupils become normal again. Respiration very slow—13 per minute.

5.20 P.M. Tries to rise. Very feebly.

5.22 „ Fallen quite over.

5.23 P.M. In same condition. Makes feeble efforts to rise. Pupils dilated again.

5.27 P.M. Again tries to rise. Micturition.

5.29 „ Convulsions.

5.30 „ Dead.

No local symptoms, *i.e.*, no extravasation about the puncture. No congestion of stomach or bowels. Stomach empty. Blood coagulated *after death*.

Injected at 3.39 P.M.

Died at 5.30 P.M.

Death in one hour and fifty-one minutes.

The following experiments show the effect of chloride of gold in completely destroying the cobra-poison.

Experiment IV.

March 7th, 1878.—3 milligrammes of cobra-poison, mixed with 1 grain of chloride of gold, dissolved in 40 grain measures of water, injected into the hip of a white guinea-pig, weighing 18 oz., at 3.50 P.M.

4.10 P.M. Crouching quietly in corner of box. Tremor, perhaps fright.

4.15 P.M. Seems uneasy; crouching in corner. No other change. Recovered without any bad symptoms.

Experiment V.

March 14th.—In this experiment a very large dose of poison was used.

30 milligrammes of cobra-poison, mixed with $1\frac{1}{3}$ c.c. of a 10-per-cent. solution of chloride of gold, were injected into a guinea-pig weighing 20 oz., at 3.30 P.M.

75 c.c. of water was used to wash out glass, and then injected. The poison and the chloride form a yellow creamy precipitate.

3.30 P.M. Began to jerk and twitch immediately, excited, running about the box.

3.35 P.M. Crouching in corner, twitching, but not otherwise affected.

3.42 P.M. Not apparently affected.

3.52 P.M. Crouching; does not appear affected, but is weak in the hind legs when he runs.

4.10 P.M. Very little affected; hind legs weaker, but he is very active otherwise.

4.20 P.M. Much the same; active, except that hind legs seem rather weak.

4.55 P.M. Remains the same. Recovered perfectly without any further symptoms.

In order to make sure that the dose of cobra-poison would certainly prove fatal if administered alone, the animal, after its recovery, was injected with a quantity of pure cobra-poison, fifteen times less than that from which it had recovered, and, as will be seen from Experiment VI, death rapidly occurred.

Experiment VI.

March 14th.—White guinea-pig that recovered from 30 milligrammes of cobra-poison, mixed with chloride of gold.

At 4.45 P.M., 2 milligrammes of cobra-poison were injected into the hip.

4.50 P.M. Very restless; scratching his skin.

4.52 „ Twitching; very restless.

4.59 „ Squeaking; very restless.

5.10 „ Injected leg weak; not so restless.

5.15 „ Trying to vomit; twitching movement of head, jerking upwards; violent efforts to vomit; a sort of cough; flows from nostrils and mouth; getting gradually paralysed, he still crawls; nearly violent efforts to vomit.

5.24 P.M. The animal creeps along, putting his head along the ground.

5.26 P.M. Apparently dead; heart still beats.

At 4.45 P.M. the injection was made, and at 5.26 P.M. the animal was dead. Death in 41 minutes.

Experiment VII shows that chloride of gold is a chemical, and not a physiological antidote, and does not prevent the action of the poison after its absorption.

Experiment VII.

March 14th.—Guinea-pig, weight 16 oz.

5 milligrammes of cobra-poison dissolved in 1 c.c. of water and injected into the right hip at 3.39 P.M.

In three minutes afterwards $1\frac{1}{3}$ c.c. of a 10-per-cent. solution of chloride of gold were injected into another spot (the left hip, at 3.42).

3.43 P.M. Very restless.

3.45 „ Very restless; head twitching; drops the left leg.

3.53 „ Restless.

3.55 „ Weak, dropping both hind legs; left appears quite paralysed.

4.5 P.M. Getting weaker; paralysis creeping over him.

4.10 „ Barely moves; hind quarters completely paralysed.

4.12 „ Convulsions.

4.19 „ Heart still beats feebly.

4.20 „ Dead.

Experiment VIII shows that permanganate of potash destroys the action of the venom.

Experiment VIII.

