

**On the physiological actions of the ordeal bean of Calabar, and on its antagonism to tetanus and strychnia-poisoning / by Eben Watson, M.A.**

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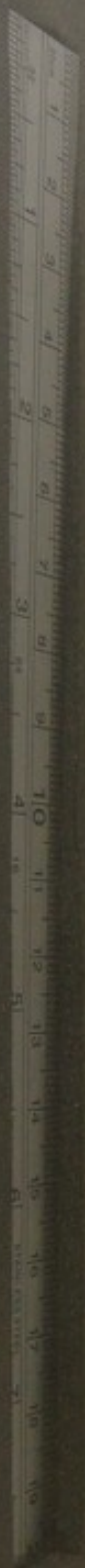
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ON

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THE PHYSIOLOGICAL ACTIONS

OF THE

ORDEAL BEAN OF CALABAR,

AND ON

ITS ANTAGONISM TO TETANUS AND  
STRYCHNIA-POISONING.

BY

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THE PHYSIOLOGICAL ACTIONS

OF THE ORGANS OF CALVARIA

ITS ANATOMY TO THE  
STYLOID BODY

REPRINTED FROM THE EDINBURGH MEDICAL JOURNAL FOR MAY 1867.

BY J. W. M. M.D.

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## THE ORDEAL BEAN OF CALABAR.

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I BELIEVE that I need make no apology for prefacing the account of my investigation of the physiological actions of the Calabar bean with the following notes written by the Rev. W. C. Thomson, who was lately a missionary in Calabar, and is at present studying medicine in Glasgow, where he became acquainted with my employment of the bean in the treatment of tetanus, and I with his knowledge of its administration in trial by the ordeal. I was thus led to request him to commit to paper his recollections of what he had observed in Calabar, and these are now published here, with his consent, because they form an important contribution to the subject of my paper. I am not aware that any such detailed or accurate account of the symptoms presented by persons under the Calabar ordeal has previously been communicated to the profession.

"The Calabar ordeal bean, *Physostigma venenosum* of Professor Balfour, comes to us, as its name intimates, from Calabar, a name by which Europeans designate a small but influential tribe of negroes inhabiting the left bank of the Old Calabar river, which flows into the Bight of Biafra, west coast of Africa, immediately to the north of the island of Fernando Po. By the natives of Calabar the bean is called *esere*,—has long been known to them, and has long been used by them as an ordeal, for the purpose of detecting and extirpating the superstitious crime of witchcraft.

"The plant from which the beans are obtained is a *climber*, attaining often to very considerable dimensions, and frequently found growing on the banks of the river, at the water's edge, where it climbs the overhanging trees, almost entirely masking their foliage with its own rich festoons. About the month of August it makes an abundant display of pretty pink and white papilionaceous flowers, of which, however, comparatively few come to maturity. The fruit, which is ripe in November, is a pod not unlike that of our own horsebeans, containing rarely three, commonly one or two beans. On the 29th October 1862, rather too early in the season perhaps, I gathered the fruit of two considerable plants, one of them having a stem an inch and a half or two inches in diameter, and at its lower part towards the root so twisted upon itself as to simulate a cable of three or four inches in diameter. From the first of these plants 230 pods were procured, representing about 170 clusters of



flowers, and yielding exactly 375 beans. From the other plant the number of pods obtained was 261, representing at the same average about 190 clusters or racemes of flowers and yielding exactly 430 beans. These beans when gathered were still full of moisture, nearly as large again as the dry bean, of a dark grey colour—not the dark chocolate brown which they ultimately acquire—and they averaged in weight 54 beans to the pound.

“The natives of Calabar obtain their supply from the shores of the river, where the beans are cast up in sufficient quantity to serve their purpose. In former days every free man of the least consequence in his village kept a stock in hand, so as to be able to contribute his quota as occasions of public trial by the ordeal might require; or to test the loyalty of suspected wives or slaves of his own; or even in case of his being threatened with a public trial, to put himself quietly to the proof, with proper remedies at hand, so as to obtain a prognosis that might encourage him to face the ordeal with hopes of an honourable acquittal, or else warn him in time to flee from certain and ignominious death. And yet it is a curious fact, that hardly any of these people know anything at all of the plant; indeed one may safely venture to say, that none of them are able to identify the plant in new situations, except by the aid of the fruit.

“According to Dr Fraser, of the Edinburgh University, who has written on the subject, the dry bark of the plant is quite harmless, though the sap which exudes from it when a fresh part is wounded is first astringent and then acrid to the taste. The leaves also are quite harmless. Goats devour them greedily without any deleterious effects ensuing.

“In publicly administering the Calabar bean as an ordeal, it is commonly given both by the mouth and in the form of a clyster. The suspected person has some entire beans handed to him, which he is compelled to eat up in this condition. Meanwhile others are bruised in a mortar or on a slab, and being well mixed with water, one part is taken as a draught and the rest administered as an enema. If after vomiting and purging, when the ordeal has been given in both forms, the person recovers, he is declared to be innocent and harmless, if not he is pronounced guilty, and the community congratulates itself on having thus avenged past and prevented future mischief.

“It would be very gratifying indeed to be able to say, though it were only now after the presence of missionaries amongst them for some twenty years, that the negroes of Calabar have quite abandoned this stupid and most fatal custom,—a custom by which formerly hundreds of lives were sacrificed annually, and by which many still occasionally perish. A few such cases have come under our own observation, and of these I proceed to give such particulars as I can clearly recall to mind.

“CASE 1.—This was the case of two men and a woman who were subjected to the ordeal out of a company of twenty-one persons



accused. The trial took place during the night, and was conducted by lamplight in the public square. The two men had been dosed ere we reached the spot, and were sitting on the ground quite motionless with their legs gathered in their arms, and their faces resting on their knees. The woman was in the act of receiving the draught portion of the ordeal, which was no sooner swallowed than it was rejected by the stomach. The quantity of the mixture taken could not have been less than a quart, and might contain the substance of four or five beans at least. After this, immediately after she had vomited, she was removed in charge of her female friends to receive the remaining portion as an injection, while the men were taken into the town hall or palaver house for the same purpose. There was no opportunity in this case of observing effects, but next morning it was found that one of the men had died, and that the remaining man and woman had so far recovered as to be able to go the round of many friends to receive the congratulations and presents customary on such occasions. Both were living and in vigorous health two years afterwards.

"CASE 2.—This was the case of a young woman,—a mere girl indeed, twelve or fourteen years of age perhaps,—who had devoured a bean for the purpose of self-destruction. At the time our attention was called to her she was sufficiently sickened to be very penitent, but not sufficiently so to feel quite safe. She could not vomit, much as she desired to do so. A dose of the sulphate of zinc, however, speedily cleared her stomach, and she was soon quite herself again. In this case the circumstances were such, that the poison must have lain more than twenty minutes on the girl's stomach before the emetic took effect.

"CASE 3.—This also was that of a female—a young woman of about twenty years of age. She had quarrelled with a neighbour,—had been called a witch,—and took it so much to heart that she straightway went off to the woods and there quietly put her character to the test by eating up half a bean. This being discovered she was brought to the public square of the village to be put through the ordeal before the headman in regular form. Meantime we were sent for, and reached the spot before the beans in process of preparation for her were ready. But the half-bean she had taken was already beginning to affect her. There was very obvious twitching of the muscles of the back, pretty profuse perspiration, and she repeatedly and urgently begged for water. Yet she resolutely for several minutes refused to receive a solution of tartar emetic from a lady missionary who was pressing it on her acceptance. At length, however, her sufferings appeared to persuade her; she received the emetic, threw up the poison, and the case being considered spoiled, further proceedings were abandoned. She was quite well next morning. In this case the poison—half a bean—must have lain from twenty minutes to half an hour on the stomach before the emetic was taken.

