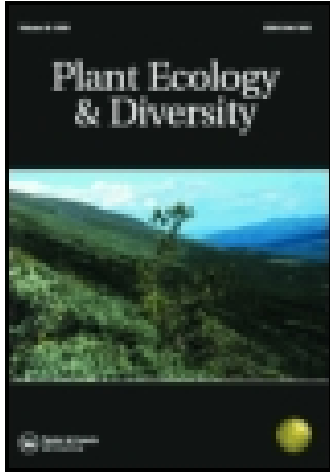


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IV. Notes on the Physiological Action of the Calabar Poison Bean (*Physostigma venenosum*, Balfour)

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LAHORE, PUNJAB, 2d December 1862.

“ I write a line enclosing fresh seeds of *Meconopsis aculeata*, a most beautiful plant, which will, no doubt, be acceptable to Mr M'Nab. I am the guest of Col. Robert MacLagan, and I am much engrossed in putting together my notes after ten months of continuous travel. I have lately crossed the Indus, and examined the vegetation of the Peshawur Valley, and the banks of the Cabul river. The great trunk road passes through a well cultivated plain. The wheat, barley, maize, and cabbage, are superb. The fields are fenced with *Rhamnus*. The avenues consist chiefly of *Melia* and *Tamarix*. Extensive sandy tracts are clothed with *Aerua*, *Andropogon*, and *Calotropis*, but the most common plant on both banks of the Indus is *Peganum Harmala*. The islands in the bed of the Indus are self-sown with *Populus euphratica* and *Dalbergia Sissoo* which yields the most valuable wood we possess, both for house-building and for agricultural purposes. The trade in deodar wood will undoubtedly increase on the Indus and Cabul rivers, and it seems desirable to encourage commercial relation with the wild tribes on our frontier. They are much divided among themselves, and only a few Mahomedans, who have great religious influence, can travel with safety through the wooded tracts of Suwat and Kafiristan. At the time of my visit (the end of November) snow was falling on the surrounding mountains, and all the herbaceous vegetation was withered. A few months hence (April) the plain is covered with a rich carpet of various colours. The most interesting plants noticed on a rapid excursion were *Alhagi maurorum*, the Camel-thorn; *Withania coagulans*, DC. (*Pumeceria coagulans* of Stocks, see Hook. Icones, ix. 801) used in Scinde and Afghanistan for coagulating milk; and the prophet's flower, *Arnebia echinoides*, much esteemed by the Mussulman population, who assert that the fine purple spots on the corolla are the marks of Mahomet's fingers. The seed will be sent to you. It is a rather showy plant. Enclosed are the seeds of *Diospyros tomentosa*, the fruit of which is dried and sold in the bazaars. It is about the size of a pigeon's egg, and tastes like a plum. There are also enclosed the seeds of *Delphinium Brunonianum*, the Musk plant, gathered at an elevation of 14,000 feet. It is mentioned in the 2d vol. of Hooker's Journal, p. 95. There are also seeds of *Convallaria cirrhifolia*.”

IV. Notes on the Physiological Action of the Calabar Poison Bean (*Physostigma venenosum*, *Balfour*). By THOMAS R. FRASER, M.D., Res. Phys. Roy. Infirmary, Edinburgh.

A considerable amount of attention has been directed, within a comparatively recent period, to the seed of a leguminous plant of West Africa, the Ordeal Bean of Calabar. First scientifically noticed by Dr Daniell, about the year 1840, and alluded to in a paper read by him before the Ethnological Society in 1846, the attention of Europeans residing in this district, and especially of the various missionaries who are there stationed, has been attracted to it. And, certainly, its virulence as a poison, and the savage barbarity of its employment, are of themselves sufficient points

of attraction. The bean is employed in Africa almost only as a state poison: as a supposed means of discovering crime, and a certain method of punishing it,—suspicion being in itself a cause of death.

The region included in the term *Calabar* is a district of West Africa in the neighbourhood of the Bight of Biafra, and extending along the course of a considerable river, the Rio Calbary. Its boundaries are indefinite; it may be reckoned to have a length of 100 miles and a breadth of 50, and is situated between 4° and 8° N. Lat. and 6° and 12° E. Long.

