

On the characters, actions, and therapeutic uses of the ordeal bean of Calabar, (Physostigma Venenosum, Balfour) : a graduation thesis, for which a gold medal was awarded by the Edinburgh University, August 1862 / by Thomas R. Fraser, M.D.

Contributors

Fraser, Thomas R. 1841-1920.
University of Edinburgh.
University of Glasgow. Library

Publication/Creation

Edinburgh : Oliver and Boyd, 1863.

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From the Author.

ON THE
CHARACTERS, ACTIONS, AND THERAPEUTIC USES
OF THE
ORDEAL BEAN OF CALABAR,

(*Physostigma Venenosum*, Balfour:)

A GRADUATION THESIS,

FOR WHICH

A GOLD MEDAL WAS AWARDED BY THE EDINBURGH UNIVERSITY,
AUGUST 1862.

BY

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EDINBURGH: OLIVER AND BOYD, TWEEDDALE COURT.

REPRINTED FROM THE EDINBURGH MEDICAL JOURNAL, JULY, AUGUST, AND SEPT. 1863.

THE
CHARACTERS, ACTIONS, AND THERAPEUTIC USES
OF THE
ORDEAL BEAN OF CALABAR.

SECTION I.—HISTORY, EMPLOYMENT AS AN ORDEAL, BOTANICAL
CHARACTERS, ETC.

SOCIETY, in sacrificing much to the hazardous cause of geographical exploration and discovery, has frequently been rewarded by the acquisition of materials which have proved of great service to man in a civilized state. There can be little doubt, that a further careful study of the properties of many substances so discovered, would increase our list of economic materials, and especially add to the catalogue of the therapist many agents possessing medicinal virtues.

Within a comparatively recent period a considerable amount of attention has been directed 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 1846,¹ it has since attracted a large amount of attention from Europeans residing in the district in which it occurs. This bean is used principally as a state poison, as a supposed means of discovering crime and a certain method of punishing it,—the suspicion of guilt being held to be verified if it prove the cause of death.

The mode of trial by ordeal, in one or other of its forms, is of extremely ancient origin. It may be stated generally to have existed in every race and country during its stage of infantile barbarity. The ancient annals of Greece² show its existence. In

¹ Edinburgh New Philosophical Journal, vol. xl., 1846, pp. 319, 320, 321.

² Antigone of Sophocles, v. 270.

the Bible one of the earliest accounts of such a trial is found, where a cup of "bitter water" is commanded to be drunk for the detection of conjugal unfaithfulness.¹ In Hindostan and China, in Japan, Pegu, Java, the Canary Islands, and many other places, various forms of ordeal were, and in many are still employed; and in our own country the practice existed to a great extent until the thirteenth century, when, in the reign of Henry III., a law is stated to have been passed for its abolishment.² In the other countries of Europe it had the like prevalence during the medieval periods. It would occupy too much space to attempt to enumerate the many and ingenious methods which were made use of in such trials. They may be naturally classified under two great divisions,—those whose application was *external*, and those in which some substance was introduced into the system, or where it was *internal*.

The *first* includes the well-known trials by fire, water, the combat, and the balance.

The *second* class comprises what may be regarded as the more curious and interesting forms, and it includes the large section of the vegetable ordeal poisons. This description prevails, as might be expected, in the tropical latitudes, where plants containing principles of active energy are more abundantly to be met with. The actions of these vegetable agents have, no doubt, been narrated in very exaggerated terms, and in many instances erroneously. Merolla describes the "Ncassu," a plant employed as an ordeal at Congo, as possessing properties so pernicious, that birds even "fly from the tree, for if they settle on its branches they immediately fall down dead."³ Many of them must, at the same time, really possess energetic actions, in order to suggest the assertion of such absurdities, and many may yet become valuable as therapeutic agents.

The general *rationale* of the use of the ordeal will be more satisfactorily explained by entering on a few details as to its employment at Calabar. The region included in the term Calabar occupies 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, Old Calabar, or Oude Calburgh. Its boundaries are indefinite. It is situated between 4° and 8° N. lat., and 6° and 12° E. long., and is estimated to have a length of one hundred miles, and a breadth of fifty. The natives are descended from the Ibibio tribe, who inhabit a region extending westward from Calabar to the river Niger. Their government is oligarchical. Several chiefs rule the towns, each of which separately forms an independent government, joining with others in times of danger for the common cause, and possessing with them a common council.

¹ Book of Numbers, chapter v., 17–31.

² Blackstone's Commentaries, vol. iv.

³ Merolla's "Voyage to Congo." See Pinkerton's "Voyages and Travels," 1814, vol. xvi. p. 222.

This is presided over by one of their number, who, on this account, receives the title of king, though he possesses no special authority, and has no jurisdiction beyond his own village. Next in power are the medicine-men,—“*mbia-idiong*” and “*mbia-ibok*,” whose duties include the superintendence and conduct of the usual round of processions, feasts, incantations, and the other juggleries of heathenism. In their condition of ignorance, superstition reigns supreme. Everything unexplainable, and all that occurs beyond the ordinary course of things,—with events even of everyday occurrence, as the usual occasions of sorrow, joy, disease, and death,—are ascribed to the mysterious agency of witchcraft. And it is for the discovery of the operations of this evil genius that the discriminating property 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 summoned, the accusation is heard, and the 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 always granted. The ordeal is administered 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 receive the ordeal bean, either in the form of infusion or of the dry kernel. Sometimes a portion of one bean is only taken, at others as many as twenty-five: according to the discretion of the priest, or until innocence is held to be declared by the production of vomiting, or the guilt of the accused proved by his death. 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 compensate for the slowness or failure of the action of the poison.

Should the accused escape, the accuser is liable to undergo the same trial, to show that he does not possess “free-mason” or witchcraft against the accused. A salutary check is thus placed on treachery or private enmity.

The confidence of the natives in the power of the bean is remarkable. They do not believe that any peculiar virtue resides in it, or even that it possesses any disagreeable or dangerous properties, but consider it an instrument indifferent in itself, but employed by the gods to show who is and who is not guilty. The evident denial which is given to such a theory, by the fatal effects which are known to be produced when the administration is without the sanction of a chief, and, therefore, illegal or in violence of their strict rules of trial, is overcome in a very simple and ingenious manner. In such cases the administration is regarded as a murder, and punishment follows. The gods are displeased because the victim consented to eat, and they kill him. But they are also

aware that a death so caused will be investigated by the chiefs, and thus they make sure that the administrator will be charged with murder and himself executed.

The number of deaths occasioned by this ordeal is very considerable. The population of Calabar is roughly estimated at 100,000, and of these upwards of 120 are reckoned annually to be thus sacrificed.

Botany.

The bean is the product of a leguminous plant, the *Physostigma venenosum* (Balfour), found in the neighbourhood and to the west of Calabar Proper, in the territory of a tribe called Eboe (Ibio, Aboi, Abo, or Ibo), who inhabit a region extending westward from the source of the Niger. The plant is described as a *runner*, climbing on the bushes and trees in its neighbourhood; and this character was well shown in the plants which have been cultivated in the Edinburgh Botanic Garden. Its habitat is on the sides and edges of streams, thriving best on swampy river banks. The ripe beans are frequently dropped into the stream, and carried down to Calabar in considerable quantity, so that the natives obtain their supply principally from the banks of the river, irrespective of what is used judicially by the "idol-priests." From this source also was derived one of the parcels of the bean for which I am indebted to the Rev. John Baillie. The plant is perennial, probably producing fruit only after some years. The fruit ripens at all seasons of the year, in common with that of many other tropical plants; but the most abundant crop is produced in the rainy season from June to September inclusive.

