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Contributors

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Royal College of Surgeons of England

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ON THE

NATURE AND PHYSIOLOGICAL ACTION

OF THE

POISON OF *NAJA TRIPUDIANS*

AND OTHER

INDIAN VENOMOUS SNAKES.

(PART II.)

BY

T. LAUDER BRUNTON, M.D., Sc.D., M.R.C.P.,

AND

J. FAYRER, C.S.I., M.D., F.R.C.P. LOND., F.R.S.E.,

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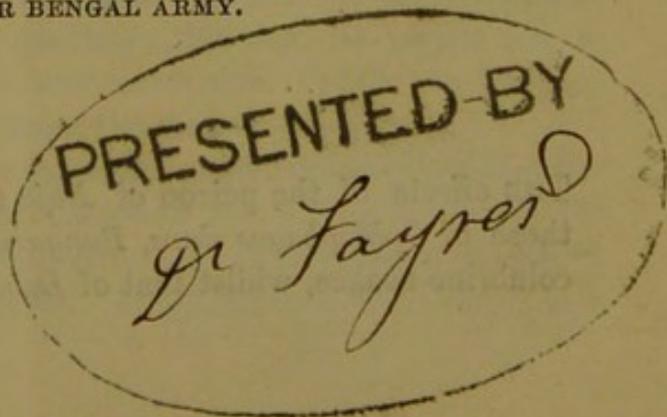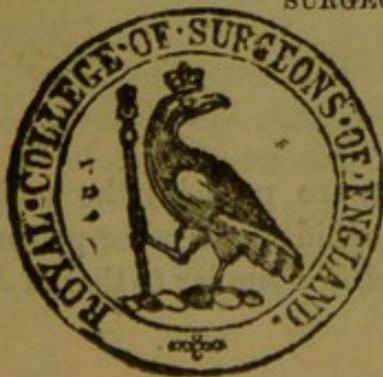
For Part i

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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. cœruleus, 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 *Craspedocephalus* 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, guineapig, 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, guineapigs, and rabbits peculiar twitching movements occur, which seem to represent vomiting in them; occasionally, in fact, dogs and guineapigs (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 coordinating power of the muscles of locomotion.

Hæmorrhage, relaxation of the sphincters, and involuntary evacuations, not unfrequently of a sanguineous or muco-sanguineous character, often precede death, and 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 guineapigs 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 guineapig. In one pigeon, killed by *Daboia*-venom, the blood remained permanently fluid after death; but in the other, and also in the guineapigs, 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 27*th*, 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 sunk 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 paralyzed; 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 paralyzed.

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 paralyzed. 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 paralyzed. 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 cubic centimetre of a mixture of *Daboia*-poison with alcohol (1 part poison with 4 of alcohol) was injected into the left thigh of a small guineapig 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 paralyzed. 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 11.—About 1 cubic centimetre of *Daboia*-poison (1 part poison mixed with 4 parts of alcohol) was injected under the skin of the left thigh of a guineapig 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 cubic centimetre 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 paralyzed, 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 paralyzed. 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 11*th*.—About ½ a cubic centimetre of milky-looking cobra-poison was injected into the right thigh of a guineapig 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 paralyzed, 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 paralyzed.

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

Exp. *a.*—*March* 10*th*, 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.

Exp. *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.

Exp. *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.

Exp. *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.

* 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.

12.39. Almost paralyzed; 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.

Exp. *e.*—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.

Exp. *f.*—A small rat-snake (*Ptyas mucosa*), about 2 feet long, was bitten by a *Bungarus cœruleus* 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.

Exp. *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.

Exp. *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.

Exp. *i.*—A *Bungarus cœruleus*, 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.

Exp. *j.*—A young and very small, though lively, cobra, 14 inches long, was bitten in the muscular part of the body by a large krail (*Bungarus cœruleus*), 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.

Exp. *k.*—*July* 10*th*, 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.

Exp. *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.

Exp. *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.

