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“Note on the Effect of various Substances in Destroying the Activity of Cobra Poison.” By T. LAUDER BRUNTON, M.D., F.R.S., and Sir JOSEPH FAYRER, K.C.S.I., M.D., F.R.S. Received June 20, 1878.

In a paper, read some time ago before this Society, by Mr. Pedler, he mentioned his discovery of the fact that the activity of cobra poison was completely destroyed by admixture with perchloride of platinum. This substance, however, could only be regarded as a chemical and not as a physiological antidote to the poison, inasmuch as it had no power to modify or prevent the action of the venom after its absorption into the blood. Mr. Pedler expressed his opinion that the proper method of pursuing the investigation was to investigate separately the action of platinum salts and of cobra poison upon the animal body. In the discussion which followed we stated that the method proposed by Mr. Pedler was in the present instance not likely to lead to any results, and that as the action of the substance employed by him was in all probability due to its simply forming an insoluble compound with the cobra poison and not to any action of the platinum *per se*, certain other metallic salts would have a similar action to the perchloride of platinum. Experiments have confirmed the opinion we then expressed,* and we find the action of chloride of gold is precisely similar to that of perchloride of platinum, the cobra venom being rendered entirely inert by admixture with the gold salt before its injection into the body. Chloride of gold, however, like perchloride of platinum, is merely a chemical antidote, and does not modify the action of the venom after its absorption into the circulation. Permanganate of potash, which has been recommended as an antidote, also destroys its activity completely. Chloride of zinc, chloride of mercury, nitrate of silver, and carbolic acid all diminish the activity of the poison, and prolong life when mixed with it before its injection; but they do not prevent death, nor do they prolong life to any great extent. Perchloride of iron has very much

* The Poison of the Cobra, by A. W. Blyth, M.R.C.S. “The Analyst,” 28th February, 1877, p. 204.

less action upon the poison than one would expect, and it prolongs life to a very slight extent. *Liquor potassæ* impairs the activity of the poison very considerably, and prolongs life for several hours. When a large dose of cobra poison is injected, none of these substances prevent death even when applied immediately to the wound. The reason of this probably is that they do not come into such perfect contact with the poison as to destroy the whole of it, and the portion which escapes destruction is sufficient to kill. It is possible, however, that when minimum doses only are injected, the local application of one or other substance may turn the balance between life and death, but this point we must reserve for a future paper.

Our first experiment was made in order to compare the action of chloride of platinum alone with that of cobra poison alone, and of chloride of platinum injected after cobra poison.

Experiment I.

February 25th, 1878. A cat weighing 4 lbs. had about 1 cub. centim. of the chloride of platinum solution of the British Pharmacopœia injected into its flank.

3.44 P.M. Injection completed.

3.55 ,, No apparent effect. The cat well and playful.

No symptoms whatever were observed, but after some days a slough formed at the point of injection. Chloride of platinum thus appears to have no physiological action whatever when injected subcutaneously beyond its effect as a local irritant.

In Experiments II and III similar doses of cobra poison were subcutaneously injected into two cats ; but in Experiment III the injection of the poison was followed immediately by the injection of a solution of chloride of platinum into the same spot, so as if possible to destroy the venom which had not yet been absorbed. In this case death was delayed, but not to a very great extent, as it occurred in an hour and fifty minutes after the injection of the venom and chloride of platinum, and in an hour and two minutes in the animal which received the poison alone.

Experiment II.

Black cat, weight 5 lbs.

25 mgms. of cobra poison dissolved in 1 cub. centim. of distilled water injected into skin of flank at 3.26 P.M. of 25th February.

3.28 P.M. Vomiting. It had taken chloroform to keep it quiet whilst being weighed, and was recovering from the chloroform. Micturated. Drooping head on one side.

3.32 P.M. Vomiting again. Looks much depressed. *Defecated.*

3.40 ,, Breathing slow. *Shallow.*

3.41 ,, Vomiting again.