The following botanical details are extracted from Professor Balfour's paper in the Transactions of the Royal Society of Edinburgh:—

Natur. order—Leguminosæ. Sub-order—Papilionaceæ. Tribe—Euphaseolæ.

Genus and Species—*Physostigma venenosum*.—It has generic characters closely resembling those of *Mucua* and *Phaseolus*, but is separated from the former by the characters of the flower and pod, and from the latter by its seed. It has accordingly been placed by Professor Balfour in a separate genus, *Physostigma*, and is itself the only known species, *venenosum*.

Generic Charact.—Root, spreading with numerous fibrils, often having small succulent tubers attached. Inflorescence, axillary; on pendulous multifloral racemes; rachis of each raceme zig-zag and knotty. Calyx, campanulate, four cleft at apex, the upper division being notched and its segments ciliated. Corolla, papilionaceous; veined with a pale pink, having a purplish tinge, and curved in a crescentic manner. Stamens, ten, diadelphous. Pistil, more than one. Stigma, blunt, covered by a remarkable ventricular sac or hood, which extends along the upper part of the convexity of the style, having a resemblance to an "admiral's hat set in a jaunty manner." Legume, dark brown and straight, when mature, about seven inches

in length, elliptico-oblong, with an apicular curved point, and with outer and inner integument easily separable. Seeds two or three, separated from each other by a woolly substance.¹

Characters of the Seed or Bean.

The part of the plant of interest on account of any known properties is the *seed* or *bean*.

Synonymes.—Esērē nut; the bean of the Etu esere; chop nut; the ordeal bean of Calabar.

Form.—Irregular reniform, having the appearance of a somewhat flattened fusiform body bent on one of its edges. It has two margins, a shorter or concave and a longer or convex, and two flattened surfaces. Extending along the convex margin is a sulcus, having a minute aperture near one of its extremities.

Colour.—As obtained from Calabar the beans have a grey colour, and are incrustated with earthy matter. This is readily removed by washing, and a somewhat shining integument is exposed of various shades of brown, ranging from a light coffee to an almost perfect black.

Sulcus.—On the convex edge is the furrow or sulcus already alluded to, with elevated edges, which have, externally, a reddish black hue, while, within, the sulcus is generally brown with a shade of yellow. It extends unequally towards either extremity; at the more extended portion, it runs along a part of the extremity of the bean, and terminates in a narrow furrow; at the shorter end, it has a more rounded termination, and is pierced by a foramen. The bottom of the sulcus is of a grey or reddish black colour, and has two parallel markings extending down its centre.

Dimensions.—The average length is 1 and 1-16th of an inch, and varies from 1 inch to 1 and 8-16ths. The average breadth is 12-16ths of an inch, and varies from 10-16ths to 14-16ths. These measurements are the extremes in each direction, and the sides slope from the greatest breadth to the comparatively narrow extremities. The average thickness or breadth from one flattened side to the other is 8-16ths, the maximum 11-16ths, and the minimum 6-16ths of an inch.

Weight.—The specific gravity is about .946, therefore less than that of spring-water, and we can thus understand how the beans should be conveyed down the rivers to the seacoast. A very few, however, sink in distilled water; out of 300, I have found eighteen such, or 6 per cent. The bean weighs, on an average, 63.263 grains. The greatest weight met with was 94, and the least 25 grains.

When the covering was removed from the bean, the embryo was found to weigh, on an average, 46.2 grs., varying from 21 to 73 grs., and the removed spermoderm 16.73 grs., varying from 13 to 19 grains.

¹ See Professor Balfour's paper in the Transactions of the Royal Society of Edinburgh, vol. xxii. Part II.

The external tegument is of great hardness and toughness. It is with difficulty cut with a knife, and considerable force is required to break it in a mortar. Its internal surface is of a bluish grey colour.

So slight is the absorbing power of this covering, that the bean may be exposed to the action of *cold* water for a long time without undergoing any change. A bean was carefully measured and weighed, and placed in a covered vessel containing water, in which it was left for four months. When examined, no change had been produced in the dimensions or weight of the bean.

When exposed to the action of water of a temperature of 212° , or to the action of steam for a few hours, the bean swells by imbibing a quantity of fluid, which may be found in the central cavity, and the spermoderm becomes soft, and can be cut readily into sections with a knife. If the heat be prolonged, the spermoderm cracks and fissures, and the colour of the kernel is changed from a yellowish white to a brownish hue. A fractured portion has a distinct odour of *cocoa*.

When a transverse section of the spermoderm is examined microscopically, the following structures are shown:—

1. At the bottom of the sulcated hilum are two bodies separated in the median line, forming the floor of the sulcus, and extending a considerable way up its edges. They are about the 1-157th of an inch in perpendicular thickness at the centre, and taper towards the ends. They consist of an aggregation of rods, each extending through the whole depth of the structure, and terminating at both ends in thickened extremities.

2. *Outer Layer of the Spermoderm.*—It is very similar in structure to the above, and forms the external envelope of the spermoderm. It extends over the entire surface of the bean, except at one end of the floor of the sulcus, where the opening of the foramen occurs. It is between the 1-138th and 1-117th of an inch in perpendicular thickness, and consists of a number of rods placed side by side, each rod being about the 1-2250th of an inch in thickness, and terminated by broad extremities.

3. Internal to this is the *middle* and principal *layer of the spermoderm*. It varies in thickness at different places from the 1-8th to the 1-130th of an inch, having its smallest measurement at the narrow convex edge of the bean, and its greatest at the hilum. Its structure is cellular, consisting of stellate cells, having six or eight branches which communicate with others from the neighbouring cells. The cells diminish in size and in the length of their branches as they approach the exterior, and here they appear to form a separate membrane. This is in reality a compressed collection of cells, which extends over the exterior of the middle coat of the spermoderm to a fibro-vascular body to be presently described, and from this to the internal surface of this middle layer.

4. *Inner Coat of the Spermoderm.*—It consists of dark ligneous

tissue, forming a continuous layer immediately below the former, and varies from the 1-470th to the 1-20th of an inch in thickness.

5. *A Fibro-vascular structure* embedded in the middle layer, immediately below and extending along the whole length of the sulcus. In a transverse section it is seen to possess an elongated ovoid form, and from its lighter colour it is apparent to the naked eye. It has a perpendicular diameter of about the 1-65th of an inch, and a transverse diameter of about the 1-120th. In a transverse section, it appears to contain a number of irregularly oval cells, with transverse markings, having their long axes in the same direction as that of the containing structure.

6. *Kernel or Embryo*.—It consists of two large concavo-convex cotyledons, of a creamy white colour, and easily broken in a mortar or scraped with a knife. In a transverse section these are seen to be in close contact externally with the spermoderm, and internally to be quite separated from each other, except at the margins of the bean. A large cavity is thus left in the centre, which communicates with the external atmosphere by means of a minute foramen so small and so narrow as to give no opportunity for the escape of the contained air when the bean is immersed in water. Projecting into this cavity, immediately below the broader extremity of the hilum, may be found the plumule with its two radicles.