Exp. *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.

Exp. *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.

Exp. *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.

Exp. *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.

Exp. *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 &c. on the Action of the Poison.

The activity of the poison is not destroyed, and scarcely impaired, by drying. We have made no comparative experiments 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 guineapig 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. Fayrer in India.

Experiment XI.

October 28*th*, 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 ½ a grain diluted with alcohol (in which it was only imperfectly soluble), was injected into the thigh of the same guineapig 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 his 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, paralyzed.

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 centimetres.

Experiment XII.

May 19*th*.—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 guineapig's hip at 3.25. Twitching began almost immediately.

3.30. Restless. Hind leg paralyzed.

4. Twitching acute in hind leg.

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

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 paralyzed.

4.45. In convulsions. Dead.

Experiment XIII.

May 19*th*.—Dried cobra-poison, dissolved in liquor ammoniæ, injected into a guineapig'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 guineapig becomes immediately very restless.

4.15. Paralyzed. 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 cubic centims. of water.   Another piece, treated in the same way, was laid in 9 cubic centims. 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 ten lettuce- and ten cress-seeds were dropped into each.   Ten drops of a solution of dried cobra-poison, containing ·0355 gramme in 3 cubic centims. 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 ten 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 21*st*, 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 paralyzed 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 paralyzed. 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 paralyzed. 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 7 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 28*th*, 1872.—1.49. One quarter of a drop of cobra-poison put into a guineapig'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 29*th*.—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 paralyzes 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 guineapig 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. ·018 gramme of dried cobra-poison, dissolved in 1 cubic centim. of water, was injected into the flank. Almost immediately the nose of the animal began to twitch up every few seconds.

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

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

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 cubic centimetre 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 curarized frog.

Experiment XXIV.

September 4th.—The motor nerves having been tested and found to be completely paralyzed, 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 centimetres.

The poison paralyzes 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 5 or 6 drops of a strong but not perfectly concentrated solution of dried cobra-poison into the muscles of the left thigh of a guineapig.

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

12.47. The leg seemed paralyzed 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 guineapig 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 guineapig (No. 1), and immediately after decapitated another, healthy guineapig 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 paralyzes 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 paralyze 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 cubic centims. of serum ; but, with this exception, all the conditions under which the two legs were placed were exactly alike.

July 19*th*.—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 supervened 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 8*th*, 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 paralyzed, 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 ¾ cubic centimetre 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 guineapig was killed by decapitation. On opening the thorax of No. 1 (the poisoned guineapig) 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.

Guineapig, No. 1. No contraction. Coil at 0.

Guineapig, 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 paralyzed 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 paralyzed sooner than those which are paler (Experiment XXV.).

Experiment XXIX.

September 4th.—A cannula was placed in the carotid of a large guineapig, and ½ cubic centimetre 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 twenty 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 befor⋅ 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., & XXXII., where poison, which had undergone partial coagulation, was employed.

Experiment XXX.

January 14*th*.—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 14*th*.—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 15*th*.—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 15*th*.—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 9*th*.—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 in-

troduction 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 curarized 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 disorganizing 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 diffluent, 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 ¾-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 17*th*.—About three drops of cobra-poison were injected under the skin of the flank of a guineapig at 12.48 P.M. Immediately afterwards the guineapig 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 coordinating 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 coordination 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 paralyzed 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 Exp. XXXVII. and those succeeding it. Its occurrence in man is indicated by the symptoms of a case described by Dr. Hilson (Ind. Med. Gaz., Oct. 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 paralyzed, as is seen from Exp. 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 (Exp. XLVII. &c.); 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 Exp. 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 (Exp. 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 (Exp. VI. & 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, &c. 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 paralyzed; 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 paralyzed.

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. 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 paralyzed, 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 paralyzed; 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 paralyzed. 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 14*th*.—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 paralyzed. 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 centimetres 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 tetanized. 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 centims., 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 paralyzing action of the poison on the ends of the motor nerves becomes very evident.