"CASE 4.—Here again the unhappy person is a woman, thirty-five



or forty years of age. Having lost her son, she accused a sister-in-law of having caused the young man's death, and demanded that she should be tried by the usual ordeal of the bean. In such a case, when one individual thus challenges another, if the accuser be willing to partake of the ordeal along with the other, it is customary for the authorities to compel the accused to yield. It was so in this case. The bereft mother ate up several whole beans, quite deliberately, taking an occasional sip of water to facilitate deglutition. When next seen—little more than half an hour afterwards, perhaps—she was perfectly helpless. She was sitting on the ground supported by a female friend, who sat on a low stool behind her. She seemed to be perfectly flaccid. Leaning against her friend, her drooping head had to be supported, while she rested, hung by the axilla on her friend's thighs, over which her arms hung lifelessly as over the arms of a chair. Her back was much bent backwards, and her legs thrust out flat on the ground before her. At this time she was still able to speak, and obstinately refused everything in the shape of an emetic, observing that if she were such a one as the bean should destroy, it were best for all that she died. She complained of intense nausea; there was a constant flow of mucus; occasionally an attempt to vomit, when small quantities of mucus were thrown up, which friends anxiously but vainly searched in the hope of finding the larger particles of the bean, the appearance of which is, in their estimation, a hopeful sign of innocence and of life. In a few hours she was dead. The other unfortunate woman, whom, however, I did not see, also died.

"CASE 5.—This also was the case of a female, of about the same age as the preceding. Finding herself named along with certain others in connexion with a great feast of witches, she indignantly determined to purge her character, and demonstrate her innocence. Her own brother gave her a bean, or perhaps more than one, which no dissuasion on the part of others could prevent her eating. I reasoned with this woman for more than ten minutes, vainly endeavouring to get her to receive an emetic from me, and she must have taken the poison ten minutes or a quarter of an hour before I saw her. Indeed her friends were already becoming anxious about her, and even joined with me in urging her to use means to clear her stomach. This she stoutly refused to do, and became quite angry with us for proposing such a thing. All this while the poison seemed only to render her a little uneasy. By-and-by, as we still urged her to receive an emetic, she started up and went off in a fury, calling myself and all who sided with me all the hardest and worst names her vocabulary could supply. This was early in the forenoon. In the afternoon I saw her quite lively and comfortable, and in excellent humour. She had vomited after I saw her in the forenoon, and had so escaped.

"CASE 6.—This case happened at the same time as the last, and was that of a strong man of middle age. Having snatched up and swallowed a handful of bruised beans that had been prepared for



others, he ran about wildly for sometime, pursued by his friends, who at length captured him, and brought him back to his house. I saw him just as he was brought back,—it might be about a quarter of an hour from his taking the poison,—perhaps less than that. He was greatly agitated,—was evidently afraid that it was going to be a bad case with him, and he perspired profusely, which his so recent violent exercise might sufficiently account for. He would not hear of an emetic being prepared for him, and even refused to receive water from his friends, who had urged him to accept an emetic, and desired him to drink with the view to encourage vomiting. An hour or more after I saw him it was reported that he had vomited. The same afternoon he visited his friends, danced before them as is customary, and received their congratulations. However, in the evening, as he was proceeding to his farm, three or four miles from the village, the vomiting returned, and he died in about a week thereafter.

“CASE 7.—This was the case of a little boy of about eight years of age. Some extravagant gestures that he had indulged in for his own amusement and the diversion of his little companions had appeared, in the estimation of the wise men of the village, to implicate both himself and his mistress in certain witch proceedings of a frightfully cannibal description. In consequence of this both he and his mistress were subjected to the ordeal. The latter I did not see after she had received the poison. By all accounts, however, it was rapidly fatal in her case. As respects the little boy, I was summoned on his behalf almost immediately on its being determined that he should have the ordeal; but before I could reach the spot he had been largely drugged. I found him sitting firmly on the ground, with his belly greatly distended, apparently from the large quantity of the mixture he had been compelled to swallow. My efforts to get possession of this little boy, or to have an emetic given to him, were all in vain for many minutes, nor was I allowed to remove him till his case was deemed beyond remedy. At this time he was lying apparently quite flaccid, overpowered by the poison. He was removed by two persons, one seizing him by the wrists, the other by the ankles, and, while being thus conveyed from the place, it was observed that his head hung back without any appearance of muscular effort to support it. By this time he had also lost command of the lower sphincter muscles, contents of the bladder and rectum were both escaping. He was still, however, able to answer to his name by a feeble, abrupt moan. I could not get him to swallow any part of the emetic we poured into his mouth. It was quickly poured back again as soon as given. Beyond this quiet extrusion of the emetic from his mouth, and the feeble answers he gave to his name, I cannot recollect that he made any voluntary movement from the time he came into my hands till his death. He quickly became, to all appearance, quite unconscious; there was much frothy mucus about his mouth and nose; his pulse



grew feebler, and in two hours from the time I was summoned to his help he was dead.

"CASE 8.—This was the case of three persons,—an elderly woman, a young woman, pregnant, and a young man under trial for the third time. The elderly female, a strong masculine sort of woman, died. I saw her but for a moment or two, and she was then quite overpowered, and was sitting, supported by a female friend, exactly as described under Case 4, and in the very same flaccid state. The younger woman survived, but in her case the poison had the effect of causing abortion. As respects the young man, I saw him swallow what might be the substance of five or six beans, very coarsely bruised. To this quantity must be added what he received as a clyster. When I next saw him, on the following morning, he was quite well. Each of these persons had had the poison exhibited to them in both forms.

"In concluding these observations, I cannot help regretting that they are not more precise and particular,—the more especially as one can hardly wish to have such opportunities as the cases afforded repeated over again. But, such as they are, I trust they may be useful as, to their limited extent, a kind of corroborative evidence; and now that the Calabar bean has fallen into wise and good hands, I feel assured that it is on the way to become henceforth, instead of the curse it has been, a restorer of health and preserver of life."

In my experiments with the Calabar bean, I have used several preparations of it, but chiefly those of the kernel; because I believe that to be by far the most active, if not the only active part of the bean. I found this opinion on the following experiment. I had a very concentrated tincture made from three drachms of the spermoderm of the bean, and I injected this to the amount of one drachm of fluid into a cavity carefully prepared beneath the skin of a dog. He soon became sleepy, and in fact fell asleep on his legs. He did not fall, but nodded his head and closed his eyes; but he was easily startled, and ran away quite briskly. In about half an hour he had completely recovered from his drowsiness.

I concluded that this state was not the specific effect of the spermoderm. It did not agree with the results of Dr Fraser's more numerous experiments, and it might be accounted for by the very cessation of the excitement just previously undergone during the injection of the tincture, and perhaps also by the operation of the alcohol. I am quite willing, however, to consider this a doubtful experiment, as it is negative in its result, and was not repeated. I do not think that the question of the possibly different actions of the spermoderm and kernel of the Calabar bean is of any great importance; since the former is a very small quantity compared with the latter, and they are not likely to be separated by pharmacutists in their preparations. Indeed I have discovered that they really are not separated by them, but that the alcoholic extract, for instance, is made from the powder of



the whole bean, which, in my opinion, only serves to make it a little weaker, and therefore more manageable as a drug than otherwise it would be.