5 milligrammes of poison were dissolved in 1 c.c. of water, and mixed with 1 c.c. of liquor potassæ permanganatis of the British Pharmacopœia, and injected under the skin of a guinea-pig. No symptoms were produced, and the animal remained quite unaffected.

Experiment IX.

Two rabbits of the same litter, each weighing exactly 2 lbs., were taken. 5 centigrammes of cobra-poison dissolved in 1 c.c. of distilled water were mixed with 1 c.c. of liquor potassæ permanganatis (B.P.), and allowed to stand for about 8 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. 5 milligrammes of cobra-poison dissolved in 2 c.c. 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 30 minutes.

Chloride of zinc delays the action of the cobra poison, but does not prevent it, as appears from Experiments X and XI, in which a guinea-pig that had received 3 milligrammes of pure cobra-poison (Experiment X) died in 45 minutes, whereas one that had received a similar dose, previously mixed with chloride of zinc, lived for about 3 hours (Experiment XI).

Experiment X.

March 1st, 1878.—3 milligrammes of cobra-poison, dissolved in 2 c.c. of distilled water, injected at 3.43 P.M. into a guinea-pig's hip. Weight of guinea-pig, 20 oz.

3.46 P.M. Twitching.

3.50 „ Restless twitching.

3.53 „ The same. Irritable; squeals; quarrels with the other guinea-pigs; respiration jerky.

4 P.M. The same.

4.5 P.M. Drags the injected leg, which is nearly paralysed.

4.15 P.M. Much the same.

4.19 „ Paralysed, and crawls with difficulty; all hind quarters invaded by poison's influence.

4.21 P.M. Paralysis extending; struggles to rise; can only move the head. Reflex from eye diminished.

4.25 P.M. Convulsive movements.

4.28 „ Dead in 45 minutes. Heart continued to beat after apparent death.

Experiment XI.

Red guinea-pig, weight 16 oz. At 3.46 P.M., March 1st, 3 milligrammes of cobra-poison, dissolved in 2 c.c. of distilled water and mixed with 0.01067 chloride of zinc, were injected subcutaneously. The poison and the chloride were mixed 5 minutes before injection.

5.53 P.M. Guinea-pig restless; twitching; grunting; keeps licking the puncture; irritable with other guinea-pigs.

4 P.M. Very restless. Puncture seems irritable; leg partially paralysed.

- 4.15 P.M. Much the same.
 4.29 „ Much the same.
 4.35 „ Not quite so restless.
 4.45 „ Active; runs about.
 4.45 „ Restless; not worse.
 5 „ Seems pretty well now.
 Died about 7 o'clock.

Liquor potassæ impairs the activity of the poison, but does not destroy it, as will be seen from Experiment XII, in which the dose of the poison, which had usually proved fatal considerably within an hour, did not cause death until 8 hours had elapsed.

Experiment XII.

March 14th.—Guinea-pig, weight 16 oz.

5 milligrammes of cobra-poison, dissolved in 1 c.c. water mixed with 1 c.c. of liquor potassæ, injected into hip at 3.52 P.M.

3.53 P.M. Twitching.

4.0 „ Leg paralysed.

4.20 „ It seems much the same.

4.35 „ Appears much the same.

4.55 „ Appears much the same.

5.35 „ Much the same.

At 11.30 it was lying with left hind leg paralysed, could walk when irritated, mouth opened, head twitching back frequently.

11.45 P.M. its respiration ceased, but when the skin of the belly was pinched the animal took a breath and respiration continued for about a minute afterwards. The heart continued to beat until 11.50.

Liquor ferri perchloridi fortior (B.P.) has much less action upon the cobra-poison than one would have expected, as will be seen from Experiment XIII, in which death occurred in an hour and a half.

Experiment XIII.

March 14th.—Guinea-pig, weight 16 oz.

5 milligrammes cobra-poison, dissolved in 1 c.c. water mixed with 1 c.c. of liquor ferri perchloridi fortior (B.P.), injected into the left hip of the guinea-pig at 4.4 P.M.

4.20 P.M. Dropped the hind leg, but otherwise seems active and well.

4.35 P.M. Very active, but leg drops.

5.10 „ Hind leg paralysed.

5.15 „ Tries to crawl, cannot, struggles, convulsed.

5.16 „ Jerking convulsions.