Experiment XXXIX.

May 12*th*, 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.
Right.	37·5	Distinct contraction.
Left.	7·0	No distinct contraction. When the muscles were irritated by single induced shocks, applied to them directly,
Single shock.	7.5	they contracted almost equally.

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 14*th.*—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 paralyzing 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 15*th*.—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 20*th*, 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.

Distance of primary from secondary coil.

Time.	Frog 1.	Frog 2.	
About 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.
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 21*st.*—The sciatics of the other legs were exposed and irritated.

Time.	Distance of primary from secondary coil.		
	Frog 1.	Frog 2.	
..	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.

Dec. 4*th.*—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.

Aug. 27*th.*—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 com-

pletely 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 paralyzed.

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 paralyzed 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 paralyze them, or at least greatly to diminish their power.

This is evident from the following experiment.

Experiment XLV.

A dog was etherized 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 paralyzed; 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 paralyzed, 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 paralyzed; 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. Paralyzed. 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 centims. There was movement of left hand.

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

At 12 centims. also faint movement of left leg.

At 15 centims. 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 centims., the right leg contracts.

Coil at 42 centims. 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., &c.

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 paralyzed 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 19*th*.—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 paralyzed; 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 centims. distance, faint contractions in both arms. At 0 centim. 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·centims. 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 centims., 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 (1st supply), diluted with ½ cub. centim. 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 paralyzed; the fore limbs still move, but much less than before.

1.30. Frog almost motionless. Contractions of the fore llimbs 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 paralyzed before the motor nerves. It is indeed difficult to say whether the motor nerves were paralyzed in this case or not, as the muscles themselves were distinctly weakened.

Experiment XLIX.

Dec. 1*st*, 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.   Do.   do.
Right. Distinct contraction of whole leg. Coil 50.
Left.   Do.   do.
Sciatics exposed and irritated.
Right. Contraction. Coil 77·0.
Left.   Do.   ,, 52·0.
3.28. Right. Do.   ,, 50.
Left.   Do.   ,, 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.

Sept. 13*th.*—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 paralyzed.

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 12*th*, 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 sprung 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 paralyzed 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 Türck's method, shows that in cobra-poisoning the diminution of reflex action is due to the latter of these causes.

Experiment LIII.

May 19*th*, 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 Setchenow'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.
„ 16*th.*—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	
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.

Time	Left	Right
1.3	6	3
1.6	5	5
1.11	6	6
1.16	6	12
1.18	5	6

Time.	Left.	Right.	
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 guineapig.

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 paralyzed. 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 30*th*.—A cannula was placed in the trachea of a cat, and 1½ decigramme of dried cobra-poison was weighed out and dissolved in a small quantity (about 2 cub. centims.) 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 ·02 grain dissolved in a little water, as the cat did not seem about to die.

6.2. Injected 1½ cubic centimetre 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 paralyzed.   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 paralyzed.

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 14*th*, 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 25*th*.—At 3.34 a little cobra-poison was injected into the peritoneum of a guineapig. 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 np.

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 coordination; but the animal could run up to the last, although it could not walk. This indicates that the higher coordinating centre (probably the cerebellum) was paralyzed before the lower ones, just as in the case of a man who is drunk.

Experiment LX.

August 29*th*, 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 two cubic centimetres 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 dark 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 intestines 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 paralyzed; 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, &c., 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.

<center>*Experiment* LXI.</center>

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

2.36.30. One cubic centimetre 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 grs. to 1 fl. oz.) was injected into the side.

2.57. Twitching 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 paralyzed, 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.

<center>*Action of Cobra-poison on the Stomach and Intestines.*</center>

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 guineapigs, though to a less degree. Its occurrence in guineapigs 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 LXIV. after that nerve had been divided in the neck; and the failure to bring any thing 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 aërated, 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 aërated ; 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 aërating 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 arterialization 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. & LXVI., is very remarkable. The want of coordination 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 connexion 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.

