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# BLOWPIPE DART POISON FROM BORNEO

BY

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Mr. Rodney Needham recently sent from Sarawak a block of poison used on darts by the nomadic Pĕnan of Borneo. The block weighed 9 grammes and was wrapped in stout dried leaves. Mr. Needham said that it was a two years' supply for blowpipe darts. He described the method of using it. "A little of it is scraped into a large leaf folded to make a slight hollow; on to this is poured a little hot water, and the mixture is smeared on the darts for a length of about three inches from the point, more thickly at the actual point than elsewhere because usually little of it enters the animal. An alternative method is to pour a little hot water on to the block of poison itself, and to rub the darts along the grooves in it." The dart is about eight inches long.

We now describe a pharmacological examination of this poison.

## RESULTS

*Experiments on Blood Pressure.*—The block of poison was found to powder easily, and the powder was soluble when ground up in water or in saline to form a solution with a slight brownish tinge. The effect of injecting this solution intravenously into cats anaesthetized with chloralose was determined, recording the blood pressure and in some experiments the respiration also by Gaddum's method (1941). Fig. 1 illustrates the effect in one experiment. A volume of solution containing 0.4 mg. powder caused a rise in blood pressure and after 2 min. cardiac irregularity. Later, twice this dose caused a rise and then a fall of blood pressure which continued abruptly to zero. During the action of the first injection there was a slight slowing of the respiration from 28 to 22 per min., and during that of the second to 18 per min.

In all experiments both in cats and rabbits in which the respiration was recorded, it was observed that the usually abrupt fall of the blood pressure to zero occurred without any more serious change in the respiration than that in Fig. 1, so that it was clear that death did not result from respiratory failure. When the heart was examined after death the left ventricle was found to be tightly contracted and hard.

*Slow Intravenous Injection.*—The time elapsing between the injection of the poison and the arrest of the heart, the abrupt fall in blood pressure, and the arrest of the heart in systole all suggested that the poison had an action not unlike that of a glycoside of digitalis or strophanthus. We therefore studied the effect of the slow intravenous infusion of the poison in a solution containing 1–2 mg. in 40 ml., since when administered in this way the cardiac glycosides produce characteristic changes. Observations were made in rabbits under urethane anaesthesia and in cats under chloralose anaesthesia. Some parallel observations were made in cats using a solution of ouabain (crystalline strophanthin, from *Strophanthus gratus*).

An infusion of ouabain causes at first a progressive fall in the heart rate. A fall was observed with the arrow poison, though it was often small; thus in one cat the heart rate fell from 180 to 146 per min.; in a second it fell from 232 to 196 per min., and in a third from 196 to 180 per min. Later the heart rate rose and the beat became irregular as it does when ouabain is infused. During the later part of the infusion artificial

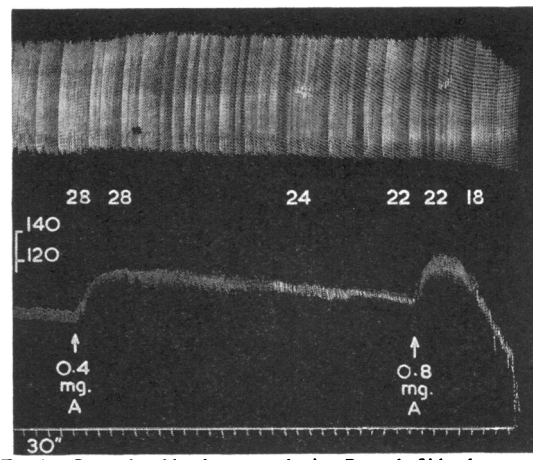


FIG. 1.—Cat under chloralose anaesthesia. Record of blood pressure (below) and respiratory movements (above) showing injection of 0.4 mg. and of 0.8 mg. of the poison (A). Note that 4 min. after the injection of 0.8 mg. the blood pressure fell to zero; the respiration became slower as indicated by the figures giving the rate per min. below the record.

respiration was usually given to ensure that death did not occur from respiratory failure. In some experiments the blood pressure fell more abruptly than in Fig. 1. In all experiments the arrest of the heart was the cause of death. The amounts of arrow poison calculated per kg. necessary to cause death in different animals are given in Table I, together with similar figures for ouabain.