5.17 „ Almost dead.

5.18 „ Dead.

Carbolic acid likewise delays the action of the poison, but to a very much smaller extent than liquor potassæ, as is proved by Experiment XIV.

Experiment XIV.

March 14th.—Carbolic acid, $\frac{1}{3}$ c.c. mixed with 5 milligrammes of cobra-poison in 1 c.c. of water, injected into hip of a guinea-pig weighing 14 oz. at 4.55 P.M.

5.55 P.M. Much the same.

7.50 „ Very slight convulsions.

7.55 „ Much the same.

8.0 „ Dead.

Experiment XV.

March 7th.—3 milligrammes cobra-poison mixed with 1 grain of nitrate of silver dissolved in 40 grains of water, injected into hip of black guinea-pig, weighing 14 oz., at 3 P.M.

4.10 P.M. Twitching; crouching in corner, crying out slightly as guinea-pigs are wont to do when restless.

4.15 P.M. Restless, crouched in corner of box, twitching of muscles, cries as before.

4.25 P.M. Restless, crying fretfully.

Died in about $1\frac{1}{2}$ hours afterwards, about 2 hours after the injection of the poison.

Experiment XVI.

March 7th.—3 milligrammes of cobra-poison mixed with 10-grain measures of a saturated solution of chloride of mercury (corrosive sublimate), injected into hip of guinea-pig (black and white), weighing 14 oz., at 3.56 P.M.

4.10 P.M. Twitching, uneasy, tremors.

4.15 P.M. Quiet, crouching in the corner.

4.24 „ Restless, but does not seem to twitch; cries like the other guinea-pigs occasionally.

About 6.0 the animal lay quiet, with occasional twitches, and about 6.30 it died.

In order to ascertain which substance would be most likely to save the life of the animal by local application to the point of injection, either by destroying the poison itself or by preventing its absorption by the tissues, we applied chloride of gold, permanganate of potash, chloride of platinum, and carbolic acid locally, the method adopted being to inject the poison under the skin of the leg, immediately afterwards to apply a ligature tightly above that point, and then to make an incision and apply the substance in just the same manner as we would have done if the animal had actually been bitten. From the following experiments, however, it will be seen that the absorption of the poison is so rapid that all local applications were useless. It should be noted that the quantity of poison we employed was large, and it still remains to be seen whether these local applications may turn the balance between life and death when the quantity of the poison would be just sufficient to kill in case of no remedy being applied.

Experiment XVII.

Guinea-pig weighing 1 lb.

4.27½ P.M. Injected 2 gr. 9 centigrammes of cobra-poison into thigh, ligature applied immediately.

4.29½ P.M. Solution of chloride of platinum applied.

4.31 „ Twitching violently.

4.33 „ Twitching violently; ligature remains on limb.

4.40 „ Not worse; the ligature is evidently delaying the action of the poison.

4.47 P.M. Getting weaker.

4.50 „ Convulsed.

4.52 „ Dead.

Death delayed in this instance.

Experiment XVIII.

April 4th, 1878.—Guinea-pig weighing $1\frac{1}{2}$ lb.

4.11' 10" P.M. Injected 3 centigrammes of cobra-poison.

4.13 P.M. Chloride of gold solution, 1 in 10; ligature kept on until chloride of gold was applied.

4.15 P.M. Twitching.

4.16 „ Leg paralysed.

4.17 „ Animal nearly paralysed.

4.19 „ Animal dying.

4.20 „ Convulsions.

4.22 „ Dead.

Experiment XIX.

April 4th, 1878.—Guinea-pig weighing $1\frac{1}{2}$ lb. Injected 4 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 „ Dying.

4.13 „ Convulsion.

4.14 „ Dead.

Experiment XX.

April 4th, 1878.—Guinea-pig weighing 1 lb.

3.45' 20" P.M. Injected $\frac{3}{4}$ gr. = 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.

3.55 „

3.57 „ Dying.

3.58 „ Dead—less than 13 minutes.

EXPERIMENTS ON A METHOD OF PREVENTING DEATH FROM SNAKE BITE, CAPABLE OF COMMON AND EASY PRACTICAL APPLICATION.