Of the kernel I have used the powder, the tincture made from it by percolation, the alcoholic extract in the semi-solid form and suspended in water and in sherry; and re-dissolved by boiling in alcohol. I have also used the watery extract, and have found it extremely active. It was prepared by slowly boiling seven pounded beans in four ounces of water for three-quarters of an hour. The result, after straining, was one and a half ounce of a starchy fluid, which was mixed with milk, and about a third of it was poured down a dog's throat. The usual characteristic symptoms of the poison were produced in less than a minute, and he had ceased to breathe in five minutes more. A similar extract is produced by boiling in acetic acid, but I have not used it. It is extremely bitter to the taste. All these facts point to the existence in the bean of an active principle which is soluble in alcohol, water, and I believe also in acetic acid at the boiling temperature, but which has not yet been separated. There is no doubt that this principle is a very subtle poison, but, as it exists in the bean, it is not so very virulent as many others with which we are already acquainted; as, for instance, woorara, which is in many respects similar to it. In some of the cases observed by Mr Thomson, large quantities of the crushed bean were taken and retained in the stomach for nearly half an hour, yet, when vomiting had been induced by sulphate of zinc, no bad effects followed. In those of his cases in which death occurred, several hours elapsed before the fatal event, and in all of them the most remarkable phenomenon was paralysis of voluntary motion, without pain or impairment of the mental faculties.

In my experiments on the lower animals quite similar effects were produced. All were paralyzed, and some recovered after a time from what seemed a very thorough influence of the bean. I subjoin a short account of these experiments.

EXP. I.—Performed, 21st December 1866, on a Guinea pig. At 4.35 P.M. I injected m. v. of the tincture of Calabar bean under the skin of the right flank by means of a hypodermic syringe. Almost immediately it was found to have lost the power of moving the right leg, and, soon afterwards, of the left also. It lay down on its belly and seemed averse to any exertion whatever. When its ear was pinched it immediately cried, but did not move. When I aimed a blow at its head with a cane, and struck the floor in its near vicinity, making a sharp noise, it started and winked, but did not attempt to move any part of its body to escape the threatened blow. It therefore saw and heard, and knew the danger of a blow, but could not or would not try to escape.

In a few minutes more the palsy had reached the anterior extremities. At 4.45, only ten minutes after the commencement



of the symptoms, vomiting of frothy fluid like saliva occurred, and, at this time, by way of attempting an antidote,  $\text{m iii.}$  of vinum belladonnæ were given and soon repeated; but they had no effect, and the animal ceased to breathe at 4.53.

I immediately opened the chest, and found the heart pulsating quite regularly, which it continued to do for some minutes afterwards; and when, some hours later, a more extended inspection was performed, it was found that the lungs were congested and airless, while the cavities of the right side of the heart were distended with dark partially coagulated blood, and those of the left were nearly empty.

EXP. II. 21st December 1866.—The subject of this experiment was a large and very strong cat, which struggled very much and was difficult to manage.

After two previous, and, as we thought, unsuccessful attempts to make it swallow doses of the bean, the third attempt was really successful; and at 4.15 P.M., one grain of the alcoholic extract was administered by the mouth (mixed with a little water). The animal's eyes soon became filmy and the pupils somewhat contracted. Bloody saliva poured from the mouth, and the tongue was protruded, hanging over the jaw. It could not stand, but lay on its side, having apparently lost the power of its four legs almost simultaneously. Soon after this it began to kick out convulsively, with its fore-legs chiefly, but it never seemed to attempt to rise or to run away. The respiration then became jerky and gasping, and the cat died somewhat suddenly about 4.30.

On inspection some time after death, the body was found quite rigid. The lungs were much congested, and, when incised, dark venous blood escaped from them. The left side of the heart was hard and firmly contracted; its cavities contained almost no blood, while the cavities on the right side were fully distended with dark and partly coagulated blood.

EXP. III.—Performed on 27th December 1866, on a small but active rabbit.

At 8.53 A.M., a dose of  $\text{m x.}$  of the tincture of the bean was given by the mouth, and as it produced no effect, a second dose of other  $\text{m x.}$  of the tincture was given at 9.52. Soon afterwards a very copious discharge of both urine and fæces took place. There was no other effect, and therefore, at 10.20, a third dose, consisting of a grain of the alcoholic extract mixed with water, was administered. In eight minutes thereafter, the rabbit sank upon its hind-legs in a sitting position, and apparently could not move. When held up by the ears it kicked out, but not vigorously, with the hind-legs. When set down again it trembled on its legs and quivered in all its muscles. The pupils were quite natural. When suddenly threatened, it did not move its body, though it showed by winking and moving its ears that it knew what was meant.



At 10.30, it lay down, but immediately struggled, and after a great effort got up and stood weakly, supporting itself against the wall. Then it fell down and lay on its side with its eyes half shut. Again it rose upon its legs merely to fall down in a different position, viz., on its belly, with its legs stretched out before and behind in a most unnatural way, only to be accounted for by their utter powerlessness. The respiration was very labouring, so that its nostrils were widely dilated for each inspiration.

At 10.38, the pupils were still natural, and the rabbit started when the candle was brought close to the eye. It can get up on its legs, but instantly falls again as if quite unable to stand. Its legs fold under it in any way and appear quite powerless, but it held its head curiously erect all this time.

At 10.43, it was breathing very badly and lying quite still. No threat could make it move, and physical motions were elicited feebly and with difficulty. It would not drink water. Pupils were quite natural. I thought the animal was dying at this time, it looked so very weak and breathed so ill. It continued in much the same state until 11.5, when it began to recover; first breathing more fully, and then exhibiting power over the muscles of the limbs; for, when touched, it could now get up on its legs, and very soon it ran nimbly about. But this was only on compulsion, and when permitted it stood still, leaning against the wall. By-and-by it became more natural, shook and licked its fore-paws, and by 11.13 it seemed quite recovered.

EXP. IV.—Performed on 29th December, on a small and active rabbit.

At 9.37 A.M., I gave it a pill, containing gr.  $\frac{1}{2}$  of the extract of the bean. At 9.55, it seemed to be a little frightened, but quite active. At 10.5, it ran about the room as if pursued, with great and unnatural activity. At 10.18, the same state continuing, I gave it a whole grain of the extract at once by the mouth.

At 10.24, it rocked itself to and fro from side to side, still standing on its legs, which seemed weak. When a sudden noise was made near it, it moved its ears and seemed startled, but did not move or try to escape. It soon fell on its belly, with its legs stretched out front and back. The pupils were rather small.

At 10.29, the only change was that it occasionally uttered cries like those of a peacock. It was very easily startled, and got up weakly on its legs, tottering for a few seconds and then falling down again. This was repeated several times till 11.10, when it seemed stronger. Then, for the second time, it became unnaturally active and lively, as if under some strong excitement, and by-and-by it became quite well. It was now put among some pet rabbits and fed, but it was found dead before night.

EXP. V.—Performed, 11th March 1867, on a middle-sized mongrel dog. This is the experiment referred to at page 1005.

At 9.45 A.M., I gave him the third part of the water which had



been boiled on seven pounded beans. In one minute, he had lost the power of his hind-legs and fell down on his haunches. He trembled all over and panted in breathing, moved his fore-legs reluctantly, though he could by using them crawl along, dragging his hind-legs. He answered to his name and seemed quite sensible, but did not appear to suffer any pain. The pupils were about half contracted.

In about two minutes more, he kicked aimlessly with his fore-legs and then lost the power of them, falling down on his side. The respiratory movements were almost imperceptible. He passed urine and fæces and frothy saliva. Pupils the same as formerly. He soon afterwards lost the power of holding up his head, and finally ceased to breathe in six minutes after the administration of the poison.

