

Observations on the poison of the Upas Antiar / by Professor Albert Kölliker.

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“Observations on the Poison of the *Upas Antiar*.” By Professor ALBERT KÖLLIKER, of Würzburg. Communicated by Sir B. C. BRODIE, Bart. Received December 1, 1857.

During my stay in England, in the autumn of 1857, I was so fortunate as to acquire the rare poison of the famous *Antiaris toxicaria* (Lesch.), with which no experiments have been tried since the time of Magendie, Brodie, Horsfield, and Schnell and Emmert (1809–1815). I owe my specimens of the Antiar poison to my friend Prof. Christison, of Edinburgh, who had it from Borneo, and to Dr. Horsfield, of London, who collected it himself during his stay at Java in the beginning of this century; and as both specimens were fully active—as some preliminary experiments made in company with my friends Dr. Sharpey and Dr. Allen Thomson showed—I thought it well worth while to devote some time to the study of the poison, and to try to elucidate its manner of action on the animal organism. The following are the principal results which I obtained in my experiments with frogs, and I hope that they will not be deemed unworthy of notice by those who take an interest in the physiological action of poisons in general.

The Antiar, like most other poisons, acts from the intestinal canal, and from wounds; but it must be remarked, that it is much more energetic and rapid when introduced into a wound. The symptoms which are observed in frogs, in the latter case, are the following:—First of all, the *voluntary movements* become less energetic, and at length cease totally, 30 to 40 minutes after the introduction of the poison (after 21^m min. and 1^h 21^m max.). Then follows a time in which reflex movements may be caused by stimulating the skin; but this faculty also is lost very soon, viz. at from 50 to 60 minutes (at 33^m min. and 85^m max.); and the animals die without the slightest trace of convulsions or tetanic spasm. If now the frogs are opened, we find that, without any exception, *the heart has ceased to beat*.

The auricles are dilated, the ventricle corrugated, rather small, and generally red, as if blood had been extravasated into its muscular parietes; but very soon the exposure of the heart to the air causes the ventricle to shrink a little more, and to become pale and stiff, as if in the state of *rigor mortis*. All interior organs, especially the lungs, liver, stomach, intestine, and kidneys, are gorged with blood, and in a state of great, especially venous, hyperæmia. The blood is fluid and rather dark, but soon coagulates when exposed to the air, and assumes a brighter colour. The lymphatic hearts cease to beat as soon as the reflex movements are lost. At the same time the nerves are yet found excitable, but their power is very low, and generally vanishes in the second hour after the application of the poison. The same must be said of the muscles, which contract very feebly when directly stimulated by galvanism, and in most cases lose their power totally in the second or third hour, and generally a little after their nerves. The *rigor mortis* begins early, sometimes in the sixth hour, and is generally well established at the eighteenth hour.

Amongst all these symptoms, to which we may add some signs of vomiting occurring now and then, there was none which attracted my attention more than the cessation of the movements of the heart, considering the great energy which this organ possesses in frogs; and I tried, therefore, before all, to elucidate the action of the Antiar upon the heart. For this purpose I instituted a new series of experiments, in which I exposed the heart by the section of the sternum, before the poison was introduced into a wound of the back; and in this way I easily got the result, that the heart ceases to beat as soon as from the fifth to the tenth minute after the introduction of the Antiar; and so, that first the ventricle stops, and half a minute or one minute later, also the auricles. Now, as the frogs at this time are not at all deprived of their faculty to move, we may have the rather astonishing view of an animal, with artificially-paralysed heart, which moves and leaps as freely as if nothing had happened.