The natives are an offshoot from the “Ibibio” tribe, who inhabited a region extending westward from Calabar to the river Niger. Their government is oligarchical, and all their institutions and customs are under the influence of a superstitious ignorance. Everything unexplainable, and all that occurs beyond the ordinary course of things, events even of every-day occurrence, as sorrow, joy, disease, and death, are ascribed to the mysterious agency of witchcraft. And it is for the discovery of this evil genius that the discriminating power of the ordeal bean is required.

Any person may lay a complaint against another. The charge is made before one of the chiefs of the village. A council of neighbouring chiefs is called, the accusation is heard, and reasons in support are stated. The accused is then asked for his or her defence; the answer is invariably a demand for “chop-nut,” which is as constantly granted. The ordeal is given in the most public part of the town, and the whole proceedings are watched by a crowd of onlookers. The priest, as administrator, offers up a prayer that the gods may continue to the bean its power to kill the guilty. The accused is then permitted to eat the ordeal either in the form of an infusion, or by simply chewing the kernel. Sometimes a portion of one is only taken, at others as many as twenty-five, according to the will of the priest, or until innocence is declared by the production of emesis, or death proves the guilt of the accused. The medicine-men are by no means scrupulous in the accomplishment of their object, and if, from any cause, they desire the death of their victim, a club is employed to hasten the action of the poison.

Should the accused escape, the person bringing the charge

is liable to undergo the same trial, to show that he does not possess "free mason" against the accused. A salutary check is thus placed on treachery or private enmity.

The number of deaths by this ordeal must be very considerable, even since the efforts of a large and enthusiastic body of missionaries have been directed against the custom. The population of Calabar is roughly estimated at 100,000, and in one year the number of deaths by this ordeal was 120, which gives an average percentage of 1.2. What the symptoms are which are stated to be produced by this administration will be described with greater advantage in another portion of this paper.

In an inaugural thesis which I presented to the Medical Faculty of the University of Edinburgh last session, details were given of a number of experiments on the physiological action of the ordeal bean, and from this have been extracted the following notes of the action on the lower animals and on man. Through the kindness of Professor Balfour, and of Messrs Baillie, Edgar, and Thompson of Old Calabar, a sufficient supply of the bean was obtained to permit of a satisfactory investigation of its physiology.

It was found that when an extract representing one ounce of the dried stem was introduced into the system of a rabbit, no effect was produced, and nearly the same quantity was swallowed by a pigeon without any symptom being caused. Various other experiments were made with different preparations of the stem, and seemed to prove that this part of the plant is perfectly inert. This is opposed to the popular belief among the natives of Calabar, who regard the whole plant as poisonous. An alcoholic extract of the spermoderm produced well-marked symptoms, the most important of which could be referred to the Medulla spinalis, on which it appears to exert a *depressing* action, producing paralysis of the muscles supplied by the cord. In addition to this, an energetic cathartic action was caused, diuresis was produced, and in many experiments long-continued and powerful emesis. These last symptoms were by no means the results of the general constitutional depression, which might be supposed to have followed the poisonous action of this agent, but were caused before any such effects, and were indeed

the means of preventing fatal consequences. For in a direct ratio with the dose administered was the degree of the cathartic, diuretic, and emetic actions, which thus caused the speedy elimination of the poison. It was found impossible to cause death in the lower animals, even with doses of the alcoholic extract representing 64 grains of the spermoderm.

A specific action, therefore, appears to be exerted on the secretions of the intestinal canal and kidneys. It is very doubtful if the cathartic and diuretic actions can be referred to any stimulation of the muscular coats of the bladder or intestines, because this is opposed to the general result on the muscular system, which was never excitation; and we may explain the passage of fæces and the escape of urine without involving this agency. The experiments appeared to show an increased action of the intestinal glands and the kidneys, and this would naturally cause the reflex action which follows an increase in the contents of the intestines, and produces the evacuation of a distended bladder. In one experiment, also, I emptied the bladder, and still frequent diuresis was produced. The most prominent actions of the spermoderm are therefore sedative on the spinal cord, hydragogue cathartic, and diuretic.