By Sir LAUDER BRUNTON, M.D., F.R.S., Sir JOSEPH FAYRER, Bart., K.C.S.I., F.R.S., and LEONARD ROGERS, M.D., B.S., etc., Indian Medical Service.

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ALTHOUGH this paper is a joint one, the authors wish to mention that each has had a different part in its production. The whole research may be fairly regarded as the natural outcome of the work begun in India nearly forty years ago by one of us (Fayrer), and this is the only ground on which his name can be associated with this paper. The instrument employed was designed by another of us (Brunton), and the actual experimental work was entirely carried out by a third (Rogers).

The first experiments on the use of permanganate of potash as an antidote to snake-poison was made by one of us (Fayrer) in 1869, both by the local application of a solution and by injection into the veins,* on the ground of its being a chemical antidote. The animals experimented upon were dogs, but the permanganate of potash did not seem to have any power to avert the lethal action of the poison. It was shown also by Wynter Blyth† that cobra-venom, when mixed *in vitro* with permanganate of potash, becomes innocuous. His results were confirmed by two of us, who showed that some other substances had a similar power.‡ They tried, by the injection of strong

* J. Fayrer, M.D., London, J. and A. Churchill, *The Thanatophidia of India*, 1872, p. 95.

† A. Wynter Blyth, M.R.C.S., "The Poison of the Cobra," *The Analyst*, February 28th, 1877, p. 204.

‡ Brunton and Fayrer, "Note on the Effect of Various Substances in Destroying the Activity of Cobra-Poison," *Proceedings of the Royal Society*, June 20th, 1878, vol. 27, p. 465.

solution of permanganate of potash, and also by its local application to an incision made over the bite, to destroy the lethal action of cobra-poison previously injected, but their experiments were unsuccessful, the permanganate appearing to be unable to overtake the poison which had got the start of it.

In 1881 Messrs. Couty and Lacerda* made a number of experiments upon the effect of permanganate of potash on serpents' venom, and Lacerda found that permanganate of potash not only destroyed the lethal action of the venom when mixed with it *in vitro*, but also preserved life when a 1-per-cent. solution of permanganate was injected into the tissues close to the place where the venom had been previously injected, and also when both venom and antidote were injected directly into the vein. At the time of presenting his note to the Academy of Science, in Paris, M. Lacerda was apparently unaware of the previous experiments by Blyth, Brunton, and Fayrer. In a later publication† he discusses their experiments, but claims for himself to have scientifically demonstrated permanganate of potash to be a precious antidote to serpent venom, and to have brought it into common use, and thinks, therefore, that the priority belongs to him; but he was apparently unaware that instructions for its use with the ligature had many years before been promulgated by Fayrer in India.

In the winter of 1881 a number of experiments were made by Dr. Vincent Richards, who found, like the previous experimenters, that cobra-poison was completely destroyed by permanganate of potash when mixed with it *in vitro*, so that death did not follow the injection of the mixture either hypodermically or into a vein. He found also that when cobra-poison was injected into a dog, and the injection followed either immediately or after an interval of four minutes by a hypodermic injection into the same part of a solution of permanganate of potash, no symptoms of cobra-poisoning resulted, but after the development of symptoms of cobra-poisoning permanganate of potash failed to have any effect, whether injected locally or into a vein or both.

* Couty and Lacerda, *Comptes Rendus*, vol. xcii, p. 465.

† Lacerda, *Comptes Rendus*, vol. xciii, p. 466.

These results obtained both by Lacerda* and Richards seemed to give good hope that permanganate of potash might be used to lessen the appalling fatalities from snake bite in India, but it is evident that the hypodermic injection of a solution can never be widely employed, because the hypodermic syringe is expensive, it is liable to get out of order just at the times that it is wanted, and the solution may become dried or spilt, or may not be available. It is evident that the first requisite for any antidote to snake poisoning is that it shall be always at hand; second, that it shall be easily applied; and thirdly, that it shall be cheap.