The experiments just mentioned prove, that the first action of the Upas Antiar is to paralyse the heart; and I am therefore quite in accordance with Sir Benjamin Brodie, who, by his experiments on mammalia, came to the same result in 1812; whilst I cannot otherwise than disagree with Schnell (*Diss. de Upas Antiar*, Tubingæ, 1815), who assumes that this poison acts in the first place on the spinal marrow. Now this point fixed, the further question arises, whether the other symptoms mentioned, viz. the paralysis of the voluntary and reflex movements, and the loss of the irritability of the muscles and nerves, are only the results of the paralysis of the heart, or must be attributed to a specific action of the Antiar. For the elucidation of this question, I found it necessary to study the consequences of the suppression of the heart's action on the organism of frogs, which I did in the same way as it had been done by others, especially by Kunde (*Müller's Archiv*, 1847); viz. by cutting out the heart, or by putting a ligature around the base of it, so as to stop the

circulation totally. The results of these experiments were in both cases the same, that is to say, the voluntary movements ceased in from 30 to 60 minutes, and the reflex movements after one or two hours. Hence it follows that these two symptoms of the poisoning with Antiar are simply dependent on the paralysis of the heart caused by it. With reference to the irritability of the muscles and nerves, on the contrary, it is easy to show that the ligature or excision of the heart has not the same influence as the Antiar; inasmuch as in the first case the muscles and nerves are found irritable six or seven hours, and more, after the experiment has been made. Therefore it may be said that the Antiar has a direct action on these organs.

These points once demonstrated, there remained one more question to elucidate, namely, whether the Antiar acts only upon the muscles, or also upon the nerves. If we consider that the Antiar undoubtedly paralyses the muscles, we may easily see that the loss of the excitability of the nerves possibly depends merely upon the impairment of the muscular contractility, and is therefore not real, but only apparent. With a view to determine the real state of things, I tried a third series of experiments—poisoning frogs in such a manner that the muscles of one limb were kept free from the influence of the poison. This was done in two ways: first, by putting a ligature round the crural artery and vein of one leg; and secondly, by cutting through a leg entirely, after the ligature of its vessels, with the exception only of the ischiadic nerve. In poisoning frogs treated in one of these ways, through a wound of the back, I found that, with the exception of the heart, the Antiar acts in the first instance upon the muscles. This is shown by the fact, that in the second hour, at the time when the muscles of the poisoned parts have lost their irritability, the nerves of the sacral plexus in the abdomen still possess their full influence upon the muscles of the leg which has been kept free from the action of the poison. One might be inclined from this to conclude, that the nerves are not at all acted upon by the Antiar; but this inference would be erroneous. In fact, the experiments just mentioned, if followed a little longer, show that in the third or fourth hour the sacral plexus also becomes inactive, at a time when the muscles of the non-poisoned leg are fully contractile. The Antiar, therefore, paralyses also the nervous trunks, but later than the muscles.

From all these experiments, it seems to follow that the Antiar is a poison which acts principally upon the muscular system (the heart and the voluntary muscles), a conclusion, in favour of which I may further add, that the muscles and the heart of frogs poisoned by Urari (Woorara, Curare) lose their irritability totally, and in a short time, if Antiar is introduced into a wound some time after the Urari. If we consider that, as I have shown (see Proceedings of the Royal Society, 1856, p. 201), the Urari only acts upon the terminations of the nerves in the muscles, and does not affect the irritability of the heart and muscles at all, we may conclude, that a poison, which, as the Antiar, is capable of paralysing the muscles after the Urari, has really a direct action upon the muscular fibre.

The results of my investigation into the effects of the Antiar upon frogs, are therefore the following:—

1. The Antiar is a paralysing poison.
2. It acts in the first instance and with great rapidity (in 5 to 10 minutes) upon the heart, and stops its action.
3. The consequences of this paralysis of the heart are the cessation of the voluntary and reflex movements in the first and second hour after the introduction of the poison.
4. The Antiar paralyses in the second place the voluntary muscles.
5. In the third place it causes the loss of excitability of the great nervous trunks.
6. The heart and muscles of frogs poisoned with Urari may be paralysed by Antiar.
7. From all this it may be deduced, that the Antiar principally acts upon the muscular fibre and causes paralysis of it.

So much for this time. My experiments with the Antiar upon warm-blooded animals have only begun, and I am not yet able to draw any conclusion from them. As soon as this will be possible, I shall take the liberty to submit them to the Royal Society, together with the results of my experiments with the *Upas tieuté*, which poison I had also the good fortune to obtain through the kindness of Sir Benjamin Brodie and Dr. Horsfield. With regard to the Antiar I may further add, that experiments made independently, and at the same time, by my friend Dr. Sharpey with this poison, have conducted to the same results as my own.