TABLE I

LETHAL DOSE (MG. PER KG.) BY SLOW INTRAVENOUS INFUSION

| Arrow Poison | | Ouabain |
|---|---|---|
| Rabbit | Cat | Cat |
| 0·73 | 0·39 | 0·123 |
| 0·31 | 0·53 | 0·115 |
| 0·48 | 0·35 | 0·099 |
| 0·58 | 0·56 | 0·082 |
| | 0·66 | |
| | 0·46 | |
| Mean 0·52 | 0·49 | 0·105 |

The mean figure for ouabain, 0.105 mg. per kg., agrees with other published figures. Macdonald (1934) found a figure of 0.098 mg. per kg. for cats and Baker (1947) found a figure of 0.095 mg. per kg. for rabbits. Thus the toxicity of ouabain for rabbits is the same as that for cats; the figures in Table I show that the toxicity of the arrow poison for rabbits was the same as that for cats. Moreover, the arrow poison from Borneo, although a crude preparation, contained activity equal to 20% of that of crystalline ouabain.

*Action on Isolated Cat Heart.*—Experiments were carried out on the isolated cat heart perfused with Locke's solution through the aorta by Langendorff's method. An example is given in Fig. 2. Perfusion with Locke's solution containing 5 mg. per litre of the poison caused the rate of beat to fall at first from 164 to 126 per min. After 7 min. the rate became very much faster, the amplitude of contraction then steadily diminishing. Finally the ventricles stopped and then contracted firmly, the auricles continuing to beat. The record is not unlike that obtained when a digitalis glycoside is similarly perfused.

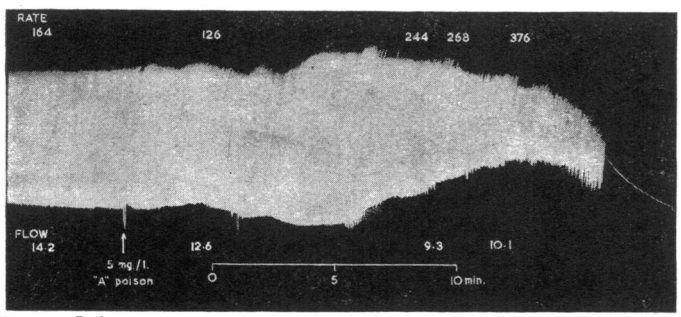


FIG. 2.—Isolated cat heart (Langendorff method). Effect of perfusing Locke containing 5 mg. of poison per litre. Figures above the record are the heart rate per min. Note the initial fall in rate and the later period of great quickening of rate. The beat was then arrested and the ventricle contracted firmly though the auricles continued to beat. Figures below the record are the coronary flow in ml. per min.

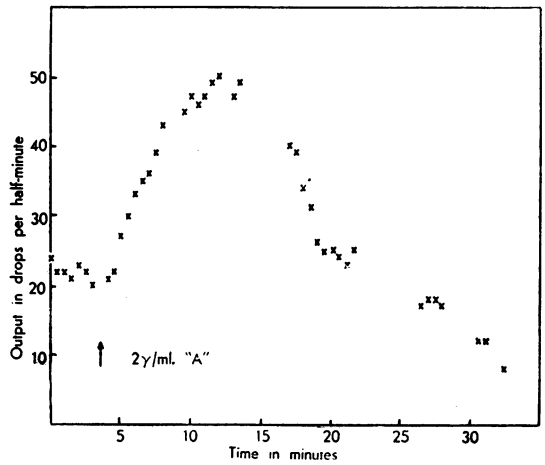


FIG. 3.—Frog heart perfused by Bülbring's method using Ringer containing one-quarter the normal amount of calcium. Ordinate: Output in drops per 30 sec. Abscissa: Time in min. Perfusion at the arrow with the poison (2 μg./ml.) caused a rise in the output resembling that caused by ouabain, when perfused in the same concentration.

*Action on the Isolated Frog Heart.*—In the observations so far recorded there was no evidence of any save a toxic action on the heart muscle. A substance which has the characteristics of a cardiac glycoside such as digoxin or ouabain should have an early beneficial action by which the force of the beat is improved and the output increased. This effect can be demonstrated very simply for ouabain by using the Bülbring (1930) preparation of the frog heart in which the inferior vena cava is cannulated for perfusion from a Marriotte bottle, and one aorta is cannulated in order to measure the output, the other being tied. When the heart is perfused with frog-Ringer containing one-quarter the normal amount of calcium, the change to a fluid containing in addition ouabain (2 μg./ml.) causes a large rise in output.

A series of seven experiments was therefore carried out with this preparation, using instead of ouabain the poison under examination in a concentration of 2 μg. poison per ml. Fig. 3 illustrates the effect observed, which closely resembles the effect obtained with ouabain (see Burn, 1952). Thus the poison resembles a cardiac glycoside such as ouabain in this important respect also.