About two years ago, one of us (Brunton) was asked, on behalf of a young officer going out to India, to design an instrument which might be used in case of snake bite. He did so accordingly, and he has since had a similar one made for him by Messrs. Arnold and Sons, which seems to combine the three requisites just noted. It consists of a lancet-shaped blade about half an inch long, long enough, in fact, to reach the deepest point of a bite by the largest snake. He has had some instruments made with a double edge, like an ordinary lancet, and others with one edge sharp and the other edge blunt, so as to press in the permanganate. The lancet is set in a wooden handle about an inch and a half long, which is hollowed at the other end so as to form a receptacle to hold the permanganate. Two wooden caps are fitted over the ends of the instrument, one to keep in the permanganate, and the other to protect the lancet. Such an instrument, if turned out in large numbers, could be sold at such a small price as to be within reach of even the Indian labourer, and might be sold everywhere in the same way as packets of quinine are at present.

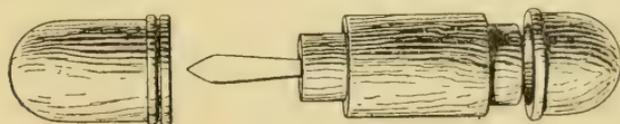


FIG. 1.—Lancet for use in snake bite, showing the steel blade, the cap which covers it, the hollow wooden handle for holding crystals of permanganate of potash, and the cover which retains them.

* Dr. J. B. de Lacerda, Rio de Janeiro, Lombaerts, etc., "O Veneno ophidico e seus antidotos," 1881, p. 64.

The plan now proposed is to make a free opening into the site of the bite, and to rub in crystals of permanganate. For this purpose the limb should be surrounded by a tight bandage above the bite, the puncture of the tooth or teeth should be freely cut into by the lance-shaped blade and the crystals of permanganate introduced and rubbed round. A few drops of saliva may be added.

To test the efficacy of the proposed plan, several lethal doses of venom dissolved in a few drops of water, so as to resemble, as far as possible, the natural poison, are to be injected into the limb of an animal, a ligature placed round the limb above the seat of injection, an incision made, and crystals of permanganate placed in the wound, moistened and rubbed in.

Experimental Investigation, by Leonard Rogers.

In order to test in as practical a manner as possible the value of the suggestion of the two first-named authors of this communication, the following experiments were carried out at the Physiological Laboratory of the London University by the third-named author. In the first place it was necessary to ascertain if crystals of permanganate destroy the activity of other venoms besides that of the cobra, for we are not aware that its action in this direction has been tested against any extensive series of snake venoms. As the value of the suggested treatment would evidently be greatly enhanced if the permanganate could be shown to act efficiently against every class of snake venom, a series of experiments were carried out to test this point. The venoms in solution were mixed with small quantities of a 10-per-cent solution of pure crystalline permanganate of potash in 0·9 per cent. NaCl, and after given times the mixtures were injected into pigeons, several times a lethal dose of each venom being used, so that if recovery took place it would be evident that the permanganate had destroyed the activity of the poisons. The following table (p. 154) summarises the results of these experiments.

It will be seen that the table includes venoms of each main subdivision of snakes, namely the two true vipers, the *Daboia Russellii* of India and the Puff Adder of Africa, the Pit Viper,

the *Crotalus horridus*, the Colubrine snake the *Bungarus fasciatus*, and one of the Hydrophidæ or Sea-snakes, namely, the *Enhydrina bengalensis*. In the case of each, ten or more lethal doses were neutralised by very small quantities of permanganate in solution, and in most of them 20 lethal doses were readily thus rendered harmless. The only failure was in Experiment 7, in which 32·2 milligrammes of *Bungarus fasciatus* venom was added to 25 milligrammes of permanganate of potash in solution, and in this case by far the greater part of the poison must have been neutralised, for in previous experiments one-eighteenth part of the venom per kilogramme, used in Experiment 7, killed a pigeon in one hour. Further experiments showed that 25 milligrammes of the permanganate of potash did entirely neutralise 16·1 milligrammes of *Bungarus fasciatus* venom. It is evident, then, that the salt will neutralise about its own weight of this venom, but that its power in this direction has a definite limit, as might have been expected. It is clear, then, that this agent does act on every class of snake venom and renders them inert.