3.45 ,, Twitching of muscles.

- 3.52 P.M. The same state.
- 3.58 ,, Defecating. Micturating.
- 3.59 ,, Retching. Vomiting. Moves about in a restless manner.
- 4.6 ,, Moving *backwards* with staggering gait.
- 4.12 ,, Staggers, and head droops.
- 4.13 ,, Falls over on its side. The respiration is slow. Reflex from eye and ear almost gone.
- 4.14 P.M. Reflex from head and legs when irritated. None from tail.
- 4.15 ,, Attempts to rise.
- 4.18 ,, Got up, but fell over again. Tried to walk. No reflex from the head.
- 4.20 P.M. Head raised and fell over again. Touching the eye seems to rouse the cat, but no reflex of lids. Tries to get up, but cannot. Fell over on the opposite side.
- 4.24 P.M. Again a struggle to rise.
- 4.27 ,, Touching the eye produces no reflex. Breathing very slow. Convulsive twitching of limbs.
- 4.28 P.M. Apparently dead. Heart still beating one hour and two minutes after injection of poison.
- The blood, after death, formed a *firm* coagulum.
- Intestines much congested. Patch of congestion in stomach. Red serum effused into the peritoneal cavity.
- No local symptoms or changes.
- A good deal of food in the stomach, notwithstanding the vomiting. Digestion was in full action.
- In these and other experiments the dose of cobra poison was regulated according to the weight of the animal, the same proportion per pound weight being given in each case.

Experiment III.

A grey cat 4 lbs. weight had 20 mgms. of cobra poison, dissolved in one cub. centim. of distilled water, injected under skin of flank at 3.39 P.M. of 25th February.

At 3.40 P.M. a solution of chloride of platinum injected at the same spot.

- 3.42 P.M. Very restless.
- 3.43 ,, Drinks water.
- 3.52 ,, Vomiting.
- 3.55 ,, Dull and depressed.
- 4.10 ,, Same condition.
- 4.20 ,, Sluggish.
- 4.30 ,, Restless. Moving about.
- 4.45 ,, Staggers. Getting very sluggish. Walks with difficulty. Head drooping.

4.54 P.M. Shivering. Head fallen over.

5 P.M. Fallen over. Slow paralysis creeping over limbs. Respiration slow. Gets up, rolls over again. On touching the eye the eyelid moves. Reflex not gone from the ear.

5.6 P.M. Fallen over. Paralysed. Reflex nearly gone, still slight from ear. Pupils dilated.

5.9 P.M. Convulsions. Pupils become normal again. Respiration very slow—thirteen per minute.

5.20 P.M. Tries to rise. Very feebly.

5.22 ,, Fallen quite over.

5.23 ,, In same condition. Makes feeble efforts to rise. Pupils dilated again.

5.27 P.M. Again tries to rise. Micturition.

5.29 ,, Convulsions.

5.30 ,, Dead.

No local symptoms, *i.e.*, no extravasation about the puncture. No congestion of stomach or bowels. Stomach empty. Blood coagulated *after death*.

Injected at 3.39 P.M.

Died at 5.30 P.M.

Death in one hour and fifty-one minutes.

The following experiments show the effect of chloride of gold in completely destroying the cobra poison.

Experiment IV.

March 7th, 1878. Three mgms. of cobra poison, mixed with 1 grain of chloride of gold, dissolved in 40 grain measures of water, injected into the hip of a white guinea-pig, weighing 18 oz., at 3.50 P.M.

4.10 P.M. Crouching quietly in corner of box. Tremor, perhaps fright.

4.15 P.M. Seems uneasy; crouching in corner. No other change. Recovered without any bad symptoms.

Experiment V.

March 14th. In this experiment a very large dose of poison was used.

30 mgms. of cobra poison, mixed with $1\frac{1}{3}$ cub. centims. of a 10 per cent. solution of chloride of gold, were injected into a guinea-pig weighing 20 oz., at 3.30 P.M.