Microscopically, the kernel consists of a cellular texture, with cavities of hexagonal, and often of very irregular one-sided form. These cells vary from the 1-650th to the 1-140th of an inch in diameter. They contain from one to six starch corpuscles, which are readily detached by washing, and give the usual reactions with iodine, bromine, and boiling water. The general form of these starch granules is an elongated oval, frequently approaching an irregular reniform shape or rounded parallelogram. They have usually a regular margin, but this is often indented. The surface has, in the majority of cases, a central line in the long axis, surrounded by concentric rings, but frequently the central line is superseded by a dark space containing amorphous granules. Occasionally, dark radial lines extend, from the central line or space, more or less completely to the circumference, presenting an appearance similar to radiated cracks in a transparent sphere.

The average length of the starch granule is 1-440th of an inch, varying from the 1-700th to the 1-300th. The average breadth was found to be 1-625th of an inch, and varied from the 1-920th to the 1-400th.

The bean has been always received remarkably free from all disease,—only one form of abnormality, scarcely deserving the name of disease, having been found. This occurs between the spermoderm and kernel, and affects the inner surface of the former and the outer of the latter. It consists, on the kernel, of a circular, somewhat dark, indented space, varying in diameter from the 1-6th to the 1-8th of an inch, and having a central irregular depression from

which a number of faint lines diverge towards the circumference. The kernel is found much softer than usual within this area. On the inner surface of the spermoderm a corresponding space is found, of a brownish colour, and distinct from the usual bluish grey. This appearance is probably due to the attack of an insect, although our research has never succeeded in finding one.

SECTION II.—PHYSIOLOGICAL ACTIONS.

Physiological Action of the Seed or Bean.

No part of the *Physostigma venenosum* is known to possess active properties except the seed or bean. Experiments, with results of a completely negative character, were performed with the stem, of which I received a supply from Professor Balfour.

A. *Actions of the Spermoderm.*—When a considerable quantity of the alcoholic extract of the spermoderm is introduced into a part of the cellular texture of a rabbit, the animal, after the first few struggles, shows symptoms of uneasiness by a restless and disturbed manner. In five or six minutes, urine is voided in a copious stream, paralysis commences in the extremities, the posterior generally yielding in the first place, and in a few minutes the animal ceases to struggle when lifted by the ears. Fæces are soon passed, and this evacuation persists during the effects of the administration, —the fæces being at first normal, but becoming gradually softer, and ultimately nearly fluid. In about twenty minutes from the commencement of the administration, the pupils are observed to be contracted, not however to any extreme degree, and always remaining under the influence of light. About the same time the muscles of the neck become affected, and the head appears to be supported with difficulty. It has a trembling motion, and is soon after laid on the table. The whole body is then extended, and the animal lies on the thorax and abdomen. Urine and fæces continue to be frequently voided, and in about *thirty minutes* the respirations become noisy. The animal may recover its proper position, and stand for a short time in a shaky manner, but it soon falls again; and this process is repeated until the paralysis is completely recovered from,—generally in about *two or three hours* after the administration.

Consciousness is retained during the whole time. The animal can hear, and is sensible to impressions which cause pain. Reflex action is impaired, but never completely lost. Fæces and urine are passed very frequently for about *twelve hours* after the recovery from the paralysis. The paralysis is a most striking symptom. It is most distinctly shown by the inability of the limbs to support the body, and by the shaking of the head from incomplete enervation of the muscles of the neck.

Fatal results have not been produced in any experiment, although doses of the alcoholic extract, varying from one to four grains, have

been given. Each grain of this extract is equal to sixteen of the powdered spermoderm, and it follows that the alcoholic extract from sixty-four grains did not produce death.

The spermoderm has evidently an action on the spinal cord of a sedative nature, as is shown by the muscular paralysis and the contraction of the pupils. On the relation of this latter symptom, with the effects of neurotic agents, I shall have occasion to enter more fully when treating of the actions of the kernel. There is, besides, what appears to be a specific action exerted on the secretions of the intestinal canal and kidneys, both of which are increased in quantity, causing micturition, with the escape of very fluid fæces.

The most prominent actions of the spermoderm are therefore sedative on the spinal cord, hydragogue cathartic, and diuretic.

B. *Actions of the Kernel.*—I. *On Vegetables.*—The infusion of the powdered kernel appears to produce no bad effects on certain plants, while on others it exerts a sedative action. No explanation can be advanced of this variety of effect.

This infusion serves as a menstruum for the generation of infusoria with as great rapidity as one of ordinary vegetable matter.

II. *On Animals.*—a. *Constitutional.*—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 at the posterior regions, and this extends forwards to the anterior extremities and the head. The limbs yield immediately afterwards, the posterior becoming generally first paralyzed, and the animal lies extended in a state of almost complete muscular flaccidity. A few attempts may be made to recover the normal position, but they are usually ineffectual. The bowels, in some cases, are evacuated. The pupils *contract*; as the symptoms advance, the respiration becomes slow and irregular, with a distinct stertor accompanying both inspiration and respiration, 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. By and by the eyelids do not contract when touched, or even when the eyeball is pricked. On lifting by the ears, the limbs hang inertly, 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. During incomplete paralysis, proofs of sensation may be obtained by pinching the ears or pricking the skin. Immediately after death the pupils dilate.

On opening the body, the various muscles which are cut contract. The diaphragm and muscles of the extremities may be excited to action by pinching the phrenic and sciatic nerves, and the contractility of the muscles generally is retained for some time after death. The heart is found acting regularly, and the intestines exhibit

distinct vermicular action. The heart may continue its action for one hour and a half after death. Its chambers usually cease to contract in a definite order, the left auricle first losing its contractility, then the right and left ventricles, and after an interval the right auricle. The large veins in the thorax are found distended. The surface of the brain is injected, and of a dark colour, and the spinal cord appears normal as to its supply of blood. The lungs are engorged: in two experiments, this had proceeded to such an extent that detached portions sank in water (Experiments 2 and 7). The kidneys and liver are dark, and their vessels appear full of venous blood. The back of the tongue is injected, and the fauces contain frothy mucus, which covers the top of the larynx, but seldom extends to the trachea. Serous fluid is found in the abdomen to a greater or less extent. The stomach is usually full, and no change can be detected in the digestive tract.

When a *large* fatal dose of the kernel is administered, the hind-limbs almost instantly yield, and the animal falls. It lies flaccid and in any posture on the table, and exhibits muscular power only by a few twitches. The pupils contract; in a few cases fluid escapes from the nostrils, and the lachrymal secretion is increased. 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, a few muscular twitches occur, less strong and numerous than when a small dose is given. The heart is found distended and passive: irritation, however, produces contraction for about ten minutes after death. The vermicular action of the intestines is very much diminished, and can scarcely be observed. Pinching of the sciatic and phrenic nerves produces no muscular contraction. The mesenteric arteries and veins may be readily distinguished by the colour of their contents. The same difference is evident in the aorta and venæ cavæ, and the whole vascular system is well-filled. The brain and spinal cord never presented any abnormal appearance, but had their vessels full without any injection.

On incising the heart's chambers, they are found full, and the contents of each distinctly different in colour (Experiments 13, 15, 26, etc.). The stomach and intestines are usually full and the bladder distended. The liver, lungs, and other organs appear quite normal.

These effects were produced whatever the channel of introduction. I have made experiments in which various preparations of the kernel were introduced by means of the principal tissues and systems of the body,—

By means of the *circulatory* system, through direct injection and application to a wounded surface (Experiments 1, 2, 13, etc.).

By means of the *nervous* system, through immediate contact with nerve substance (Experiments 16 and 18).

By means of the *respiratory* system, as by injection into the tissue of the lung (Experiments 14 and 15).

By means of the *nutritive* system, through introduction into the stomach and rectum (Experiments 7 to 12).