Owing to the limited time available and the small number of animals for which a license had been obtained, the actual experiments on the treatment after injection of the venoms have been so far limited to those of the cobra as a typical representative of the Colubrine class, and of the *Daboia Russellii* as a common and deadly viper. Rabbits and cats were used in the investigation, the latter on account of their mixed diet and firmer tissues resembling more closely the human subject. The venoms were dissolved in as small a quantity of sterile normal saline solution (0·9 per cent. NaCl) as possible, so as to resemble in concentration the natural venom. The portion of the limb to be operated on was cleaned of hair by scissors beforehand (as the human subject is free from this obstacle to treatment). The strong solution of venom was then injected into the subcutaneous tissues of the cleaned part of a hind limb a little above the paw, as most snake bites in the human subject occur on the distal parts of the extremities. After a given measured time a ligature consisting of a piece of bandage was tied loosely round the thigh and twisted up tightly by means of a piece of stick or a pencil so as to temporarily stop

Table I.

Number of experiment.	Weight of pigeon.	Dose in milligrammes.	Number of lethal doses.	Dose per kilogramme weight.	Amount of 10 per cent. K_2MnO_4 .	Time mixed before injection.	Symptoms.	Result.
I. <i>Daboia</i> Venom.								
1.....	grammes. 350	3.5	3	milligrammes. 10	c.c. 0.5	mins. 30	Nil	Recovered.
2.....	320	6.2	7	20	0.5	10	Do.	Do.
3.....	280	14	17	50	0.5	10	Do.	Do.
4.....	300	15	10	50	0.5	10	Do.	Do.
II. <i>Crotalus horridus</i> Venom.								
III. African Puff Adder.								
5.....	270	21.6	20	80	0.25	5	Do.	Do.
6.....	300	12	10	40	0.25	5	Do.	Do.
IV. <i>Bungarus fasciatus</i> .								
7.....	230	32.2	20	140	0.25	5	Colubrine	Died in 2 hours.
8.....	230	16.1	10	70	...	10	Nil	Recovered.
V. <i>Enhydra bengalensis</i> .								
9.....	250	25	20	...	0.25	10	Do.	Do.

the circulation through the distal part of the limb in order to check further absorption of the poison. An incision was then made in the long axis of the limb over the seat of injection of the poison, and the edges dissected up slightly on either side so as to fully expose the affected tissues and to form a small pocket, into which the crystals of permanganate were next placed, and after moistening with a few drops of sterile normal salt solution (water, or even saliva, would serve in an emergency) they were well rubbed in until the exposed tissues presented a uniformly blackened appearance. About 3 minutes were usually occupied by the little operation, on the completion of which the ligature was released and a dressing and bandage applied to the wound. The animals were under chloroform throughout the operation, including the injection of the venom. The amount of permanganate held by the instrument made for these experiments was $\frac{1}{4}$ gramme, this quantity being used in each of the experiments.

The results of the experiments so far performed may most conveniently be summarised in the following table, by means of which they may readily be studied. The actual doses of venoms injected are given in Column 4, and the dose per kilogramme weight in Column 5. The time which was allowed to elapse after the injection of the poison before the application of the ligature (Column 6) was usually $\frac{1}{2}$ minute, which it was calculated would be sufficient to allow a handkerchief, or, in the case of a native, a strip of a pugari or of the cotton garments commonly worn by the poorer classes in the tropics, being tied round the limb and twisted up to form an efficient ligature. In a few of the later experiments this application of the ligature was delayed for 5 and 10 minutes. In Column 8 the time is shown which was taken over the operation from the application to the release of the ligature, while the ultimate result is shown in Column 9. In most of the control experiments a ligature was applied round the thigh for about the same time as in the operations, as it appeared possible that the ligature might delay somewhat the absorption of the poison, although it could scarcely affect the ultimate result of its action, owing to the poison being an essentially cumulative one.

Table II.—Experiments with Cobra Venom.

No.	Animal.	Weight.	Actual dose.	Dose per kilogramme.	Time of ligature.	Amount of permanganate.	Ligature released after.	Result.
1	Rabbit	kilogrammes. 1	milligrammes. 10	milligrammes. 10	30 secs.	gramme. 0·25	mins. 2	Died, 1 hr.
2	"	1½	7·5	5	2½	" 3½ hrs.
3	"	1½	3·75	2½	3¼	" 3½ "
4	"	2¾	2·75	1	3	" 3½ "
5	"	1·8	1·8	1	...	Nil (control)	...	" 1½ "
6	"	2½	1·25	0·5	30 secs.	"	3½	" 3½ "
7	Cat.....	1¾	17·5	10	...	0·25	3	Recovered.
8	"	3	30	10	...	Nil (control)	3½	Died, 3 hrs.
9	"	3	15	5	...	0·25	3	" 30—38 hrs.
10	"	2¾	13·75	5	3½	Recovered.
11	"	4	20	5	5 mins.	...	3½	"
12	"	3	15	5	...	Nil (control)	3	Died, 28 hrs.
13	"	3½	10·5	3	10 mins.	0·25	3¼	Recovered.
14	"	2	4	2	5 secs.	...	3	"
15	"	3½	3½	1	...	Nil (control)	...	Died, 50 hrs.