75 cub. centims. of water was used to wash out glass, and then injected. The poison and the chloride form a yellow creamy precipitate.

3.30 P.M. Began to jerk and twitch immediately, excited, running about the box.

3.35 P.M. Crouching in corner, twitching, but not otherwise affected.

3.42 P.M. Not apparently affected.

3.52 ,, Crouching; does not appear affected, but is weak in the hind legs when he runs.

4.10 P.M. Very little affected; hind legs weaker, but he is very active otherwise.

4.20 P.M. Much the same; active, except that hind legs seem rather weak.

4.55 P.M. Remains the same. Recovered perfectly without any further symptoms.

In order to make sure that the dose of cobra poison would certainly prove fatal if administered alone, the animal, after its recovery, was injected with a quantity of pure cobra poison, fifteen times less than that from which it had recovered, and, as will be seen from Experiment VI, death rapidly occurred.

Experiment VI.

March 14th. White guinea-pig that recovered from 30 mgms. of cobra poison, mixed with chloride of gold.

At 4.45 P.M., 2 mgms. of cobra poison were injected into the hip.

4.50 P.M. Very restless; scratching his skin.

4.52 ,, Twitching; very restless.

4.59 ,, Squeaking; very restless.

5.10 ,, Injected leg weak; not so restless.

5.15 ,, Trying to vomit; twitching movement of head, jerking upwards; violent efforts to vomit; a sort of cough; flows from nostrils and mouth; getting gradually paralysed, he still crawls; nearly violent efforts to vomit.

5.24 P.M. The animal creeps along, putting his head along the ground.

5.26 P.M. Apparently dead; heart still beats.

At 4.45 P.M. the injection was made, and at 5.26 P.M. the animal was dead. Death in 41 minutes.

Experiment VII shows that chloride of gold is a chemical, and not a physiological antidote, and does not prevent the action of the poison after its absorption.

Experiment VII.

March 14th. Guinea-pig, weight 16 oz.

5 mgms. of cobra poison dissolved in 1 cub. centim. of water, and injected into the right hip at 3.39 P.M.

In 3 minutes afterwards $1\frac{1}{3}$ cub. centims. of a 10 per cent. solution of chloride of gold were injected into another spot (the left hip, at 3.42).

3.43 P.M. Very restless.

3.45 ,, Very restless; head twitching; drops the left leg.

3.53 P.M. Restless.

3.55 „ Weak, dropping both hind legs; left appears quite paralysed.

4.5 „ Getting weaker; paralysis creeping over him.

4.10 „ Barely moves; hind quarters completely paralysed.

4.12 „ Convulsions.

4.19 „ Heart still beats feebly.

4.20 „ Dead.

Experiment VIII shows that permanganate of potash destroys the action of the venom.

Experiment VIII.

5 mgms. of poison were dissolved in 1 cub. centim. of water, and mixed with 1 cub. centim. of liquor potassæ permanganatis of the British Pharmacopœia, and injected under the skin of a guinea-pig. No symptoms were produced, and the animal remained quite unaffected.

Experiment IX.

Two rabbits of the same litter, each weighing exactly 2 lbs. were taken. 5 centigrammes of cobra poison dissolved in 1 cub. centim. of distilled water, were mixed with 1 cub. centim. of liquor potassæ permanganatis (B.P.), and allowed to stand for about 8 minutes. The mixture was then injected under the skin of the flank of one rabbit. No symptoms whatever were produced, and the animal though kept under observation for some weeks remained quite unaffected by the poison. 5 mgms. of cobra poison, dissolved in 2 cub. centims. of water, were injected into the other rabbit at the same time. During the injection a little of the poison was lost, so that the animal did not receive the full dose, yet it died in 30 minutes.