The chest was immediately opened. The heart had ceased to pulsate. Its cavities were full to distention on both sides, the blood being of different colours. When this was allowed to escape by incisions, the wall of the heart began to contract, and continued to do so feebly but regularly for some minutes. The lungs contained very little blood, and were pale and crepitant.

In these experiments, as well as in Mr Thomson's cases, the two phenomena observed were, first, and most remarkably, the paralysis, and, second, a peculiar effect on the secretions.

I.—The paralysis has struck every one who has studied the actions of the Calabar bean as most extraordinary and unusual in many of its features. Let me mention the chief of them:—It is preceded by a more or less marked stage of twitchings or tremblings of the muscles of the whole body. Then it always commences in loss of the voluntary movements of the lower extremities (posterior in the inferior animals), and gradually extends upwards, first implicating the superior or anterior limbs, and then the chest and neck, when the respiratory movements cease, and the animal dies of asphyxia. In some cases, however, when the dose of the poison is strong, the paralysis affects the heart directly and thus causes death. When this paralysis is fully established, the physical or diastaltic movements can only be very feebly excited, and sometimes do not at all respond to their accustomed stimuli. Yet this paralysis seems to be intermittent in its power, for the animal sometimes rises out of the state of helplessness and moves for a short distance, again to fall down quite powerless; and this is repeated perhaps frequently till death happens. During the whole operation of the poison the sensibility of the body remains unimpaired, but no pain seems ever to be felt, and the mental faculties are quite unaffected.

Now, in investigating the physiology of this very extraordinary state in order to arrive at some knowledge of its proximate cause, it will be admitted without question that the poisonous agent enters the blood and then affects some of the nervous centres. The



analogy of other poisons is enough to establish this point, but when we inquire more precisely into the kind of effect and the precise centre acted on, we meet with considerable difficulty. Professor Christison, in a private communication to me on this subject, has suggested four possibilities as to the cause of the paralysis, which are so exhaustive, and from the fact of their coming from him so worthy of consideration, that I shall state them in his words, and reason upon them from the facts before me.

1st, "*It may depend on reduction of the circulation and consequent great debility;*" that is, a general effect on the nervous system analogous to what we find in shock after a severe bodily injury. But it is quite evident that this is not the right explanation of the paralysis caused by the Calabar bean, for the paralysis always affects the posterior extremities first, and the rest of the body remains under the power of the will for sometime longer. The animal can hold his head erect, and walk with the fore-feet, dragging the posterior limbs behind. Besides, the arterial pulses may be felt beating strongly when the animal has lost all power to move; and even after death the heart is found to beat, sometimes vigorously for many minutes. These circumstances are obviously incompatible with such an amount of general debility as would account for the paralysis.

2d, "*It may be the result of coma, through action of the poison on the brain.*" But it is still more obvious that this is not the case of animals poisoned with Calabar bean; for nothing approaching to coma is ever noticed, except, of course, just when the animal is expiring. Then, certainly, as the circulation through the vessels of the brain is arrested, it ceases to perform its functions, but this is death, not coma. Indeed, in the case of one rabbit experimented on (Exp. IV.), the animal seemed to be even excited and to run about as if under the influence of a stimulant; and in the case of the woman (Case 5) observed in Calabar by Mr Thomson, the effect of the bean seemed to be to excite the cerebral functions. I suspect, however, that these were exceptional cases, and that in general the bean exercises no influence at all on the brain.

3d, "*It may depend on volition being suspended or impaired, though not necessarily, with the other phenomena of coma.*" This idea originated in Dr Christison's own feelings when under the influence of the poison. He then experienced great inability to move, but he found after several ineffectual trials that he really had the power still; that is to say, he could after a short time make the exertions in which he had failed just before. Now it is certain, that in order to a voluntary movement, the cerebral centre (corpus striatum) of the voluntary nerves must receive some sort of impression or impulse from the mind to be conveyed to the muscles; but if the mind be prevented from giving this impulse, no such movement can be produced, though the nervous apparatus is untouched by disease.

It seems to me, however, that the only mental state in which such communication between the mind and the nervous centre is



necessary, is just the state of volition, and in Dr Christison's own case, the volition was strong, while the inability to move was nevertheless complete. Some three times he tried to raise himself on his elbow, but failed to do so. Surely this is proof of his will being strong enough,—so strong, indeed, that he did not cease to make an effort to obey it; and on the fourth attempt he succeeded, and did get up on his elbow to vomit.

Again, in Mr Thomson's cases, the poisoned persons showed strong will in obstinately refusing for a time the emetics offered by the missionaries; stating as their reason that the ordeal would then be unfulfilled and their characters still suspicious.

In my experiments on the lower animals, they could see and try to avoid a blow when threatened,—they winked, turned their ears to one side, and tried to run away, which, after several unsuccessful attempts, they often accomplished, tottering a few steps before they fell down unable for further exertion. They showed their will, however, in thus running as far as they could.

There seems, therefore, to be no failure of volition. The mind is clear and active in all its operations, and, what is very strange, it retains the power of willing to move the parts which are palsied. This is not usually the case in ordinary palsy of voluntary motion. The patient does not feel that he can even wish to move the affected limbs, but it is different in the palsy produced by Calabar bean. The person can wish to move his limbs which are lying apparently powerless, and though he fails to move them, yet he renews the attempt again and again, and often, by a strong effort of the will or under some powerful emotion as of fear, he overcomes the paralysis and succeeds in moving the limbs.

All this, I think, interestingly shows that the defect is in the nervous apparatus itself, for it is not in the mind, and it is not in the muscles, which I have stated already remain, even after death by poisoning with the bean, quite irritable on application of the ordinary stimuli.

4th, "*It may depend on complete annihilation or suspension of the action of the spinal cord.*" This I believe to be the true explanation of the phenomenon in question. *First*, Because none of the other explanations is applicable or satisfactory; and I believe that no other feasible explanation could be suggested. *Second*, Because the parts paralyzed by the influence of the bean are such as receive their nervous supply from the spinal marrow and its nerves. *Third*, Because this paralysis is never confined to one side, as one often sees, in cases where the affection springs from a local or a cerebral cause, but it is always a paraplegia which is produced by the bean; just as might be expected in the case of an agent affecting the whole of one segment of the spinal cord. *Lastly*, Because of the way in which the bean causes death. In almost all cases this is by asphyxia, brought on by paralysis of the external mechanism of respiration. This effect is produced more or less rapidly according to the dose of the bean administered, but



it seems to be the universal mode of action of the poison that it affects the lowest segment of the cord first, then those above, and lastly, the part in the neck, soon after which the animal expires. If the chest be then opened at once, the heart will be found pulsating, but, of course, ineffectually. The circulation is arrested in the pulmonary capillaries by the stoppage of the respiration, and the enfeebled heart's force cannot overcome the *vis inertiae* of the blood in them; hence we have the usual post-mortem appearances of asphyxia, viz., gorged right side of the heart and empty left side, while the lungs are rather more than usually bloodless.

There is no doubt, however, that when the dose of the bean is very powerful, the animal seems to die of paralysis of the heart, in which case the mechanism of respiration is paralyzed at the same time, and it is very difficult to tell which is the cause of death. In opening the body, however, in these cases, both sides of the heart will be found enormously distended with blood of different colours, the walls thin and flaccid, and no pulsation will be noted. But I have remarked, that after opening the cavities of the heart and relieving their over distention, the heart begins to pulsate feebly again, showing that it had been prevented from pulsating and emptying its left side by a paralysis of its walls occurring just previous to the systole, while its muscular fibres remain contractile. Now, this may be attributed to the sudden change in its nutrition and in its nervous supply caused by the complete cessation of the respiratory changes in the lungs, the effect of palsy of the muscles of respiration; or it may be ascribed to a direct influence of the bean on the cervical portion of the cord, and therefore of the sympathetic nerve, which is in close connexion with it in that region.