*Toxicity for Mice.*—Although the glycosides of digitalis and strophanthus have a high toxicity per unit of body weight for cats and for rabbits, they have a much lower toxicity for mice. If the active principle in the poison was similar to one of the cardiac glycosides, then it should be found to have a low toxicity for mice. A comparison was therefore made between crystalline ouabain and the arrow poison on mice.

That the arrow poison had a low toxicity for mice was soon evident. Whereas the lethal dose for cats and rabbits was about 0.5 mg. per kg., that for mice was approximately 40 mg. per kg., an amount about 80 times as great. To compare the arrow poison with ouabain, several preliminary experiments were made, and then four experiments each on 40 mice were carried out. The results of the four experiments are given in Table II.

TABLE II

TOXICITY FOR MICE BY SUBCUTANEOUS INJECTION

| Exp. | Arrow Poison | | Ouabain | |
|---|---|---|---|---|
| | Dose (mg. per kg.) | Mortality | Dose (mg. per kg.) | Mortality |
| 1 | 40·0 | 12/20 | 14·0 | 13/20 |
| 2 | 40·0 | 12/20 | 12·5 | 10/20 |
| 3 | 27·5 | 11/20 | 9·5 | 11/20 |
| 4 | 19·0 | 2/20 | 6·5 | 7/19 |

The different experiments were done on different days and the mice were not equally sensitive on the different days. Thus in Exp. 3 the mice were more sensitive both to the arrow poison and to the ouabain, since a lower dose of both agents killed almost the same proportion of mice as in Exp. 2. However, a comparison could be made between the arrow poison and ouabain in each of the experiments; evidently the ouabain was about three times as toxic as the arrow poison, since ouabain in one-third the dose killed about the same proportion of mice. The experiments could also be combined, since of the mice injected with arrow poison (in Exps. 1, 2, and 3) 35 out of 60 were killed, and of the mice injected with ouabain 34 out of 60 were killed. These mortalities being the same, it could be said that the mean of the three doses of arrow poison, namely 35.8 mg., was equivalent to the mean of the three doses of ouabain, namely 12.0. Hence, the arrow poison had 33% of the toxicity of ouabain for mice; thus like ouabain it was much less toxic for mice than for cats and rabbits.

*Difference from Aconitine.*—When the first observations were made on the cat which showed that the arrow poison had a lethal action on the heart, it seemed possible that the active principle might resemble aconitine. The foregoing results appear to us to establish the close similarity of the arrow poison to ouabain, but it is perhaps worth while recording how it differs from aconitine. When this substance was injected by slow intravenous infusion into four cats under chloralose, the mean lethal dose was not much greater than that of ouabain; it was 0.145 mg. per kg. The effect on the respiration and the blood pressure was, however, very different from that of ouabain and from that of the arrow poison. When only 1–2 ml. of the solution had entered the cat the respiration was profoundly depressed and the blood pressure fell to a low level as seen in Fig. 4. Both blood pressure and respiration recovered later, and the cats died from the action on the heart, though the hearts were not always arrested in systole. Fig. 4 can be compared with Fig. 1, in which the arrow poison was injected. Experiments in which the arrow poison was slowly infused gave

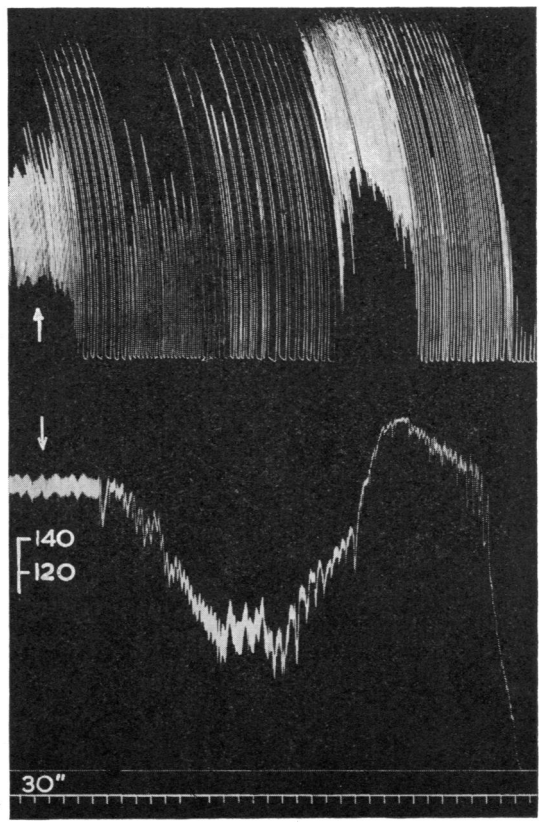


FIG. 4.—Cat; chloralose. Upper record is of respiratory movements, lower record is of blood pressure. At the arrow aconitine was given by slow intravenous infusion until the heart ceased to beat. Note the great slowing of the respiration and the fall of blood pressure, which did not occur when the arrow poison was similarly administered.