Action of Kernel.—As the most violent and marked effects are produced by the kernel, the greater number of the experiments was undertaken with the view of investigating its special actions.

The infusion of powdered kernel appears to cause no bad effects on slips cut from certain plants, as the species of the *Primulaceæ*; while on others, as the species of the *Amaryllidaceæ*, it exerts a sedative action. No explanation can be advanced of this variety of effect. This infusion served as a menstruum for the germination of infusoria as effectively as one of ordinary vegetable matter.

When a *small fatal* dose of the kernel is administered to one of the lower animals, a train of symptoms is produced usually in the following order:—A slight tremor is first seen, especially in the posterior regions, and extending upwards to the anterior extremities and the head. The limbs immediately afterwards yield, the posterior becoming generally first paralysed, and the animal lies

extended on the thorax and abdomen in a state of almost complete muscular flaccidity. A few attempts may be made to recover the normal position, but they are usually ineffectual. Fæces are in some cases passed. The pupils contract. Respirations become slow and irregular; as the symptoms advance, with a distinct stertor accompanying both inspiration and expiration, and frothy mucus escapes from the mouth. A few muscular twitches occur, especially in the extremities. Reflex action cannot be produced by either pinching or pricking the skin. On lifting by the ears, the limbs depend in a loose manner, and the only sign of life is an occasional gasping inspiration, which also soon ceases, and the animal appears dead. Consciousness is preserved during the whole time, until the power of expression is lost. Immediately after death the pupils dilate. In the autopsy the usual signs of fatal asphyxia are found.

When a *large fatal* dose of the kernel is administered, the hind limbs almost instantly become powerless, and the animal falls. It lies flaccid, and in any posture, on the table. The pupils contract. The lacrymal secretion is increased, and in a few cases fluid escapes from the nose. Reflex action cannot be produced by irritation, and the respirations, after a few gasps, cease. The pupils dilate immediately after death. On opening the body, appearances are found strongly characteristic of death by syncope, and the action of the heart cannot be excited even by direct irritation.

These effects were produced whatever the channel of introduction into the system. Experiments were made in which this entrance took place through each of the principal tissues and systems in the body. Various preparations were introduced through the circulatory, nervous, respiratory, and nutritive systems, and by contact with the muscular, serous, and mucous tissues. The effects of each have only varied in their rapidity; and a connection apparently exists between this rapidity and the class of symptoms produced.

In those cases where the results are produced with comparative slowness, the symptoms and *post mortem* appearances indicated death by asphyxia, and in those in which an

extremely rapid and energetic action was produced, death was apparently caused by syncope.

Generalizations.—From these results, and especially from the two varieties of action and appearance after death, it is probable that the bean exerts its influence primarily on the spinal cord, and that its action is one of *depression*. Along with this there are various special actions, as the paralysis of the heart, and the contraction of the pupils.

The special paralysis of the heart is apparently of a complicated nature, resulting from the peculiar action of the kernel on muscular fibre, and on an extension of a spinal effect to the nervous ganglia of the heart.

The contraction of the pupils may be of considerable importance in illustrating the action of the bean.

Valentin,* from a series of experiments on the ganglionic system of nerves, and especially on the mixed ganglia of the neck, has arrived at the conclusion that the iris derives its nervous supply from two sources, from cerebral and from spinal filaments. He has shown that the *cerebral* filaments are supplied to the circular muscle, or contractor of the pupil, and the *spinal* to the radiating fibres of the iris, or dilator of the pupil. The actions of these two nervous supplies must be regarded as antagonistic. When, therefore, the influence of one set of fibres is removed, that of the other will be unchecked, and will produce a greater degree of its proper action. Thus, when the influence of the cerebral supply is removed, the fibres which are acted on by the spinal nerves will be unchecked, and dilatation of the pupils will result, in the same manner as a direct irritation of these nerves would act.