By means of the *muscular* tissue, by direct contact (Experiment 17).

By means of the *serous tissue*, as into the cavities of the pleura, pericardium, and peritoneum (Experiments 4, 5, and 6).

By means of the *mucous tissue*, as by contact with the Schneiderian, auditory, and conjunctival membranes (Experiments 23, 24, etc.).

The effects in each have only varied in their rapidity, and a connexion apparently exists between the degree of this rapidity and the class of symptoms produced. Direct injection caused the most rapid results; then introduction into cellular and serous tissues; and, lastly, contact with the mucous membrane.

I have never succeeded in producing any symptoms in the rabbit by application to a surface denuded of cuticle (Experiment 21).

b. Topical Action.—When the alcoholic extract is placed in contact with living contractile tissues, their function is suspended. When a muscle is dissected, and carefully painted over with a small quantity of the syrupy extract, in a very short time it loses all power to contract, when irritated either directly or through the medium of its nervous supply (Experiment 17).

The cardiac muscle may be so affected by injecting the syrupy extract into one of its cavities (Experiment 19).

When the exterior of the heart is painted, a temporary effect only is produced, and the contractions recur after an interval (Experiment 20).

The vermicular action of the intestines is almost instantaneously stopped, in a limited portion, by painting a small quantity of the syrupy extract over that portion (Experiment 21). A similar result follows the injection of the infusion into the rectum (Experiment 9).

The same effect is produced on the eye by direct application, as by introduction through the system; contraction of the pupil, confined in this instance to the eye on which the preparation is applied, being very soon caused (Experiment 25).

A local inflammatory action results where the preparation has been in contact with certain of the tissues, a distinct congestion being apparent on examination after death. This is only seen when the preparation has been in contact with cellular and serous textures, never in the case of a mucous membrane. It appears to be an example of the general phenomenon of a foreign body producing a local inflammation, and not of any specific irritant property of the poison.

When the syrupy extract is applied to the cutis of worms, a very rapid action ensues. A little uneasiness is evidenced by wriggling.

This is quickly followed by inability to progress, and by absence of reflex action or irritation. Soon after the worm lies motionless and contracted, slimy mucus is exuded, and death ensues (Experiment 23, *a.*). When a limited portion, as one-half, is carefully painted over with this extract, the paralysis and other symptoms are for some time confined to that portion, whether anterior or posterior (Experiments 23, *b.* and *c.*).

The physiological actions of the bean were produced with the greatest energy on birds. Experiments were made with rabbits, cats, dogs, guinea-pigs, frogs, lizards, beetles, flies, leeches, worms, and several genera of the molusca.

Generalizations.—From these results, and especially from the two varieties of action and appearances after death, it is probable that the seed or bean of *Physostigma* 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 latter is of considerable importance in illustrating the action of the bean.

Valentin¹ has arrived at the conclusion, after an extended series of experiments, that the iris receives its motor supply from two sources,—from cerebral and from spinal nerves. He has also shown that the cerebral filaments are distributed to the circular muscle or *contractor* of the pupil, and the spinal to the radiating fibres of the iris or *dilator* of the pupil. It follows from this, that the condition of the iris, and consequently of the pupil, may be influenced by agents operating on the distributed nerves or on their origins. Thus, a stimulus applied to the spinal filaments will occasion *contraction* of the *radiating fibres* and *dilatation* of the pupils, and a stimulus applied to the cerebral fibres will cause, through the circular fibres of the iris, contraction of the pupil. An agent producing an inverse effect on either system of nerves will, in the same way, produce an inverse result.

A little consideration will show that the condition of the pupil may be influenced through its nervous supply, in at least six different methods,—

1st, By cerebral irritation.

2d, By cerebral depression.

3d, By spinal irritation.

4th, By spinal depression.

5th, By a combination of cerebral irritation with spinal depression.

6th, By a combination of cerebral depression with spinal irritation.

I have arranged several of these effects as produced by poisons in a tabulated form, and the connexion between the physiological actions and the condition of the pupil is very evident.

¹ De Functionibus Nervorum Cerebraliū et Nervi Sympathici: 1839, pp. 109, 114.

Methods in which the Size of the Pupils may be Affected.

TWO CEREBRAL.

1. Cerebral Irritation = *Contraction*, as with Opium.¹
2. Cerebral Depression = *Dilatation*, as with Belladonna,² *Æthusa cynapium*,³ *Hyoscyamus niger*,⁴ Alcohol,⁵ *Veratrum album*.⁶

TWO SPINAL.

3. Spinal Irritation = *Dilatation*, as with Strychnia.⁷
4. Spinal Depression = *Contraction*, as with *Physostigma venenosum*, *Aconitum Napellus*.⁸

TWO COMBINED CEREBRAL AND SPINAL.

5. Cerebral Irritation and Spinal Depression = *Contraction*, as with *Ruta graveolens*.⁹
6. Cerebral Depression and Spinal Irritation = *Dilatation*, as with *Cicuta virosa*,¹⁰ Nicotine,¹¹ Hydrocyanic acid,¹² *Digitalis purpurea*.¹³

The actions of the two nervous supplies for the iris may 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 spinal supply is removed from the iris, the muscles which are acted on by the cerebral nerves will be unrestrained, and contraction of the pupil will result, in the same way as a direct irritation of these (cerebral) nerves would act.

We can thus refer the action of the bean of the *Physostigma venenosum* to the spinal cord. The contraction of the pupils may be caused in three ways: positively, by cerebral irritation; negatively, by spinal depression; and, complexly, by a combination of

¹ The pupils are generally *contracted* in cases of poisoning by opium; they have, however, been observed *dilated*. The symptoms of cerebral irritation are very obscure, but I think that the mental excitement which follows a dose of opium must be regarded as an indication of such irritation. I would suggest that when the pupils have been observed *dilated*, an almost complete suspension of cerebral activity had been produced with more or less spinal irritation. See Christison "On Poisons," p. 709: 1845. It has also been observed, that although at the commencement the pupils may be contracted, as the stupor increases they gradually dilate. Taylor's "Med. Jurisprudence," p. 183: 1861.

² Christison, op. cit. p. 835. Taylor "On Poisons," p. 771.

³ Christison, op. cit. p. 865.

⁴ Christison, op. cit. p. 745. Taylor, op. cit. p. 722.

⁵ Christison, op. cit. p. 951. Taylor, op. cit. p. 729.

⁶ Christison, op. cit. p. 880.

⁷ Christison, op. cit. p. 896. It has been observed that during the convulsive paroxysm the dilatation increases. Taylor, op. cit. p. 207. Brit. and Foreign Medico-Chirurgical Review, vol. lviii. p. 536. In some experiments on rabbits, I have distinctly observed this change on the pupils (see Experiment 25).

⁸ Alex. Fleming, M.D., "An Inquiry into the Physiological and Medicinal Properties of the *Aconitum Napellus*." 1845: pp. 11 and 21. Christison, op. cit. p. 869.

⁹ Christison, op. cit. p. 891.

¹⁰ Christison, op. cit. p. 861.

¹¹ Christison, op. cit. p. 849. Nelligan, *Materia Med.*, p. 354.

¹² Christison, op. cit. p. 765. Taylor, op. cit. p. 653.