The first six experiments of Table II were performed on rabbits, with the result that only prolongation of life was obtained. Thus, after a dose of 10 milligrammes per kilogramme (Experiment 1), death took place only a little quicker than after one-tenth of this dose in a control animal (Experiment 5). Again, 5 milligrammes per kilogramme in a treated animal caused death in $3\frac{1}{2}$ hours (Experiment 2), but 0.5 milligramme per kilogramme in a control killed in the same time (Experiment 6). The rapidity of death in this last animal shows that 0.5 milligramme per kilogramme is still much above the minimal lethal dose of cobra-venom for rabbits, so that the doses used in the treated cases were many times a lethal dose (about five to fifty times), and were thus mostly proportionally larger doses than a cobra could eject in the case of a man. The tissues of a rabbit are also more delicate than those of a cat or of a man, so that absorption of the poison may be unusually rapid in rabbits, which are extremely susceptible to snake-venoms.

Turning next to the results of the experiments on cats, much more satisfactory results were obtained. Thus, the control experiments showed that 1 milligramme per kilogramme produced death in 50 hours, this being the minimal lethal dose of the cobra-venom used in these experiments for cats (Experiment 15). A dose of 5 milligrammes per kilogramme caused death in 28 hours, the time having probably been prolonged by the application of a ligature after the injection (Experiment 12). A dose of 10 milligrammes per kilogramme proved fatal in 3 hours, although a ligature had been applied as in the treated cases (Experiment 8). On comparing the result of treated cases with the above control we find only one death occurred in six experiments. The one fatal result took place after a dose of 5 milligrammes per kilogramme (Experiment 9), this having been the first case treated, in which the permanganate was not as thoroughly rubbed in, and the site of injection was not as completely exposed as in later experiments, and in this case death did not take place until over 30 hours. On the other hand, in Experiment 7 recovery took place after 10 milligrammes per kilogramme (10 lethal doses), while in two other

cases recovery took place after five lethal doses had been injected, in one of which (Experiment 11) 5 minutes were allowed to elapse before the treatment was carried out, while in Experiment 13 recovery ensued from lethal doses treated 10 minutes after injection.

The above results are very encouraging, for it appears from D. D. Cunningham's observations that the average amount of venom ejected by a full-sized cobra is not more than 10 lethal doses for a man, while other writers give much smaller amounts. Further, in many cases the full dose will not actually be injected into the human tissue for various reasons.

In Table III a similar series of experiments with Daboia venom are summarised. Here, again, in the case of rabbits, only very marked prolongation of life was obtained, although the dose used in Experiment 17 was less than four lethal doses, so that it is clear that in the case of rabbits the method was not very successful.

On the other hand, the experiments with cats were as successful as in those of the cobra series given above; for only one of the six cases treated with permanganate died, and in this instance (Experiment 21) the very large dose of 50 milligrammes per kilogramme was injected, and the treatment was delayed for 5 minutes. This dose is probably relatively larger than could be injected by any known viper in the case of a full-grown man. Further, in this case death did not take place until upwards of 24 hours after the injection, while in a control experiment with the same dose (Experiment 22) a fatal result occurred in four hours. Further, with the same large dose recovery took place when treatment was carried out half a minute after injection. Again, 30 milligrammes per kilogramme (three lethal doses) killed a control cat in $4\frac{1}{2}$ hours, but in three cases treated, $\frac{1}{2}$, 5, and 10 minutes respectively after injection, all recovered, as did one after 10 milligrammes per kilogramme, although a control with this last dose died in 30—40 hours. In all the experiments of both series the recovered animals were alive and well five days and upwards after the injection of the venoms, which is two days longer than death has ever taken place in any of the control animals.