The actions of the bean of the *Physostigma venenosum* can, in the same way, be referred to the spinal cord. The contractions of the pupils may be caused in three ways, by cerebral irritation, by spinal depression, and by a combination of cerebral irritation and spinal depression. The symptoms of the administration of the kernel disprove any cerebral irritative action, and so neither the first nor last of these can be regarded as the cause of the contraction. The symptoms, on the other hand, distinctly indicate a *de-*

* De Functionibus Nervorum Cerebraliū et Nervi Sympathetici. 1839. pp. 109, 114.

pressing action on the spinal cord. By this action the power of the cord to transmit impressions is destroyed, and so, necessarily, the power of transmitting the nervous influence to the iris. The balance between the dilator and contractor muscles is removed by the nervous supply to the dilator of the pupil being prevented, the circular fibres act, and the pupil is contracted.

In a few experiments it was observed, that some time after the contraction of the pupils had commenced, if the animal was excited to muscular exertion, the pupils very distinctly *dilated*; the spinal stimulation re-exciting the dilator muscle or radiating fibres to exert their proper function. An extension of these views may be of use in the analysis of symptoms produced by every poisonous agent.

Death is produced by the kernel of the Calabar bean in two ways,—by asphyxia, and by syncope. Death commenced at the heart when large doses were administered, and at the lungs when a more moderate quantity was introduced into the system. These two classes of symptoms may be harmonised by referring the action of the bean to the spinal cord. When this action is limited in extent and energy, the only marked effect is paralysis, and death is caused by the extension of this paralysis to the muscles of respiration, resulting in asphyxia. When this spinal action is more extensive and energetic, the heart is affected, its contractions cease, and death occurs by syncope. That the action of the heart can be in this way influenced by powerful impressions on the spinal cord, appears to have been rendered certain by the researches of Legallois* and Philip Wilson.†

From the results of our experiments we have concluded:—

- 1st, That the kernel of the seed of the *Physostigma venenosum* acts on the spinal cord by destroying its power of conducting impressions.
- 2d, That this destruction may result in two well-marked and distinct effects.
 - a, In muscular paralysis, extending gradually to the respiratory apparatus, and producing death by *asphyxia*.

* Exp. sur le principe de la Vie. 1812.

† Inquiry into the laws of the Vital Functions.

- b*, In rapid paralysis of the heart, probably due to an extension of this action to the sympathetic system, thus causing death by *syncope*.
- 3d*, A difference in dose accompanies the difference in effect.
- 4th*, The action does not extend to the brain proper, *pari passu*, with the action on the spinal cord; the functions of the brain may, however, be affected secondarily.
- 5th*, It also produces paralysis of muscular fibre, striped and non-striped.
- 6th*, It acts as an excitant of the secretory system, increasing more especially the action of the alimentary mucous membrane.
- 7th*, Topical effects follow the local application of the watery emulsion and alcoholic extract: these are, destruction of the contractility of muscular fibre, and contraction of the pupil when applied to the eyeball or eyelids.

Action on Man.—As the remarkable nature of this action on the lower animals appeared to indicate properties of therapeutical value, this investigation was continued to the physiological effects on man.

Professor Christison has accomplished the feat of eating the largest quantity of kernel without fatal results. This was about twelve grains, but as the full effect of this dose was prevented by the action of an emetic, we are still unable to describe the physiological effects which such a quantity may produce.

A case occurred in Glasgow where two servant girls eat each about five grains, perfectly unaware of the properties of their treat. I have also, on several occasions, taken portions varying from six to nine grains, and have administered small doses of the alcoholic tincture to various persons. From these data the effect of a small dose may be described as follows:—

In about five minutes after the administration, a peculiar sensation is experienced in the epigastrium immediately below the sternum. This is very slight at first, but gradually increases in intensity, until it becomes almost painful. Eructation occurs in a short time, and always takes place during the occurrence of this epigastric sensation. This