¹³ Christison, op. cit. p. 889.

cerebral irritation and spinal depression. The symptoms disprove any cerebral irritative action, so neither the first nor last of these can be regarded as the cause of the contraction. On the other hand, they distinctly indicate a depressing action on the spinal cord; by this action the power of the cord to transmit impressions is destroyed, and, necessarily, the power of transmitting the nervous influence to the iris. The balance between the dilator and contractor muscles is thus removed by the nervous supply of the dilator being stopped; the circular fibres act, and the pupil is *contracted*. In a few experiments it was observed that, sometime after the contraction of the pupils had commenced, if the animal was excited to muscular exertion, as in struggling when irritated, the pupils very distinctly *dilated* (Experiment 25).

An extension of these views may be of importance in the analysis of the symptoms produced by every poisonous agent, as they have become in the diagnosis of diseases, as in the localized affections of the nervous system.

The bean has been shown to produce death in two ways, either by *asphyxia* or by *syncope*; but from the special action of this agent on the cardiac muscle, it is extremely probable that the results are complicated by the *special* weakness of the heart's action.¹

The cases of death by *syncope* are very characteristic (Experiments 3, 6, 11, 14, 15, 26).

The cases of death by *asphyxia* are equally so (Experiments 1, 2, 5, 7, 8, 10, 16).

Death commenced at the heart when large doses were given, and at the lungs when a more moderate quantity was administered.

We have seen that paralysis is the first important symptom. This commences in those muscles that are supplied by the lower part of the spinal cord, and quickly extends upwards, until the muscles of respiration are involved, and *death by asphyxia* is produced. That such is the sequence of events, we must conclude for the following reasons:—

1st, The muscular paralysis occurred invariably as a first symptom in every experiment.

2d, The appearances in an examination after death from *small* fatal doses were those which are caused by asphyxia (Experiments 1, 2, 5, 7, etc.).

3d, The heart, in this class of cases, was found contracting with considerable regularity after death. And,

4th, The pupil contracted during the continuance of the effects, which I have endeavoured to show indicates a *depressing* action on the spinal cord.

We may also arrive at the same conclusion by disproving the

¹ The late Professor Alison refers to such a complication. See "Outlines of Physiology and Pathology," p. 332: 1836.

connexion of the symptoms and appearances after death with the known phenomena of fatal results from other causes. That the action of this agent is not *primarily* exerted on the heart is very apparent in that class of cases where death followed *small* fatal doses. For,

1st, It must be evident that if the paralysis were dependent on any cessation of the necessary supply of blood from a failing of the heart's action, this symptom could not exist without marked effects being produced in other parts of the system, and more especially in the encephalon. Indeed, the functions of the brain proper would be affected even *previous* to those of the spinal cord.

2d, After moderate and even pretty large doses, the heart has been found contracting at the rate of from 50 to 60 beats in the minute in rabbits (Experiments 1, 2, 5, etc.). This diminished action cannot be regarded as a cause of the final insensibility, as it is well known that a greater diminution may take place with scarcely any symptoms.

3d, It has been shown by various investigators, as Dr Cormack,¹ that where death is caused by a neurotic poison paralyzing the heart's action, the *respiratory movements may continue a short time after the cardiac paralysis*.

We may exclude any influence originating in the encephalon by the complete absence of any symptom which could be referred to the brain.

We therefore conclude that in certain cases this agent produces death by asphyxia.

It also occasions death, when *large* doses are given, by the symptoms of *syncope*, as has been proved by the investigation of Professor Christison.²

Dr Christison found that large doses produced languor, muscular flaccidity, and the cessation of respiration, with the preservation, as far as could be judged, of sensation and consciousness. The heart was found after death completely paralyzed, and the right and left chambers contained blood of different colours. These symptoms were also observed in my experiments, and conclusively prove that death is sometimes produced by syncope (Experiments 13, 15, 26, etc.).

If the deductions I have made in reference to a spinal action of the bean be allowed, and if the absence of mental phenomena have the import I have ascribed to it, it appears probable that this syncope is in reality caused by a rapid and energetic action of the bean on the spinal cord. It has been shown by Legallois³ and Dr Philip Wilson,⁴ that when an agent acts on the spinal cord in a partial and somewhat slow manner, it may destroy the function of the cord without influencing, or at least without directly para-

¹ "Treatise on Creosote." 1836.

² Monthly Medical Journal, vol. xx. 1855.

³ "Exp. sur le Principe de la Vie." 1812.

⁴ "Inquiry into the Laws of the Vital Functions."

lyzing, the action of the heart. On the other hand, if this action be intensified, general muscular paralysis is immediately produced, and the contractility of the heart is almost instantly destroyed. In the former case, the symptoms arise in the spinal cord, and death is produced by *asphyxia*; in the latter, the symptoms also begin in the cord, but death is produced by *syncope*.

The two varieties of symptoms following the administration of the bean may be harmonized in the same way. It exerts a special influence on the spinal cord; when this 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, causing death by *asphyxia*. When, on the other hand, this spinal action is more extensive and energetic, the heart is affected, its contractions cease, and death occurs by *syncope*.

We may therefore conclude, that the kernel or embryo of the bean of *Physostigma venenosum* has the following actions:—

1. It acts on the spinal cord by destroying its power of conducting impressions.

2. 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*.

b. In a rapid paralysis of the heart, probably due to the extension of this action to the sympathetic system, thus causing death by *syncope*.

3. A difference in dose accompanies this difference in effect.

4. This 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 influenced secondarily.

5. It also produces paralysis of muscular fibre, striped and unstriped.

6. It acts as an excitant of the secretory system, increasing more especially the action of the alimentary mucous glands.

7. Topical effects follow the local application of various preparations; these are,—destruction of the contractility of muscular fibre, when applied to the muscles, and contraction of the pupil, when applied to the eyeball.

Smallest fatal Dose.—This varies in different animals. I have found that four grains of the powdered kernel may be swallowed by a rabbit eight months old without fatal results. Five and a half grains is the smallest dose with which I have caused death in a rabbit of this age (Experiment 8).

Modified Actions.—A general impression is said to prevail among the natives of Calabar, that the varying effects of the bean is dependent on some mode of preparation by the “fetish-men.” I have found that protracted boiling in water of the powdered kernel does not to any evident degree modify the energy of the poison (Experiment 35). It is, however, possible, from one experiment which

was performed, that subjecting the entire bean to the action of boiling water for several hours may modify its action. It appeared from this experiment that a dose of the kernel so prepared, *twice as great as will usually produce death*, occasioned a train of symptoms very nearly resembling those which have been ascribed to the spermoderm, and produced no 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, *à fortiori*, when this physiological action has resulted. The active principle of the spermoderm appears to be absorbed by the kernel, and to exert its influence on the system by causing evacuation of the poison before a fatal action can be produced by the specific effect of the kernel. This also coincides with the details given by 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, but in no way opposing the previous subjection of the entire bean to such a neutralizing process.

Antagonistic Action to Strychnia.—The peculiar action of the kernel on the medulla spinalis appeared to be so directly antagonistic to that of strychnia, that it seemed desirable to discover whether the effects of the one poison might not be made to annul those of the other. For this purpose, a poisonous dose of strychnia was given to a full-grown rabbit, and when its action had been decidedly produced, a poisonous dose of the syrupy extract of the kernel was injected into the posterior flank. Almost immediately after the rigid condition of the muscles of the posterior extremities was removed, the convulsive spasms of the hind limbs disappeared, and they became perfectly flaccid. At the same time, rigidity and violent spasms alternated in the anterior extremities and anterior portions of the trunk. The animal died shortly after (Experiment 28).

It seems extremely probable that no bad consequences would result from a compound dose of strychnia and this kernel, could the exact quantities be discovered which would in each produce the same degree of their special actions. This is certainly a very great difficulty to be overcome, but it does not appear to be insurmountable.