Another most remarkable phenomenon caused by the bean when given in poisonous doses is one which I have not previously adverted to, but will now shortly describe, as it is corroborative of the theory of the spinal origin of the paralysis in the cases under consideration. It is this, that just before the paralysis becomes universal, and therefore fatal, the animal often kicks out with its fore-legs, and, strange as it may seem, with its hind-legs too. The motions certainly are not voluntary, and partake of the nature of convulsions. They never accomplish any combined effect. The animal is never able to rise from the recumbent position, or even to scratch or kick an object presented to him. The movements are quite uncoordinated, showing, in my opinion, that first the power of voluntary movement is taken away by the influence of the bean, and then that the power of coördination in the muscles is annihilated; and, lastly, the animal dies utterly paralyzed, bereft of all the actions of the spinal cord.

The state of the iris produced by the action of the Calabar bean is an interesting but very difficult subject. When a square of gelatine, containing the active principle of the bean, is placed under the eyelid, it speedily causes contraction of the pupil and abolition of the accommodating power of the eye. The vision is



only clear for a certain fixed and generally rather a short distance. The same effects, especially that on the pupil, have been observed by Dr Fraser in his experiments with the bean when acting generally on the nervous system. I must confess, however, that I have not observed this contraction of the pupil to be at all so remarkable in my experiments, or in the two cases of traumatic tetanus treated by me with the bean. From my experience, the effect on the eye is not nearly so great or so long continued when the bean is administered generally as when it is applied locally to the eye. I think the same thing might be stated with regard to atropine and belladonna. It is only when large doses or very frequent doses of any of these substances have been given that much effect is produced on the eye; and especially in my experiments on the lower animals, I have noted that the pupil was but slightly affected, even when the animal was under the full action of a poisonous dose of the Calabar bean.

It is not easy to account for this difference between what, for brevity, I may call the local and general action of the bean upon the pupil, for in both cases the action must be on the nerves and on them through absorption into the circulation. I can only suppose that in the local application more of the poison is carried directly to the ciliary ganglion than after the general administration, and that thus the effect is stronger as well as more lasting.

Then, how to explain the contraction of the pupil by the action of a substance causing depression of the spinal centres seems at first a deep mystery, and the only way of getting over the difficulty is by carefully applying the physiology of the nerves of the iris to its solution. It is well known that all the nerves of the iris pass through the ciliary ganglion, and that the short root from the third nerve, or motor oculi, is that which supplies the principal motor nerves to the iris. It has also been clearly made out, by cutting and irritating that nerve, that it supplies the sphincter muscle of the iris. So that irritation of it produces contraction of the pupil, and its section leaves it dilated. Again, it has been sufficiently demonstrated by Magendie that the ophthalmic division of the fifth nerve is a purely sensory nerve; but from recent experiments it would seem that some motor fibres are combined with its naso-ciliary branch; for irritation of that nerve produces motions in the iris with generally more or less dilatation. Now, MM. Budge and Waller have shown that irritation of the trunk of the sympathetic in the neck, or of the lower part of the cervical spinal cord, produces dilatation of the pupil by exciting contraction of the radiating fibres of the iris; while, on the other hand, sections of the sympathetic leave the pupil permanently contracted. The great probability therefore is, that the sympathetic root of the ciliary ganglion is that which supplies motor fibres to the radiating fibres of the iris, and that they are distributed along with the fibres of the naso-ciliary branch of the ophthalmic, which are themselves purely sensory.



The action of the Calabar bean on the pupil is then thus explained; for whenever it comes to affect the lower segment of the spinal cord in the neck, its influence immediately extends to the trunk of the sympathetic through its numerous branches of communication, and hence the motor nerves of the radiating fibres are paralyzed; while the third nerve, being of cerebral origin, is unaffected by this influence on the spinal centres, and so the annular fibres of the iris receive their usual nervous supply. In short, they are not antagonized by the radiating fibres, and therefore the pupil becomes contracted. Still farther, it seems to me that this theory explains the fact previously mentioned, that the local application of the bean produces more decided contraction of the pupil than its general administration; for, in the latter the animal experimented on dies very soon after the influence of the bean has reached the cervical region of the spinal cord, and in one of the two human subjects in whom I have watched its operation, a decided contraction of the pupil was only produced along with very unpleasant asphyxial symptoms. If these had not been speedily recovered from, I believe that death would have been the result, as it was in the case of the lower animals.

II.—The second physiological effect of the Calabar bean when given in poisonous doses is increase of the various secretions of the body. There is profuse perspiration, abundant flow of tears, a frothy mucous and salivary discharge from the mouth. This is sometimes tinged with blood. The urine is passed in considerable quantity, and there are fluid evacuations from the bowels.

I think that these phenomena are attributable, 1st, To the congestion of the secreting organs consequent upon the gradual arrest of the pulmonary circulation, which causes a temporary increase of their usual functions; and, 2d, It is in great measure due to the mere muscular relaxation of all the fibres of the body, the coats of the bloodvessels participating so as to permit of their great distention with slowly moving blood. Hence, there is a watery transudation from them mixed with the secretions, just as we have in cholera; and in some of the convulsive movements of the animal we are apt to have rupture of small vessels and blood escaping with the fluid, especially from the mouth and throat.

I now proceed to treat of the second section of my subject, viz., the antagonism of the Calabar bean to tetanus, and to the precisely similar state produced by strychnia in certain doses. The pathology of this state, if not quite satisfactorily explained, is, at all events, better understood by us since certain recent advances in the physiology of the nervous centres; for it was not to be expected that morbid anatomy alone could elucidate this, or, indeed, any but a few of the diseases of the nervous system. For the most of them the appeal must be made to physiology, to the otherwise known functions of the organs concerned, and to the clinical observation of their derangement during the lifetime of the



diseased. Thus, since the discoveries and writings of the late Dr Marshall Hall it has come to be an established doctrine in physiology, that "physical" movements independent of both sensation and volition can be excited by stimuli applied to the surface of the limbs in virtue of a peculiar state thereby produced in the segment of the spinal cord into which the nerve is implanted. Whether Dr M. Hall's theory of a true spinal marrow and a special set of excito-motor nerves be adopted or not, there can be no doubt of the principal facts on which that theory was built, and of the general doctrine stated above which flows from them. This peculiar state of the spinal cord has been named a "polar state," or a state of "polarity," by Dr Todd; and it is well known that in certain diseases this state of the cord is greatly increased. Hence, *e. g.*, we have the convulsions of epilepsy, the startings of paraplegic and the occasional rigidity of hemiplegic limbs, all from some morbid influence, which it may often be difficult to define, exalting the polarity of the spinal cord, and affecting, through their nerves, the limbs of the patient. Now, the only way in which we can feasibly explain the phenomena of tetanus is by assuming that the irritation of the sensitive nerves of the wounded part (in traumatic cases) is communicated to their spinal centre, and that thus its polarity becomes greatly exalted, so greatly that the slightest touch of the surface, or the making an effort to move, or perhaps even the mere internal progress of the morbid action itself, is enough to call forth the most violent contractions of the voluntary muscles, and to maintain contraction in some of them uninterruptedly for days together.

In idiopathic tetanus the only pathological difference seems to be that the irritation originates not in a wound, but in the bowels or some of the internal organs.

Lastly, strychnia seems to have the power of directly producing the same effect on the spinal centres through the blood, and therefore of exciting an artificial tetanus of the severest kind.

