

Some Experiments with the Venom of Causus rhombeatus.

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In Sierra Leone there are numbers of a small viperine snake of the genus *Causus*, known locally as “chicken snakes,” of which it has been my good fortune to get several fine specimens. The largest was 463 mm. long, the tail being only 35 mm.

The poison-gland is remarkably long, practically one-fourth the length of the snake. It lies dorsally, immediately beneath the skin, and shows no indication of attachment to any other structure. It is flat and ribbon-like, with a maximum breadth of about 6 mm. It is of a greyish-pink colour, spotted in its middle third. It stretches as far back as the posterior level of the heart. At the quadrato-mandibular joint it narrows into a flat duct which becomes attached to underlying structures and is covered by fascia. The duct ends in an ampulla which just touches the maxilla when the fang is erected. The entire gland can be seen by merely reflecting the skin.

The venom seems to be ejected by the contraction of the gland itself. In a chloroformed snake, with the gland exposed by reflection of the skin, a slight pinch of the gland with the forceps causes a vigorous contraction. If the end of the gland be pinched, a peristaltic contraction forwards takes place, towards the duct, and some venom is ejected. If the gland be squeezed in the middle, a peristaltic contraction forwards occurs on both sides of the forceps.

In the experiments here recorded the venom was used in three ways—fresh venom dissolved in sterile salt solution, dried venom dissolved in sterile salt solution, and the alcoholic precipitate of venom re-dissolved in sterile salt solution.

The action of the venom, which seemed the same in all three methods of administration, was shown in local ecchymosis, and in drowsiness and muscular weakness. In about half the cases there was marked slowing of the respiration with great difficulty in inspiration. *Post-mortem* examination showed in most cases superficial hæmorrhage into the viscera, especially the heart and lungs, the lungs being in two cases filled with fluid and deeply discoloured by hæmorrhage.

Experiment 1.—After killing the snake the two glands were at once removed and squeezed into sterile salt solution in a hypodermic syringe, and

the whole was injected into the pectoral muscles of a chicken weighing 5 ounces. 10.20 a.m., venom injected. 10.27, chicken looked sleepy, stood without moving, respiration 47. 10.55, animal propped itself up against the side of the box, respiration 40. 11.15, respiration 35, inspiration difficult, ecchymosis over abdomen and lower part of thorax. 11.45 a.m. to 2 p.m., respiration gradually slowed from 35 to 24. 2.45, the animal when placed flat on its back remained in that position with quickened respiration. 3.15, died quietly. *Post mortem*: a large, dark maroon-coloured ecchymosis over the abdomen, most of the thorax, and the root of the neck: the pectoral muscles of the side injected were deeply blood-stained. On opening the body-cavity superficial hæmorrhages were found in the gizzard, liver, and heart: the right auricle contained a small, dark, soft clot; the endocardium of the right ventricle was much congested; the lungs were pale, with no excess of fluid.

Experiment 2.—The venom, mixed with sterile salt solution, of *one* gland was injected into the pectoral muscle of a chicken weighing 8 ounces, at 10 a.m. 10.5, wings began to droop, chicken gasped and kept swallowing as if there were some obstruction in the throat, respiration 22, inspiration very difficult. 10.40, respiration 16, inspiration much prolonged. 11.40, respiration 16, chicken could not get up when placed on its side. 11.42, respiration 11. 11.45, convulsions, with emission of blood-stained froth from the mouth, death. *Post mortem*: the vessels in the neighbourhood of the puncture were much enlarged, as were those of the abdominal wall and peritoneum: the iliac veins and vena cava were engorged with dark blood: a few hæmorrhages were found in the right lung: the left lung was of a dark cherry colour and full of frothy fluid: the right auricle and ventricle contained each a dark soft clot. In this case the comparatively rapid death was probably due to some of the poison having entered a blood-vessel; for, after the injection, some clotted blood was found in the needle of the syringe.

Experiment 3.—The venom of one gland was mixed with sterile salt solution in a syringe, and half of the mixture was injected into the left pectoral muscle of a fowl weighing 17 ounces, at 10 a.m., the respiration then being 30. 10.30, respiration 24, a little irregular; fowl squatting. 1.30 p.m., fowl quite lively. 10 a.m. on following day, dark ecchymosis near puncture; vessels on both sides of thorax and abdomen, but particularly of left side, much enlarged. 7 a.m. on third day, skin of whole abdomen green; the left leg of the fowl stiff. The fowl completely recovered by the end of the third day.