III. *Actions on Man.*—(a.) *Constitutional.*—Our knowledge of the action of the bean on man is still in an unsatisfactory condition. The complete series of symptoms cannot be narrated with certainty, as no fatal case has been observed by persons qualified to describe the effects. This is certainly *satisfactory*, in a humane point of view, inasmuch as it implies a limit in the occurrence of fatal cases, none having taken place beyond the country where the bean is employed as an ordeal; but it is *unsatisfactory* when we confine ourselves to the scientific aspect of the question, and consider the great blank which is thus caused in our acquaintance

with the details of the effects on man. At the same time, we may arrive at some conception of these results, by considering the accounts of the symptoms in trial by ordeal, with their relations to the effects of smaller quantities on man, and comparing these with the conclusions arrived at by experiments on the lower animals.

1. *Symptoms of Trial by Ordeal*.—The symptoms in fatal cases, as described by unprofessional witnesses, may be arranged in the following sequence:—No sensation is experienced for about ten minutes after the commencement of the trial. At this time the victim becomes thirsty. This symptom 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. In a short time the power of swallowing is lost, mucus escapes from the mouth, convulsions and twitches are observed in the muscles of various parts, but especially of the back, and then death, 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 retained till a short time before death and after the accused is unable to swallow.

In the cases in which the ordeal is successfully undergone, nausea is produced, and is quickly followed by vomiting, when the accused is immediately declared innocent. The sickness rapidly disappears, and headache is the only symptom which persists during the remainder of the day.

2. *Small Doses on Man*.—Professor Christison has accomplished the feat of eating the largest quantity of the kernel without fatal results. This was about twelve grains. A case occurred in Glasgow, where two servant girls, perfectly unaware of the character of the seeds, ate each about five grains of the kernel of some beans which had been accidentally put within their reach. I have also taken portions varying from six to ten grains, and have administered small doses of an alcoholic tincture to various individuals. From the data thus acquired the effects of a small dose may be described as follows:—In about five minutes after the administration, a peculiar feeling is experienced in the epigastrium, immediately below the sternum. This is very slight at first, but gradually increases in intensity, till it becomes almost painful. Eructation takes place in a short time, and always occurs during an aggravation of this 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, as in Professor Christison's experiment, twitches occur in the pectoral muscles, and the dizziness is much augmented.¹

¹ Op. cit.

I have also further experienced a dimness of vision, a supposed increase in the salivary secretion, or at least an accumulation of fluid in the mouth, whatever its source, and a marked, though slight, perspiration. At this stage attempts to walk, or even to move the limbs, are difficult, and may be unsuccessful, while at the same time consciousness is perfectly retained.

These symptoms reach a certain climax and then gradually decline, dizziness being generally the most persistent, and they almost entirely subside after a night's rest.

The heart's action is described in Dr 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 cardiac contractions have been found to diminish in number. In one experiment, eight grains of the powdered kernel, in an hour and a half, reduced the pulse twenty beats. (Experiment 2, *Actions on Man*.)

These results agree, as far as they go, with the conclusions from experiments on the lower animals. The most marked symptom is the muscular paralysis, both of the voluntary muscles and of the heart. It is well known that important differences may exist in the actions of agents on different animals, as to the details of experiments, and as to the prominence which is given to one or more of these. This is well seen in the present instance, where the physiological action on the heart of man is, from the facilities of observation, shown with great distinctness.

The epigastric sensation was one of the first symptoms in every instance in which I have myself taken the powdered kernel, or any of its preparations, and in every case in which it was administered therapeutically. The sensation is rather peculiar, and its quality may be understood by some, by saying that it resembles the unpleasant feeling which is produced when a piece of solid food of too large a size is suddenly "bolted." It is at first very slight, recurs at intervals, and is first perceived about fifteen minutes after the administration. It is accompanied by eructations, which generally occur during the sensation, being preceded and followed by it. In one case it was produced by the external application of the tincture (Case 6, Section IV. *Therapeutics*).

General muscular weakness has in each of the experiments been mentioned as a prominent symptom. It is very difficult to discover the immediate cause of this action,—whether it be due to a change in the inherent property of muscular fibre, or in the nerves which convey the impressions which act as the direct stimulants of these fibres. The latter view appears to be the more probable, because we have found that the voluntary muscles are distinctly removed from the influence of the will, and in an order the reverse of that in which an agency could be brought in contact with these muscles by the blood,—as the paralysis of the lower precedes that of the upper extremities. We have also seen that the function of the

nerves to conduct impressions may be lost (Experiment 18), while the muscles to which these nerves are distributed retain their contractility and respond to direct irritation. And we have seen that when the extract was applied to the *external* surface of the heart, its effects were slow and transitory, whereas, when it was brought in contact with the *internal* surface, an immediate and permanent effect was produced, thereby proving that the greater opportunity to influence the nervous structure is followed by the greater effect (Experiments 19 and 20).

The sedative action on the heart may be explained in two ways,—*first*, by a direct local action on the proper contractile apparatus, whether nerve or muscle; and, *secondly*, by a nervous influence emanating from the cord,—a result of the change produced there by the bean. As we have seen that an energetic influence is exerted on the cord, and even on the spinal nerves, which are considerably removed from their origin, we are entitled to suppose that this special spinal action may affect the relative innervation of the heart. It is also probable that the smallest portions which may be circulating in the blood will exert their sedative action on the nerves distributed to the inner surface of the heart. That this latter is not the primary but a secondary action, I am inclined to believe, from the very significant fact that the muscular paralysis has been observed before any perceptible change in the radial pulsations (Experiment 3, *Actions on Man*).

In the symptoms of trial by ordeal, the whole details, and especially the occurrence of convulsions, appear to favour the view of death by asphyxia rather than by a slowly advancing syncope. It would, however, be extremely unphilosophical to speculate any further on this subject. We must await a complete account of the symptoms and appearances after death from the competent observation of fatal cases. We have only learnt that no effect has been described which appears to oppose the conclusions from an experimental investigation on the lower animals.

(b.) *Topical*.—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 the application. In about thirty minutes after the application the pupil becomes a mere speck, but still retains a certain degree of mobility. It continues in this state for twelve or fourteen hours, but a greater or less degree of contraction of the pupil may persist for five or six days. A slight headache and dimness of vision with myopia in the affected side, are almost always produced, but these only continue for one or two hours at the commencement (Experiment 5, *Actions on Man*). When the extract is applied to the edges and outer surface of the eyelids, there is produced, in addition to the contracted pupil, a degree of immobility of the eyelids (Experiment 6, *Actions on Man*). No effect was produced

on the pupil by friction on the temples or over the eyebrows with any preparation of the kernel.

On the Skin.—When either the tincture or extract is applied to the skin, a local action is caused, especially if a certain amount of rubbing has been employed. In about half an hour a distinct diminution in the sensibility occurs, and the skin may be pricked, very little pain only being excited (Experiment 7, *Actions on Man*).

This obtunding action is not accompanied with any irritation of the skin,—the mode of application and the nature of the preparation being sufficient to account for the slight degree of redness produced.

SECTION III.—PREPARATIONS.

The powdered kernel may be exhausted by spirits of wine, of proof or rectified strength.

Water and acetic acid have not been satisfactorily shown to dissolve any of the active principles. A few trials were made with both, and the results were that, by the process of procolation, efficient preparations could be obtained with neither; the infusion, by maceration with water, suspended such variable quantities of the starchy and leguminous constituents as to be quite unfit for any experimental purpose.