Chloride of zinc delays the action of the cobra poison, but does not prevent it, as appears from Experiments X and XI, in which a guinea-pig that had received 3 mgms. of pure cobra poison (Experiment X) died in 45 minutes, whereas one that had received a similar dose, previously mixed with chloride of zinc, lived for about 3 hours. Experiment XI.

Experiment X.

March 1st, 1878. 3 mgms. of cobra poison, dissolved in 2 cub. centims. of distilled water, injected at 3.43 P.M. into a guinea-pig's hip. Weight of guinea-pig 20 oz.

3.46 P.M. Twitching.

3.50 „ Restless twitching.

3.53 „ The same. Irritable; squeals; quarrels with the other guinea-pigs; respiration jerky.

4 P.M. The same.

4.5 P.M. Drags the injected leg, which is nearly paralysed.

4.15 P.M. Much the same.

4.19 P.M. Paralysed, and crawls with difficulty; all hind quarters invaded by poison's influence.

4.21 P.M. Paralysis extending; struggles to rise; can only move the head. Reflex from eye diminished.

4.25 P.M. Convulsive movements.

4.28 ,, Dead in 45 minutes. Heart continued to beat after apparent death.

Experiment XI.

Red guinea-pig, weight 16 oz. At 3.46 P.M., 1st March, 3 mgms. of cobra poison, dissolved in 2 cub. centims. of distilled water and mixed with .01067 chloride of zinc, were injected subcutaneously. The poison and the chloride were mixed 5 minutes before injection.

5.53 P.M. Guinea-pig restless; twitching; grunting; keeps licking the puncture; irritable with other guinea-pigs.

4 P.M. Very restless. Puncture seems irritable; leg partially paralysed.

4.15 P.M. Much the same.

4.29 ,, Much the same.

4.35 ,, Not quite so restless.

4.45 ,, Active; runs about.

4.45 ,, Restless; not worse.

5 ,, Seems pretty well now.

Died about 7 o'clock.

Liquor potassæ impairs the activity of the poison, but does not destroy it, as will be seen from Experiment XII, in which the dose of the poison, which had usually proved fatal considerably within an hour, did not cause death until 8 hours had elapsed.

Experiment XII.

March 14th. Guinea-pig, weight 16 oz.

5 mgms. of cobra poison dissolved in 1 cub. centim. water mixed with 1 cub. centim. of liquor potassæ injected into hip at 3.52 P.M.

3.53 P.M. Twitching.

4.0 ,, Leg paralysed.

4.20 ,, It seems much the same.

4.35 ,, Appears much the same.

4.55 ,, Appears much the same.

5.35 ,, Much the same.

At 11.30 it was lying with left hind leg paralysed, could walk when irritated, mouth opened, head twitching back frequently.

11.45 P.M. its respiration ceased, but when the skin of the belly was pinched the animal took a breath and respiration continued for about a minute afterwards. The heart continued to beat until 11.50.

Liquor ferri perchloridi fortior (B.P.), has much less action upon

the cobra poison than one would have expected, as will be seen from Experiment XIII, in which death occurred in an hour and a half.

Experiment XIII.

March 14th. Guinea-pig, weight 16 oz.

5 mgms. cobra poison dissolved in 1 cub. centim. water mixed with 1 cub. centim. of liquor ferri perchloridi fortior (B.P.) injected into the left hip of the guinea-pig at 4.4 P.M.

4.20 P.M. Dropped the hind leg, but otherwise seems active and well.

4.35 „ Very active, but leg drops.

5.10 „ Hind leg paralysed.

5.15 „ Tries to crawl, cannot, struggles, convulsed.

5.16 „ Jerking convulsions.

5.17 „ Almost dead.

5.18 „ Dead.

Carbolic acid likewise delays the action of the poison, but to a very much smaller extent than liquor potassæ, as is proved by Experiment XIV.

Experiment XIV.

March 14th. Carbolic acid, one-third of a cub. centim. mixed with 5 mgms. of cobra poison in 1 cub. centim. of water, injected into hip of a guinea-pig weighing 14 oz., at 4.55 P.M.