Table III.—Experiments with Daboia Venom.

No.	Animal.	Weight.	Actual dose.	Dose per kilogramme.	Time of ligature.	Amount of permanganate.	Ligature released after.	Result.
16	Rabbit	kilogrammes. 2	milligrammes. 100	milligrammes. 50	30 secs.	gramme. 0·25	mins. 3½	Died, 9—17 hrs.
17	"	2	20	10	30 "	0·25	4	" 26 hrs.
18	"	2	20	10	...	Nil (control)	...	" 3 "
19	"	2½	6·875	2·5	30 secs.	"	2½	Recovered.
20	Cat.....	1¼	87·5	50	30 "	0·25	3	"
21	"	2	100	50	5 mins.	0·25	3½	Died, over 24 hrs.
22	"	2½	125	50	30 secs.	Nil (control)	3	" 4 hrs.
23	"	2	60	30	30 "	0·25	3¼	Recovered.
24	"	1½	45	30	5 mins.	0·25	3½	"
25	"	3	90	30	10 "	0·25	1½	"
26	"	2	60	30	30 secs.	Nil (control)	3	Died, 4½ hrs.
27	"	2	20	10	30 "	0·25	4	Recovered.
28	"	3	30	10	30 "	Nil (control)	3	Died, 30—40 hrs.

The above results are very encouraging, as the Viperine poisons are much less powerful, weight for weight, than are most of the Colubrines and Hydrophidæ, so that the amount of venom ejected by them can seldom, if ever, be more than two or three times a lethal dose for man.

In the course of the experiments it was observed that, even when the incision was made only 30 seconds after the injection of the poison into the subcutaneous tissues, a distinct blood-stained effusion is found, which serves as a very useful guide to the location and limits of the injected poison; after five or ten minutes the effusion is more extensive, and in these cases the incisions were prolonged up the limb for about 2 inches in order to try and destroy as much of the venom as possible. The fact that as favourable results have been obtained after five minutes as after half a minute, may very possibly depend on the effusion noted materially checking the absorption of the poisons, so that at the end of that time the rate of absorption may become very much less rapid than during the first few seconds after its injection. That a very rapid absorption occurs during the first few seconds after the injection (probably on account of the action of the poison in preventing clotting of the blood locally) is certain, for it was shown by Fayrer many years ago that a dog bitten in the tail by a full-sized cobra died, in spite of the tail being cut off between the bitten part and the body a few seconds after the bite. In such cases, however, the dose received is relatively much larger than could be injected by a cobra in the case of such a large animal as man, so that in practice (except in the very rare cases where the poison is injected directly into a vein) a fatal dose may not enter the system for some considerable time after the bite. This probability is supported by the fact that, in the case of Colubrine poisons at any rate, the minimal lethal dose is the same whether the venom is given subcutaneously or intravenously, yet it takes one or two days to produce death when injected under the skin, but only 5—20 minutes when inserted into a vein, so that under the former conditions the whole of the poison does not enter the circulation for a long period. These facts suggest the hope that the method of treatment here

advocated may produce good results, even when it is not put into operation until considerably longer periods than in any of the above experiments, especially when only slightly *supra*-minimal lethal doses have been received into the tissues.

Conclusions.

Further experiments will be necessary to ascertain the exact limits of the value of this form of treatment, and they will be undertaken immediately by one of us (Rogers) in India, fresh venoms being tried, as it is possible that they may be more rapidly absorbed than those which have been dried and redissolved. We think, however, that the results reported in this communication are sufficiently promising to make it advisable to place them on record, with a view to a trial being given to the method in suitable cases, especially as the crystals of permanganate of potash are actively antiseptic without acting as more than a superficial escharotic, so that the treatment has no markedly injurious effect which can be weighed for an instant against the terrible results of bites by venomous snakes. The process here recommended has already yielded experimental results far in advance of anything hitherto attained.

It is worthy of note that the earlier experiments of the first two authors were stopped nearly 30 years ago by the passing of the Act for regulating experiments on animals in England, but for which this logical sequence of their earlier work might very probably have been made many years ago.

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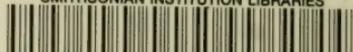
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