Rectified spirit has been usually employed as the menstruum in the therapeutic portion of this investigation, and a tincture of known strength was uniformly administered. The following is the formula for its preparation:—Take of the kernel, in the form of fine powder, ℥j. ; rectified spirit, ℥ij. Place the kernel and one ounce of the spirit in a carefully covered vessel, and allow to remain for forty-eight hours. Pack in a procolator, pour in what spirit may be left in the vessel, and add the remaining ounce of spirit. When this has ceased to escape from the procolator, pass as much more spirit through as may be required to obtain two ounces of a golden yellow tincture.

This preparation is so far objectionable, that the kernel is not exhausted by the quantity of spirit used; yet it appears preferable to one obtained by reducing to a certain standard, by distillation, a tincture obtained with a much larger proportion of spirit.

I have found five minims of this tincture a good dose with which to commence the administration. This appears to possess the activity of three grains of the kernel, as far as can be judged by the effects produced. The dose may be trebled without pushing the physiological action to any extreme. The kernel can only be exhausted by employing a much larger proportion of spirit. By using twelve ounces of rectified spirit with one ounce of powdered kernel, distilling off about eight ounces, and evaporating the remainder, first to a syrupy consistence, in a vapour-bath, and then by spontaneous evaporation, twenty-one grains of an extract of considerable consistence may be obtained, or a proportion of 4:375

per cent. This extract has a deep brown colour, and a peculiar, sweetish, and disagreeable odour, for which I can find no comparison. Its actions differ only in intensity from those of the kernel and tincture.

In the physiological portion of this investigation, the syrupy extract mentioned above was largely employed, and it is one of the preparations recommended in the application of *Physostigma*, to ophthalmic medicine. A preparation has also been employed of the extract evaporated to a firm consistence, and partially dissolved and suspended in distilled water. I have used such a preparation, obtained by acting with one drachm of distilled water on five grains of firm extract, representing 120 grains of the kernel, one minim of which possesses the activity of two grains of kernel. Of this a small drop, rather less than a minim, will maintain a contracted condition of the pupil for five days. This preparation has the objection of being extremely inelegant, as a large portion of the extract is not dissolved, and renders the fluid muddy.

SECTION IV.—THERAPEUTICS.

We are entitled to infer that the important physiological actions of the kernel of *Physostigma* may be employed with the greatest advantage in the treatment of disease.

Its special action on the spinal cord, and the result, though not entirely conclusive, of the experiment with this substance and strychnia, seem to indicate that it may be of service in all hyperæsthetic conditions of the cord. In tetanus, whether *centric* or *eccentric*, the morbidly excited condition of the spinal system may be allayed. In epilepsy, the investigations of Schröder van der Kolk have so far determined the accompanying pathological changes, that we would be even more sanguine of success from its employment. The *sedative* action on the heart will also, very probably, prove of service. Five minims of the tincture usually shows an influence on the circulation; but in almost every case this dose has been required to be considerably increased before a decided and permanent effect could be produced. When administering it with this view, I have been principally guided in my selection of cases by the condition of the pulse,—a pulse in anywise feeble being considered a decided contra-indication, while one that was strong, rapid, and hard, was considered a true indication for the employment of the tincture. I have found this action of value in erysipelas, delirium tremens, febricula, acute bronchitis, and rheumatic fever, and have detailed a few cases from a number in which this treatment was tried.

CASE 1.—Erysipelas. 15th Nov. 1861. Walter S., æt. 38. Married. Out-door labourer. Patient had been attacked four days previously, with rigors, but continued his work till yesterday morning. When first seen, at 10 A.M., pulse 96; full and hard. Whole face, and especially on right side, red and puffy. Lips and eyelids much swollen. The inflammation extended

to the scalp, ears, and neck. Tongue with slight fur. Throat and fauces red and tender. Patient has been extremely restless, had very little sleep for two previous nights, and was delirious last night.—R. Tinct. Physostigmatis, min. viij.; Aquæ, ʒj.; Ft. haust. statim sumendus. A little flour was also ordered to be dusted over the inflamed parts.

8 P.M.—Pulse 94. Attendant states that the restlessness has diminished.—Repet. Tinct. min. viij.

16th Nov.—10 A.M. Pulse 90, still full and hard. Patient slept for a short time during the night. A little delirium.—Repet. Tinct. Physostigmatis, min. viij.

8 P.M.—Pulse 86. Slept two hours this afternoon. Inflammation is decidedly less. Bowels freely opened.—Repet. Tinct., min. viij.

17th Nov.—10 A.M. Pulse 78, soft and slightly irregular. Slept well last night, and without delirium. Desquamation commenced on face.—Repet. Tinct. Physost., min. viij.

8 P.M.—Pulse 69, soft, irregular, and intermittent. Patient has slept during the day. Natural features recognisable. Tenderness of fauces gone. On being asked, patient described a sensation in the epigastrium, as of a ball rolling about, and followed by eructation. This has been perceived half-an-hour after the two last doses.—Repet. Tinct. Physost., min. viij.

18th Nov.—10 A.M. Pulse 62, soft, irregular, and intermitting. Inflammatory swelling almost gone; a little puffiness still about the ears. Patient thinks himself quite well, but is unable to stand from loss of power in the legs and thighs, and feels his arms weak and almost powerless.—Hab. Tinct. Physostig., min. v.

8 P.M.—Patient has been out of bed nearly all day. Pulse 65, soft and intermitting. Complains of extreme weakness. Erysipelas quite gone.—Omit. Tinct. Physostig. The pulse gradually rose to 70, and became much stronger in a few days. The muscular weakness disappeared in two days.

CASE 2.—Delirium tremens. W. J., æt. 36. Labourer employed at the Caledonian Distillery. Robust and plethoric. Has been lately indulging in large quantities of whisky, and has not taken any food for two days.

27th Dec.—8 P.M. Found patient with a pulse of 90, full and hard. Tongue trembling when protruded; moist, and with slight fur. Symptoms had begun two days previously. Last night patient had not slept, and was so delirious as to get out of bed frequently, notwithstanding the care of his wife and a male relative.—R. Tinct. Physostigmatis, min. viij.; Statim sum.

28th Dec.—10 A.M. Pulse 84, irregular, but hard and full. Patient slept a little, and was quiet and without delirium all night.—Hab. min. xij.; Statim.

8 P.M.—Pulse 76, soft and irregular. Patient had slept two hours after the last dose. No delirium. Bowels have been freely opened.—Repetatur.

29th Dec.—10 A.M. Pulse 68, soft and intermitting. Patient slept all night, and woke apparently recovered. Complains of great weakness of limbs when attempts are made to walk.—Omit. Tinct. Physos. Patient was soon in perfect health.

CASE 3. Delirium tremens. (This case was communicated in a fuller form to the Royal Medical Society of Edinburgh on the 13th of March 1863.) D. M'P., æt. 43, a strongly built labouring-man. Admitted to Ward VI. of the Royal Infirmary on the 28th of February, with a very limited pneumonia of the base of the right lung. In addition to the signs of pneumonia, a peculiar restless manner was observed. The eyes wandered incessantly from one object to another, questions were answered in an abrupt manner, and the patient was constantly making incoherent and unconnected remarks. A history was then obtained of seven days' constant drinking which had terminated the night before admission, and during which the patient had drunk at least six quarts of ale and three or four gills of whisky daily. Ordered an expectorant mixture.