The common cause of death in tetanus of all kinds is a more or less speedy asphyxia from fixation of the respiratory muscles by tonic spasm, which may be continued so long as to kill in the fit, or it may be repeated frequently at such short intervals as to have the same effect of stopping the respiratory changes. I can easily believe, however, though it has not occurred to me to witness such a case, that the glottis may be tetanically closed so as greatly to assist in this result, and I am quite sure that in poisoning by strychnia the heart is sometimes arrested in its action by tonic spasm of its fibres. But I think that all the morbid lesions, such as congestion and exudations in the spinal cord and softening of its tissue, observed by Mr Lockhart Clarke and others, after death from tetanus, are rather results of the primary morbid influence than its cause. I place them in the same category with the ruptured muscular fibres which have been likewise often observed in these cases. Besides, it must be remembered that none of these phenomena are constant. They have not been found by Todd and Bowman, and other equally good



observers. I conclude, then, that the true pathology of tetanus is that it is due to a greatly exalted polarity of the whole or of part of the spinal cord, and that this may originate in causes acting first on the nerves, and then on the centre, or directly upon the centre itself.

Now, in the Calabar bean, as formerly shown, we have an agent which powerfully acts on the spinal cord, and that in a depressing or depolarizing manner. The animals, when under its influence, have no power of voluntary motion, and the physical motions are only feebly or not at all excitable. It is very remarkable, too, that it causes death proximately by asphyxia, no doubt just as do tetanus and strychnia, but more remotely the asphyxia is caused by the very opposite state of the mechanism of respiration,—viz., by paralysis instead of spasm; and when the heart is affected directly by the Calabar bean, which it undoubtedly is in some cases, the same thing is true. Its fibres are paralyzed, not spasmodically contracted, as in tetanus.

Thus the influence of the bean upon the spinal centres is seen to be directly opposed to that of tetanus and strychnia, and its secondary effects on the motor apparatus is also the very opposite. Instead of increased polarity of the centres we have diminished polarity, and instead of increased excitability of the motor organs we have paralysis. If, then, we could learn to use the one agent against the other we might produce complete neutralization. The following experiments, performed with the view of counteracting strychnia with Calabar bean, will be interesting in this point of view, and let me remark that there is no chemical action of the one substance upon the other. It is simply a physiological counter-effect that is produced.

EXP. VI.—Performed, on 21st December 1866, on a Scotch terrier, apparently strong and healthy.

At 3.2, I gave him a pill of bread-crumbs containing a grain of powdered strychnia. He coughed it out after it had been held in his mouth for a few minutes, and it was thought he had got very little of it, but at 3.13 he exhibited all the usual symptoms of the drug in rapidly increasing intensity. He had a violent fit of opisthotonos before I interfered, but then I administered by the mouth the tincture of Calabar bean in  $m x$ . doses, and increased them to twice that amount. I gave these doses every five minutes for nearly half an hour, and by that time he was much more relaxed, and was able to get upon his feet, but he immediately fell down again in a fit of opisthotonos. Still stronger doses of the bean were given, but had no effect, for the spasms continued uninterruptedly, and the dog died at 3.40, just after a fit.

On inspection, the left side of the heart was nearly empty and contracted, while the right side was distended with partially coagulated blood. The lungs were congested.

In the preceding experiment the dog was evidently killed by the strychnia, while the bean did not seem to have acted at all. The



pupils were never contracted in the smallest degree, and any relaxation of the muscles that occurred was just in the intervals between the spasmodic fits. The experiment only teaches that strychnia acts much more rapidly than the bean, and that it counteracts the latter so powerfully as even to postpone its action perhaps altogether, as in the experiment, especially if it has begun to act before the bean has had time to do so.

In the following experiment the action of the bean was more obvious.

Exp. VII.—Performed, on 29th December 1866, on a large and strong rabbit.

At 9.58 A.M., I gave it  $\text{m. v.}$  of liquor strychniæ by the mouth; and in four minutes afterwards it had a tetanic fit with opisthotonos, in which it fell from the table. Still it was able to stand on recovering from the fit. I then (at 10.9) made it swallow  $\text{m. xv.}$  of the tincture of the bean. Within the next six minutes it had other two fits, the second one being very severe, and again causing it to fall from the table. I now (at 10.16) gave a second dose, the same as the preceding, and it soon afterwards seemed to be better, and was able to rise and walk a little. It had no other fit for nine minutes, and that was milder than formerly. A third dose of  $\text{m. x.}$  of tincture was then administered at 10.28, and soon after this the effects of the bean made their appearance. The rabbit lay down on its belly, and remained quite still unless touched, when slight spasms were produced. Then its breathing became panting and peculiar,—a constant effect of the bean,—and it was very sluggish. The spasms did not now seem to be produced by touching its sides as before; and therefore, to see how far it was paralyzed, it was lifted by the ears, which brought on a very violent tetanic fit, in which all the limbs, as well as neck and tail, were involved. After this it lay upon its side, its pupils were contracted, and its limbs quite palsied. In this state it died at 10.40.

On opening the chest immediately after death, the heart's action was found to have ceased, and its walls were not irritable. The lungs were empty and collapsed.

In this case the struggle between the strychnia and the bean was more observable. - Although a very strong dose of the former was given, yet the bean seems to have in some degree checked its action, and to have almost antagonized it in twenty minutes after its first administration. From that period the symptoms were chiefly those of the bean, from which it might have recovered, had it not been rudely disturbed from its state of quiescence and held up by the ears. Such a stimulation broke through the depression of the bean, and excited once more the action of the strychnia, which the animal was not now able to bear. It was, however, my own impression, and that of my assistants, that the rabbit, if let alone, would have rested quietly till the effects of the strychnia had passed by, or till it had escaped from the system; and the lessons which we learned from the experiment were, the importance of quietness



in the recovery from tetanus, even when the bean is fully acting on the patient, and also that the bean is a cause of great general prostration, in which an animal can ill bear the violence of a convulsion fit. Hence the necessity in the human subject for the exhibition of food and stimulants, and likewise for caution in the use of such a powerful agent. The great object during its administration should evidently be to give the smallest possible dose of the bean that will produce its physiological action.

In the following experiment I tried to anticipate the action of the strychnia by that of the Calabar bean.

EXP. VIII.—Performed on 29th December 1866. I took two rabbits, rather under the usual size, but very active. To one of them I gave  $\text{m v.}$  of liquor strychniæ by the mouth, and it proved almost immediately fatal. To the other I gave the tincture of Calabar bean by the mouth.

At 3.5 P.M. I gave  $\text{m v.}$ , at 3.35 I repeated a similar dose, at 3.45 I gave a double dose, viz.,  $\text{m x.}$ , still without any effect, and therefore a fourth dose of  $\text{m xv.}$  was given at 3.52. In two minutes after this last dose was taken, the breathing became panting, and the animal shivered as if from weakness of the limbs. The pupils were still natural. In other two minutes it lay down on its belly, with its legs stretched out before and behind, apparently quite paralyzed. It was very unwilling to move, but could move its face and ears.

At 4.2, while it was in the state just described, I gave  $\text{m v.}$  of liquor strychniæ, and again the effect was immediate, the animal being thrown into violent convulsions of the tetanic kind. After a short interval the fit was repeated, and then the animal died only four minutes after the administration of the strychnia. On inspection of the chest, the heart was found stiff and empty, and the lungs collapsed and containing very little blood.

In this case the life of the rabbit was no doubt prolonged by the influence of the Calabar bean, but the strychnia, in the dose employed, proved a much more powerful poison, and the result again indicated the inability of the animal to bear convulsions when its nervous power was diminished by the action of the bean. I have no doubt that the animal died of the strychnia, and that I had given too large a dose to be counteracted by the Calabar bean, before the animal's strength was worn out. I therefore performed the following experiment.