Nov. 29, 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 21, 1873.—A rabbit was etherized 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. Respiration 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 21, 1873.—A rabbit was etherized, 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.

Sept. 15*th.*—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 ·01 grain of dried cobra-poison dissolved in $\frac{1}{2}$ cub. centim. 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 ·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 9.—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 centimetres.

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 paralyzed 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 paralyzes 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 paralyzed (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 paralyzed 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 paralyzed ; 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°·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. Teperature 100°·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 any thing, more vigorously than before.

4.40. Heart beats steadily, but apparently with less vigour. Temperature 100°·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°·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 26, 1872.—Half a drop of cobra-poison diluted with $\frac{1}{2}$ cub. centim. of water was injected under the skin of a guineapig, 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 $\frac{1}{2}$ cub. centim. 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.

Jan. 14, 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 connexion 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 two grains in three 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.
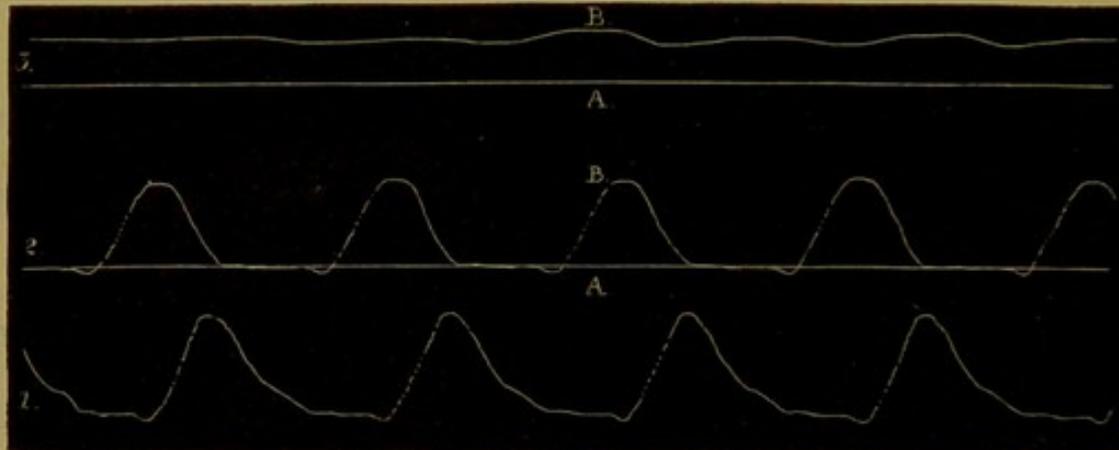
These tracings were obtained from a frog's heart by means of a small mercurial manometer connected with the aorta. The tracings all read from right to left.

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 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.

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		
1.48	57	..	Fæces passed. A clot formed in the cannula and had to be removed.
1.55	70		
About 1.58	8C	..	Injected some more poison.
1.58½	20		
1.59	55		
1.59½	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.
2.17½	..	..	Cornea still sensible.
2.18	85	..	Convulsive movements.
2.19¾	90	..	Convulsions.
2.20½	80	80	No movement.
2.20¾	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.
2.21¼	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.
2.21¾	100	64	Convulsions.
2.22¼	105	..	There were now 8 pulsations, and then an interval of 6 seconds, during which the pressure went down to 43 millims. Five beats

Time.	Mean blood-pressure. millims.	Pulse per minute.	
			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 millims. of mercury. One cub. centim. 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 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 one 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 paralyzed and motionless, it seems probable that, notwithstanding its colour, it was saliva and not bile.

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

[*] Thanatophidia, p. 43. [†] Indian Medical Gazette, May 1, 1873, p. 19.

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, cautery, 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 (*Enhydrina 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 reëstablished, 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 paralyzes 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 seventy-five 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 Med. Gazette,' Oct. 1873).

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* 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.

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.

* Such an apparatus has now been constructed.