records which resembled that in Fig. 1, in that the respiration was only slightly slowed, the depth being unaffected, and that there was no fall of blood pressure except when the heart stopped.

The second difference between aconitine on the one hand and the arrow poison and ouabain on the other lay in the high toxicity of aconitine for mice. The dose of 0.5 mg. per kg. (s.c.) killed 10 out of 10 mice; the dose of 0.4 mg. per kg. killed 12 out of 20 mice, while the dose of 0.3 mg. per kg. killed 2 out of 10 mice. Thus the LD50 was approximately 0.4 mg. per kg. for the mouse as compared with 0.145 mg. per kg. for the cat. When these figures are compared with the corresponding figures for the arrow poison, 40 mg. per kg. for the mouse and 0.49 mg. per kg. for the cat, they show that the arrow poison could not contain aconitine.

## Discussion

Mr. Rodney Needham has told us that he has seen the arrow poison prepared in North Borneo by making horizontal cuts into the bark of a tree, collecting the liquid which exudes, and evaporating it slowly in leaves above a fire. He thinks that the tree is the upas tree, *Antiaris toxicaria,* but he is uncertain of this. He has seen a monkey killed by one of the arrows. When the arrow first hit it, the monkey took little notice except that it pulled the arrow out of the wound and threw it away. After some minutes the monkey retched, though it did not vomit, and soon after it dropped from the tree dead.

Pelikan (1857) states that Brodie as long ago as 1811, and later Emmert, recognized that "upas-antiar" arrested the heart, and that Mudler in 1838 extracted the active principle antiarin. Crystals of this and also the extract, upas-antiar, were found by Pelikan to arrest the heart of the frog when the spinal cord had already been destroyed, from which he deduced that the action must have been exerted on the heart itself. Dybkonsky and Pelikan (1861) compared upas-antiar with digitaline on the frog and found that like the latter it had a direct toxic action on the heart. In 1901 antiarin was clearly recognized as a digitalis-like glycoside by Straub, who stated that it was the most powerful of these glycosides and was available in crystalline form; he found that the isolated frog heart was arrested by 0.001 mg. Hedbom's paper in the same year gives a long list of earlier work. Trendelenburg (1909) found the range of critical concentrations for the arrest of the frog heart to be the same for antiarin as for k-strophanthin. Later work includes that by Ridley (1930) and by Chopra and De (1934). Both papers describe the active principles of *Antiaris toxicaria* as glycosides with a digitalis-like or strophanthus-like action, and refer to the sap of the tree as being used as an arrow poison in Malaya, Java, and Burma.

So far as we have been able to discover, none of the many papers refer to the poison used in North Borneo, and since the tree has not been identified we cannot say for certain that the poison we have examined came from *Antiaris toxicaria.* Our evidence, however, establishes the poison as containing a principle similar to ouabain, and presumably not much inferior to it in potency.

## Summary

The evidence described shows that the blowpipe dart poison used by the nomadic Pĕnan of Borneo is a preparation containing an active principle resembling a cardiac glycoside like ouabain, and that the preparation has 20%, measured in the cat or the rabbit, or 33%, measured in the mouse, of the toxicity of crystalline ouabain. The poison causes death by arresting the heart in systole, and has no obvious action on respiratory movements or the blood vessels. The poison further resembles ouabain in having a beneficial action on the output of the frog heart which is demonstrable when the heart is perfused with low-calcium Ringer's solution. The lethal dose of the poison for mice per kg. of body weight is about 80 times greater than the lethal dose for cats and rabbits, as is likewise the relation for ouabain. The fact that the toxicity of the poison is 20% of that of ouabain on the cat, but 33% of that of ouabain on the mouse, shows that the active principle is probably not ouabain itself. Such differences in relative toxicity for different species are characteristic of cardiac glycosides.

The work has been done under the direction of Professor J. H. Burn, to whom our thanks are due.

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