5.55 P.M. Much the same.

7.50 „ Very slight convulsions.

7.55 „ Much the same.

8.0 „ Dead.

Experiment XV.

March 7th. 3 mgms. cobra poison mixed with 1 grain of nitrate of silver dissolved in 40 grains of water, injected into hip of black guinea-pig, weighing 14 oz., at 3 P.M.

4.10 P.M. Twitching; crouching in corner, crying out slightly, as guinea-pigs are wont to do when restless.

4.15 P.M. Restless, crouched in corner of box, twitching of muscles, cries as before.

4.25 P.M. Restless, crying fretfully.

Died in about one and a half hours afterwards, about two hours after the injection of the poison.

Experiment XVI.

March 7th. 3 mgms. of cobra poison mixed with 10 grain measures of a saturated solution of chloride of mercury (corrosive sublimate), injected into hip of guinea-pig (black and white), weighing 14 oz., at 3.56 P.M.

4.10 P.M. Twitching, uneasy, tremors.

4.15 „ Quiet, crouching in the corner.

4.24 P.M. Restless, but does not seem to twitch; cries like the other guinea-pigs occasionally.

About 6 the animal lay quiet with occasional twitches, and about 6.30 it died.

In order to ascertain which substance would be most likely to save the life of the animal by local application to the point of injection, either by destroying the poison itself, or by preventing its absorption by the tissues, we applied chloride of gold, permanganate of potash, chloride of platinum, and carbolic acid locally, the method adopted being to inject the poison under the skin of the leg, immediately afterwards to apply a ligature tightly above that point, and then to make an incision and apply the substance in just the same manner as we would have done if the animal had actually been bitten. From the following experiments, however, it will be seen that the absorption of the poison is so rapid that all local applications were useless. It should be noted that the quantity of poison we employed was large, and it still remains to be seen whether these local applications may turn the balance between life and death when the quantity of the poison would be just sufficient to kill in case of no remedy being applied.

Experiment XVII.

Guinea-pig weighing 1 lb.

4.27½ P.M. Injected 2 grs. 9 centigrammes of cobra poison into thigh, ligature applied immediately.

4.29½ P.M. Solution of chloride of platinum applied.

4.31 „ Twitching violently.

4.33 „ Twitching violently; ligature remains on limb.

4.40 „ Not worse; the ligature is evidently delaying the action of the poison.

4.47 P.M. Getting weaker.

4.50 „ Convulsed.

4.52 „ Dead.

Death delayed in this instance.

Experiment XVIII.

April 4th, 1878. Guinea-pig weighing 1½ lb.

4.11' 10" P.M. Injected 3 centigrammes of cobra poison.

4.13 P.M. Chloride of gold solution, 1 in 10; ligature kept on until chloride of gold was applied.

4.15 P.M. Twitching.

4.16 „ Leg paralysed.

4.17 „ Animal nearly paralysed.

4.19 „ Do. dying.

4.20 „ Convulsions.

4.22 „ Dead.

Experiment XIX.

April 4th, 1878. Guinea-pig weighing $1\frac{1}{2}$ lb. Injected 4 centigrammes of cobra poison into leg.

4.1 P.M. Ligature applied immediately. Permanganate of potash applied immediately.

4.5 P.M. Twitching.

4.10 „ Dying.

4.13 „ Convulsion.

4.14 „ Dead.

Experiment XX.

April 4th, 1878. Guinea-pig weighing 1 lb.

3.45' 20" P.M. Injected $\frac{3}{4}$ gr. = 4 centigrammes of cobra poison under skin of leg. A ligature was applied round the leg in one minute, and in five minutes permanganate of potash was rubbed into an incision made over the site of injection.

3.52 P.M. Ligature cut.

3.53 „ Twitching violently; leg paralysed.

3.55 „

3.57 „ Dying.

3.58 „ Dead—less than 13 minutes.