EXP. IX.—Performed, on 20th March 1867, on a middle-sized rabbit.

At 3 P.M., I injected, with the hypodermic syringe,  $\text{m vi.}$  of the tincture of Calabar bean under the skin of the back, and immediately afterwards  $\text{m iij.}$  of the liquor strychniæ two or three inches higher up the back.

At 3.8, the tetanic starts were very distinct, and I immediately injected other  $\text{m vi.}$  of the tincture of Calabar bean under the skin



of the opposite flank. Very soon after this, viz., at 3.10, a very severe tetanic convulsion occurred. Opisthotonos was quite marked, the very tail of the animal being bent back. Both fore and hind legs were affected with the spasms, but on coming out of it, which it did in two minutes, the hind legs lay behind the animal apparently paralyzed. At 3.14, it got up on its fore-legs, held up its head, and moved a few steps, dragging the posterior limbs behind it. At 3.16, it had partially recovered the use of the hind-legs, and ran off a short way, the hind-legs, however, being still feeble. Whenever it moved it was seized with violent shivering, which was of tetanic character. On one of these occasions (at 3.17), the shivering became a fit of rigidity, but the animal was not thrown down as before. It remained standing. The right hind-leg was exempted from the spasm, and lay out behind in a paralyzed state. It recovered from this fit in two minutes, but remained quiet till 3.21, when it got upon its legs and ran into a corner, where it sat down so as to be supported by the wall both behind and on the left side. Five minutes afterwards it moved on its fore-legs unsteadily, the hind-legs being again paralyzed, and in other two minutes (3.28) it started upon its fore-legs, with head erect, and screamed loudly, as if frightened or in pain. It then sat down in a natural position, but supported by the wall, and remained quiet till 3.55, when it turned the front of its body, using only the fore-legs. It had some tetanic starts after this, but remained still in the corner. The breathing was quite natural, and the animal seemed to be recovering. At 4.5 it ran across the floor, using the hind-legs a little weakly, and mounted on the top of an upturned basket in which it had been kept. It took food, and remained quite well during the afternoon and night.

At 8.43 next morning, the rabbit was quite well, and in every respect as before the experiment. I therefore injected *m iij.* of liquor strychniæ under the skin of the shoulder, and left it to its fate. In two minutes there was violent tetanic convulsions, from which it only relaxed in death, four minutes after the injection had been performed.

In this experiment the proportion for safe antagonism was pretty exactly reached; and, by a moderate but well-timed administration of the bean, the strychnia was prevented from producing what was afterwards proved to be its natural effect, if unresisted, viz., the death of the animal. No experiment could better prove the power of the bean in counteracting the tetanus of strychnia, the usual slowness of operation of the former being greatly modified by the hypodermic method of administration. It produced its characteristic effects in six minutes in this case, though acting against the strychnia; and in Exp. I., previously related, in which the hypodermic method was used, and not the strychnia, the bean seemed to act immediately. It is worthy of consideration, if, even in the human subject, when the tetanus either of disease or of strychnia is very violent and acute in its progress, this may not be the proper way of administering the bean. I remark, also, that by the



repetition of the injection whenever the tetanus became distinct, eight minutes after the first introduction of the tincture, its influence was prolonged over the entire period of the action of the strychnia, yet it never was so strong as to weaken the rabbit to any great or prejudicial extent. Lastly, the animal was intentionally kept from any start or rough handling which could excite the spasms, but was rather permitted to lie quiet till the effect of the strychnia had worn off. I cannot but think this experiment very encouraging, and very instructive as to the antagonism of Calabar bean to the tetanus of strychnia in poisonous doses.

EXP. X.—Performed, on 23d March 1867, on a large and strong rabbit.

At 3.3 P.M., I injected  $\text{m x.}$  of tincture of Calabar bean, and in thirteen minutes thereafter it was found very excited, as if frightened. It breathed very rapidly, and, on being approached, ran wildly about the room. This continued till at 3.16 I again injected  $\text{m vi.}$  of the tincture, and in two minutes afterwards the rabbit fell down on its belly, but with head erect. When I lifted him on to the table he started and kicked feebly. I now (3.22) injected  $\text{m iii.}$  of liquor strychniæ over the shoulder. Soon afterwards the breathing became peculiar. It was accompanied with an audible blowing noise, and the abdomen moved very much, evidently performing the chief part of the respiratory acts. Very soon the rabbit lay down on its belly with its legs stretched out before and behind. It got up again, and stood shakily. A little frothy mucus came from its mouth. All this time the symptoms were entirely due to the Calabar bean, and not at all to the strychnia; but at 3.28, *i.e.*, seven minutes after the injection of that substance, the rabbit gave a slight spring forwards on all its legs. This was quite momentary, and it was difficult to tell whether it was the effect of the strychnia or a voluntary effort, for immediately afterwards it ran across the room, and jumped into its basket, the side of which was about a foot high. Its motions were, however, stiff and ungainly; and when in the basket, it stood on its four legs and screamed violently, but showed no other sign of pain or fear. It was quite sensible, and started naturally when the floor was stamped on, even at a distance. In a few minutes more, however (at 3.33), it had a decidedly tetanic start, and touching its sides or limbs produced similar slight contractions of the muscles. When it attempted to move, its limbs seemed to be stiff, and not fully under command of the will.

At 3.37 it gave another convulsive spring; and on being touched it had a violent tetanic fit. Believing that the effect of the Calabar bean had worn off, I injected  $\text{m vi.}$  of the tincture once more below the skin of the back, and very soon after this the rabbit seemed wholly relaxed, lying on its side, and kicking especially with the fore-legs, as if to try to get up, which it was unable to do. At 3.41 it had another severe fit of opisthotonos, after which it was



very weak, and breathed so ill, that if I had not assisted it by making artificial movements of the chest, it would have ceased to breathe. When it was restored it breathed with great rapidity (68 in a minute), and very imperfectly, the air passing through mucus in the trachea. It had frequent slight twitches of the limbs till 3.52, when it had another fit of opisthotonos, and died immediately after.

On opening the chest, the heart was found to have ceased to pulsate. Its cavities were all full of blood; those on the left side of a bright florid colour, and those on the right of dark venous hue. The lungs were collapsed, and nearly bloodless. The contractility of the muscles was apparently worn out, for they did not respond to the usual stimuli.

This experiment is the last and only additional one which I have performed with these two powerful poisons, in order to investigate their antagonism; and perhaps I might not have introduced it here were it not that it completes the series of my observations; and though at first sight rather contradictory of the immediately preceding experiment, yet it is not so in reality, but rather teaches a very useful lesson in regard to the physiological action of the Calabar bean. For it will be obvious, on careful perusal of the description of this experiment, that the rabbit was first brought under the influence of the bean, which occupied nineteen minutes before it was accomplished; then the strychnia was injected, and, instead of its acting immediately, as it would have done if the bean had not been employed, it took ten minutes before doubtful and, at all events, very slight tetanic symptoms were produced; and it was not till seventeen minutes after the injection of the strychnia, and thirty-six after that of the first introduction of the tincture of the bean, that general convulsions occurred. But by this time the action of the bean had become too slight to counteract that of the strychnia, and the animal was killed by the latter before the former could be renewed by further injections, for the one practised at 3.37 never acted at all. For it is well shown in this experiment that the antagonism of the Calabar bean and strychnia is mutual; that either of them prevents the action of the other, and that the most powerful will be the one which has the greatest hold on the system at the time. Thus, at the commencement of the experiment, the bean acted alone, and got its full power over the animal. Afterwards, when the strychnia was introduced, the bean would not let it act, and so its presence was not manifested till the influence of the bean diminished. Then it, in turn, took possession of the nervous centres, and though the bean was again introduced, it was excluded by the strychnia, which kept its power over the animal till death released it. Nothing could better show the mutual antagonism of these two substances; and the lesson, in regard to therapeutics, which flows from this physiological law is, that in the treatment of tetanus, we must never allow the influence of the bean to become weak, even for a time after the disease seems to have been overcome; for if we do, we may find it difficult or impossible



to renew its force in the system, when the disease renews its attack on the patient, emboldened, so to speak, by the felt feebleness of its formerly successful antagonist. The proper medium must be struck between maintaining such an action of the bean as will diminish prejudicially the vital energies of the patient, and permitting it to become inadequate to the suppression of the morbid exaltation of the spinal polarity, which the disease seeks to perpetuate or to renew.