continues at intervals for a considerable time, and is by-and-by complicated by a feeling of dyspnoea. Dizziness is soon after experienced, and in a short time a degree of powerlessness in the muscles of the extremities. If a somewhat larger dose be taken, twitches occur in the pectoral muscles, the dizziness is much augmented, and the pupils contract. I have also experienced a dimness, with a distinct myopic condition of vision; an increase in the salivary secretion; and a marked, though slight, perspiration. At this stage attempts to walk, or even to move the limbs, are difficult, and often impossible; while, at the same time, consciousness is perfectly retained. These symptoms generally disappear entirely at the conclusion of a night's sleep. The heart's action is described in Professor Christison's case as becoming irregular and tumultuous. The same irregularity has been observed in some of the cases which have come under my notice, and in many the contractions have diminished in number. In one experiment six grains of the powdered kernel reduced the pulse twenty beats in an hour and a-half. When the alcoholic tincture or the extract are rubbed on the skin, a distinct diminution in the sensibility occurs, and the part may be pricked without causing pain. When the extract is applied to the eyeball, it immediately causes a copious secretion of tears, and, in about five minutes, a distinct contraction of the pupil, confined to the side of application. In about thirty minutes after, the pupil becomes a mere speck, it however retains a certain degree of mobility, and continues in this state for about twelve or fourteen hours. A slight headach and dimness of vision, along with myopia in the affected side, are almost always caused, but these only continue for one or two hours at the commencement.

The physiological effects of fatal doses in man can be described only by those who have witnessed the administration of the ordeal, as, fortunately, no fatal case has yet been caused by its administration for any other purpose. I am indebted to various gentlemen who have resided at Calabar for full details, from which the following more important symptoms are extracted.

No sensation is experienced for about ten minutes after

the commencement of the trial. At this time the victim is said to become thirsty. This thirst gradually increases, until the accused loses command of his Indian stoicism to such an extent as to struggle violently and entreat the bystanders for water. Soon after the power of swallowing is lost, mucus escapes from the mouth, convulsions and severe twitches are observed in the muscles of various parts of the body, but especially in the back, and death occurs, generally about thirty minutes from the commencement of the trial. During the whole time of the ordeal the victim retains complete consciousness, as is shown by the absence of delirium, and the sense and appositeness of the remarks which are made. The power of speech is preserved until a short time before death, and long after the accused is unable to swallow.

The most distressing symptom in fatal cases is the sensation of intense and insatiable thirst. It is doubtful if this is really an effect caused by the 'Esere nut,' or simply the result of an exposure to the burning heat of an equatorial sun, for the trial generally occurs during the hottest portion of the day. In no case which has come under my notice, in which any of the physiological actions were produced, has the slightest trace of this symptom been experienced.

In cases in which the ordeal is successfully undergone, nausea occurs, and is quickly followed by vomiting and violent catharsis, when the accused is immediately declared innocent. The sickness rapidly disappears, and headach is the only symptom which remains during the remainder of the day. It is very evident that in this class of cases, where death is not caused, the Ordeal Bean must have been subjected to some process by the Fetish men, by which, in place of the well-marked symptoms of the fatal administration, the poison is either destroyed or quickly removed by vomiting and purging. In order to remove this difficulty, a number of experiments were performed in support of various hypotheses, which served to supply an explanation. It was found that the protracted boiling of the powdered kernel does not, to any evident degree, modify the energy of the poison. It is, however, probable, from one experiment which I performed, that by subjecting the entire bean to

the action of boiling water for several hours, its properties may be modified.

It appeared from this experiment, that a dose of the kernel so prepared, twice as great as will usually cause death, occasioned a train of symptoms very nearly resembling those which have been described as producible by the spermoderm, and also resembling them in the absence of a fatal effect. The most characteristic of these symptoms was a violent cathartic action. The poison may thus be eliminated from the system even when no vomiting is produced, and, *a fortiori*, when this action has resulted. The active principle of the spermoderm appears to be absorbed by the kernel in the process of boiling, and to exert its influence on the system before a fatal action can be produced by the kernel.

This coincides with the description of the various Calabar missionaries, who state that the bean is produced entire at the trial, thus considerably diminishing the chances of any tampering by mixing with other substances, and in no way opposing the previous subjection of the entire bean to protracted boiling.

I have in conclusion to remark, that the physiological actions that have been shortly detailed here, indicate properties which will probably be valuable in the treatment of disease. There is every prospect of this agent becoming one of those rewards which society occasionally gains, to compensate for sacrifices in the uncertain cause of geographical discovery and exploration, and the laudable cause of the extension of the advantages of civilisation.