Experiment 4.—The venom of both glands was dried in the sun and its

weight was found to be 9 centigrammes. It was then dissolved in 21 minims of sterile salt solution, and 14 minims of the solution (= 6 centigrammes of the venom) was injected into one chicken (A), and the remainder (= 3 centigrammes of venom) into another chicken (B), at 10.15 a.m., the injection in each case being made into the right leg. 10.55: "A" respiration 29; "B" respiration 33, and sits with right wing outstretched; both fowls allow themselves to be touched without attempting to move. 11.35: "A" right leg dark blue and swollen; "B" right leg slightly ecchymosed, superficial vessels enlarged. 1.30 p.m.: "A" respiration 34, abdomen ecchymosed and superficial vessels enlarged; "B" respiration 35, some of the superficial abdominal vessels dilated, and slight ecchymosis of abdomen. 4.30 p.m.; both fowls lively and eager to feed: in "A" the leg is swollen and the ecchymosis has spread from the abdomen to the thorax; in "B" the leg is swollen and only the abdomen is ecchymosed. 6.30 a.m. on second day: "A" right side of abdomen and thorax swollen and discoloured; "B" whole of abdomen and right side of thorax ecchymosed. 6.30 a.m. on third day: both fowls limp, but are quite lively. 10 a.m. on third day: "A" quite lively, but its abdomen is still discoloured; "B" is almost normal, but has very slight ecchymosis at site of puncture. 10 a.m. on fourth day, both fowls are quite recovered.

Experiment 5.—The venom of both glands was dried in the sun, and found to weigh 16 centigrammes. 9.15 a.m., 12 centigrammes of the venom was dissolved in sterile salt solution and injected into the right pectoral muscle of a fowl. 10.30, respiration 36; ecchymosis all over right side of thorax and abdomen. 11.30, respiration 33, ecchymosis spreading to left side of thorax. 12.30, respiration 28. 2.15 p.m., respiration 28, ecchymosis spread over left side of abdomen and thorax and right wing. 2.40, convulsions, fowl died. *Post mortem*: subcutaneous tissue of abdomen and thorax full of blood-stained fluid; right pectoral muscle flabby and discoloured with blood; peritoneal vessels dilated, peritoneal cavity contains blood-stained fluid; tiny hæmorrhages in pericardium, vessels of myocardium dilated; both lungs were hæmorrhagic and contained much dark-coloured frothy fluid.

Experiment 6.—Two glands were cut up and treated with alcohol (90 per cent.). Two days afterwards the alcohol was filtered off, and the precipitate was redissolved in sterile salt solution. At 4.45 p.m. the whole of the solution was injected into the pectoral muscle of a fowl. 4.48, fowl staggered and fell, had slight convulsions and then lay quiet. 4.57, fowl staggered to rise, but failed; respiration 24. 5.10 fowl struggled to its feet; very drowsy, eyes closed, wings drooping; respiration 19. 5.22, fowl gasped, respiration 14, inspiration difficult. 5.31, respiration 18, noisy, as if the air passages

contained fluid. 10.0, fowl very unsteady, comparatively cold; abdomen ecchymosed. Fowl died during the night. *Post-mortem* examination showed ecchymosis of skin of abdomen and thorax, and effusion of blood into the pectoral muscle at the site of the puncture; the lungs were bright red and contained much blood-stained fluid.

On the Comparative Action of Stovaine and Cocaine as measured by their Direct Effect upon the Contractility of Isolated Muscle.

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It has been shown by Veley* that the affinity values of stovaine and cocaine by the methyl orange and borax precipitation methods are approximately equal. The method of measuring physiological activity of anæsthetic drugs, as described by Waller,† affords an independent control that can usefully be compared with affinity values.

Stovaine, sometimes called amyleine hydrochloride and originally prepared by Fournéau, has been successfully applied in recent years, especially for spinal anæsthesia, as also for general surgery and dentistry. As it is used for the same purposes and in doses of the same order as cocaine, the relative value of the two drugs has been compared in a series of memoirs or notices, more than 150 in number in various clinical journals. The general conclusions arrived at are: (1) as anæsthetics the drugs are of equal value, but stovaine produces vaso-dilatation, cocaine vaso-constriction; and (2) stovaine is less toxic than cocaine. The statement has even been made that stovaine does not produce any toxic effect.

Though, as stated above, the affinity values are approximately equal, yet the chemical constitution of the two compounds is wholly dissimilar. Stovaine is the hydrochloride of methyl ethyl dimethylamino-methyl carbinol benzoate $\text{HCl} \cdot \text{C}(\text{CH}_3)[\text{CH}_2\text{N}(\text{CH}_3)_2](\text{C}_2\text{H}_5)\text{OBz}$ and the base (molecular weight = 235), a benzoyl derivative of a diamino-tertiary amyl alcohol $\text{C}(\text{CH}_3)_2(\text{C}_2\text{H}_5)\text{OH}$ (Fournéau).‡

Cocaine (molecular weight of base = 303) is the methyl ester of benzoyl

* 'Trans. Chem. Soc.,' 1909, p. 763.

† 'Proc. Roy. Soc.,' June 24, 1909.

‡ 'Comptes Rendus,' 1904, vol. 138, p. 766.