It must be noted, however, that in some of these experiments the poisonous influence of the strychnia was too strong as well as too rapid for the Calabar bean, and it is not difficult to foresee that cases of tetanus from disease will arise which will be able to resist entirely even the potent influence of that subtle agent. In different persons, likewise, the nervous susceptibility may be different; so that it is more than likely that, in some, the excitement may be more easily accomplished than the repression of morbid polarity of the spinal centres, and from this cause, too, failures may arise in the application of the Calabar bean to the treatment of tetanus. Nevertheless, I think it will be acknowledged by all, that it is by far the most promising counter-agent of the tetanic poison at present known to us. Woorara is the only other that will compare with it; but the enormous rapidity and energy of that poison, as well as our want of knowledge regarding its nature, and the absence of preparations of fixed strength, all combine to exclude that curious substance from therapeutic use.

I have only as yet had the opportunity of applying the Calabar bean in two cases of traumatic tetanus, and these I have fully recorded in the *Lancet* for the 2d of March, in this present year.<sup>1</sup> I may abridge these as follows.

CASE I.—Annie W., age 11 years, admitted into the Royal Infirmary, November 12, 1866. Three weeks ago, she struck her toe against a stone, and it is still bruised, and its skin slightly ruffled. Six days ago, she began to have twitches, and now tetanus in its severest form is fully developed. The jaws are quite locked, and the body bent back in three-quarters of a circle. Chloroform was twice administered during the first night to relieve the violence of the spasms.

Such are the chief points of the report in the hospital journal as to her state on admission. After clearing out the bowels, I began to treat her with Calabar bean on the 15th. The paper used in ophthalmic surgery was first employed, and next day the extract in solution, one-eighth grain for a dose, was taken every half-hour. By the time she had taken two grains at this rate, she was found lying

<sup>1</sup> Since these cases were published in the *Lancet*, another case of traumatic tetanus has been treated in the same method with Calabar bean, by Dr Andrew Campbell, formerly a pupil of mine, and now practising at Navenby, Lincolnshire. Though the case was a most severe one, the result has been perfectly satisfactory, and will, I believe, be published in detail by Dr Campbell at an early date.



on her back in a semi-comatose state completely relaxed, with her mouth open, and her pupils moderately contracted. The breathing was quiet and regular, and the pulse rather hurried and full.

In this state of things the Calabar bean was stopped for two and a half hours, by which time the pupils were again dilated, and the spasms had begun to occur once more, when the patient was touched. Five drops of the tincture were given every hour during the night, and next day she was better in all respects, but relapsed in the evening, and seemed as bad as ever next day. I therefore prescribed one-half grain of the extract in pill, to be given every hour. Instead of this, a whole grain was given by mistake of the apothecary in making the pills. Nine pills were given before the mistake was discovered. By that time she was again thoroughly relaxed in all her muscles, except those of the back, which were still rigid; her pupils were contracted, and her heart's action was tumultuous. Her face was pale, and her eyes wide open. Her breathing was jerky, and a mucous rattle was in her throat.

From this state she recovered by the use of stimulants, *vinum belladonnæ*, and the extraction of the mucus from the throat—the first symptoms of restoration being that the respiratory movements were more freely performed, and that the pupils dilated.

In a few hours afterwards the spasms could once more be induced by touching the limbs, but generally they remained flaccid. The bean was not again administered for a fortnight, in order that she might thoroughly rally from its influence, and become stronger. During this time fits of tetanic rigidity did occur, but they never were so distressingly violent as they had formerly been, and, under the use of very small doses of the tincture for about another fortnight, she completely recovered. I had not the least doubt that the powerful influence of the bean, above described, checked the disease, and that its more continued and milder action accomplished the cure.

CASE II.—Alex. M'Ph——, aged 13, was admitted into the Royal Infirmary on 6th December 1866.

Three weeks before admission he had his finger bruised and torn, but very slightly, and two days before admission he became affected with lock-jaw. On the above date he had frequent and severe tetanic fits, with opisthotonos.

After opening his bowels I ordered him *m v.* of the tincture of the bean every two hours. Each dose had a perceptible effect in relaxing the rigid muscles, and in rendering him less susceptible to the induction of spasms on touching the limbs. In three days he was able to sit up in bed, and in seven days more he was out of bed walking, though stiffly, through the ward. In a few days more he was perfectly well.

It should be noted that in this case the doses were not so large as in the former one, and that the pupils were never so much contracted as on the two occasions in that case, when the action of the bean was greatest. The breathing was never affected at all, yet



the progress was steadily towards recovery, though no other treatment was employed but food and aperient medicine. On the other hand, it must be remembered that the girl's case was much more severe than the boy's, and therefore required larger doses to counteract it. On one occasion she took two grains of the extract in eight hours, and on another, no less than nine grains in nine hours. On both these occasions she was brought into much the same state of complete relaxation of all the muscles, but those at the side of the back-bone, and physical movements could not for a time be induced,—showing complete depolarization of the spinal marrow, or, in other words, precisely the opposite condition to that in which tetanus originates. Perhaps in the boy's case, without any such marked effect of the drug, it was more safely, and quite as efficiently, managed.

I do not think that the Calabar bean has, properly speaking, a cumulative effect, such as digitalis possesses; but, as it is necessary to keep up its effect in order to counteract the tetanus, so if the doses be rather too closely given, there will be a kind of cumulative result, for the action of the one dose will be added to that of the previous one. It is well to avoid this in the human subject, and to take care that the effects of one dose be fully worn off before another is brought into operation; and the secret of success in treating such cases will undoubtedly lie in seizing the proper moment for repetition of the drug, so that its action will never be altogether absent, and yet never allowed to become unnecessarily strong.

The time which the bean takes to act in the human subject depends on the dose. The stronger it is, the sooner it will act, and *vice versa*. Small medicinal doses, such as  $m\ v.$  of the tincture, take about twenty minutes before their action is perceived, and then this action continues for about half-an-hour, after which the effects of the drug soon disappear; and therefore the doses must be repeated about every forty minutes, if their continuance in full force is desirable. On this point the judgment of the surgeon must be his guide, as no rules can be laid down applicable to all cases. I may remark, however, that as the Calabar bean is strictly an antidote to tetanus, the doses of it which will be required and borne in cases of that disease will be directly proportionate to its severity.

In conclusion, in the case of an overdose of the Calabar bean, I believe that the best measures to be used for restoration are the clearing of the mouth and throat, mechanically, of the mucus accumulated there, and to employ artificial respiration, by moving the arms up and down, as recommended by Sylvester, and also by alternately compressing and relaxing the ribs. Electricity applied to the course of the phrenic nerves may likewise be useful, and also mustard cataplasms along the region of the spine. As soon as the patient can swallow, some stimulant properly diluted with water should be freely given.