1st March.—10 A.M. Pulse 120, full and bounding. Tongue dry, with a grey fur; trembling when protruded. Skin dry and warm. Patient has taken no food since admission. His hand trembles when raised. Did not sleep last night, and was noisy. Has now delusions.

8 P.M.—Pulse 126, full, bounding, and somewhat hard. Has neither slept nor taken food since last report. The excited manner, indistinct articulation, and trembling of the hands and tongue continue. He attempts to escape from imaginary persecutors, occasionally cries out, and says he is being thrashed. Pupils about two and a half lines in diameter, nearly equal, and mobile. Ordered min. vj. of the tincture of *Physostigma* in water, which was taken at 9 P.M.

10 P.M.—Pulse 112, still hard and bounding.—Hab. min. x.

11 P.M.—Pulse 90, rather more compressible. Patient is quieter, and says he feels better.—Repet.

12 P.M. Pulse 78, soft and regular. Patient slept shortly after the last dose, and is now in a sound sleep, so much so, that the raising of the bed-clothes to count his pulse did not waken him. He continued asleep till 1.30, when he awoke, but was very quiet, and again slept for four hours.

2d March.—10 A.M. Pulse 84, soft and regular. Skin covered with profuse perspiration. Tongue moist, with a grey fur, still trembling a little. Patient can hold out his hand with comparative steadiness. *The pupils are contracted to about one line in diameter*, but no impairment of vision can be discerned. Patient is able to read small print at the distance of six inches, and can count small objects at the other end of a large ward. Delusions gone. Patient took some breakfast.

9 P.M.—Pulse 86.—Hab. min. vj.

3d March.—10 A.M. Pulse 78. Patient slept last night as well as when in perfect health, and was found with a clean tongue, moist skin, and absence of every symptom of delirium tremens.

I should be inclined to recommend this tincture only in such cases as the above; never in weak patients, with a feeble pulse, and the other characteristics of the asthenic variety of this disease. All the symptoms in delirium tremens may be referred to the brain and heart. The most prominent symptom, and, in the present condition of pathology, the first indication for treatment, is the persistent sleeplessness. Sleep may be said to consist of a cessation of mental activity, or at least of a repose of the functions of relation, or those connecting us with external life, accompanied by a diminution in the circulatory force. It is probable that the condition of the circulation is dependent on that of the whole body, and especially of the nervous system, a *diminution* in the *demand* for blood being followed by a *diminution* in the *supply*. In this class of cases, therefore, we may explain the action of this agent by its influence on the heart. The abnormal condition of the cerebrum produced by alcohol requires and occasions an increase in the supply of blood, to produce which the heart is stimulated to contract with greater frequency. The *Physostigma*, through its influence on the nervous system, reduces the excited cardiac action; and, whatever be the condition of the circulatory *vis a fronte*, or *demand* for blood, the *vis a tergo*, or principal agent in *supplying* this demand, being controlled, the disposition to wakefulness is conquered by the large supply of blood necessary to great cerebral action being prevented. The morbid mental activity is thus removed, and a condition favourable to subsidence into sleep produced.¹

¹ This view of the pathology of delirium tremens is supported by the able Inquiry into the Physiology of Sleep, by Arthur E. Durham,—Guy's Hospital Reports, 3d series, vol. vi. 1860, p. 149-173.

CASE 4. — Febricula. A. M^l, æt. 29. Factory girl. Unmarried.
 9th Feb. 1862.—10 A.M. Patient complained last night of coldness and shivering, general lassitude, and pains in her back. This morning she is unable to leave her bed. Pulse 126, strong and hard. Tongue dry. General surface parched and hot. Patient complains of thirst.—Ordered min. vj. of the tincture of *Physostigma* in a little water.

3 P.M.—Pulse 123.—Ordered min. x.

8 P.M.—Pulse 86. Bowels have been freely opened. Tongue slightly moist. Skin soft, with a little perspiration. Repeat min. x.

10th Feb.—10 A.M. Pulse 78. Patient perspired freely during the night. Headache and pains gone.—Ordered min. xij. of tinct. of *Physos*.

8 P.M.—Pulse 72. Copious perspiration.—Repet.

11th Feb.—10 A.M. Pulse 74, irregular, and of normal strength. Tongue nearly clean; surface moist.—Rep. min. xij.

8 P.M.—Pulse 68, soft and irregular. Bowels have again moved.—Hab. Tinct., min. x.

12th Feb.—10 A.M. Pulse 61, feeble and irregular. Patient slept extremely well. Tongue clean and moist. Patient feels quite well.—Omit. Tinct. Patient was out of bed, and complained of general muscular weakness. Bowels have been moved. No further treatment was required. Pulse rose to about 72, but continued weak and irregular for several days. The muscular weakness disappeared in three days. The epigastric sensation was observed in this case also.

CASE 5.—Acute bronchitis. E. M., æt. 40. Married. Stout and robust.

2d March 1862.—8 P.M. Has been unwell for three days. Pulse 110, full and strong. Respirations 37. Frequent cough, and expectoration of considerable quantities of frothy mucus. Tongue dry and loaded. General surface dry and hot. Great thirst and considerable headache. *Physical signs*.—Percussion normal. Large and small crepitation over left lung, especially towards apex. Rhonchus over right side.—Hab. Tinct. *Physostigmatis*, min. x.

3d March.—10 A.M. Pulse 90, rather softer. Respirations 34. Bowels have been thrice moved since last night, and stools liquid. Patient vomited about two hours after taking the tincture, and this was followed by copious perspiration. Tongue cleaner, but still loaded. General surface moist.—Hab. Tinct., min. vj.

8 P.M.—Pulse 96. Respirations 34. Bowels have been moved once since last visit. Patient speaks spontaneously of a sensation of muscular weakness, and, on being questioned, admits having the epigastric sensation and eructation, which commenced about ten minutes after each dose, and continued for half an hour.—Habeat min. x.

4th March.—10 A.M. Pulse 84, very soft and compressible. Respirations 28. Had no sickness nor vomiting. Bowels have moved once since last night. Headache quite gone. Cough much relieved. Rhonchus cannot be heard on right side. No change in left lung.—Repet. min. x.

8 P.M.—Pulse 72, soft and irregular. Respirations 28. Bowels have not been moved. Surface moist. Tongue moist and nearly clean. Appetite much improved. Patient again speaks of the eructation.—Repet. min. x.

5th March.—10 A.M. Pulse 70. Respirations 30. The small crepitation is confined to the left apex, the large extends over the left side.—Repet. min. x.

8 P.M.—Pulse 66, very soft and intermittent. Respirations 27. Tongue moist and quite clean. General surface very moist; indeed, wet. Patient is very much opposed to having the medicine stopped, as she thinks it is of advantage to her.—Hab. min. viij.

6th March.—10 A.M. Pulse 68, soft and irregular. Respiration 25. Pyrexia entirely disappeared. Tongue clean. Physical signs in the lungs have very much diminished,—a limited amount of large crepitation being heard at the left apex. Muscular prostration very great.—Omit. Tinct.

This case terminated in complete recovery in about four days more, and without any further treatment. The muscular weakness disappeared in that time.

From the severity of the case and the marked effects of the treatment, I cannot avoid concluding that the tincture of physostigma was of service in producing the favourable result.

Cathartic Action.—We have seen that a decided action was exerted on the bowels in several of these cases, and this in conformity with the results obtained by experiments on the lower animals. It is possible that this action may be found of some service, but I have not specially tested its value. If Physostigma can be so employed, I think it will prove of peculiar service, from the absence in the remedy of any nauseous taste, and from the cathartic action being produced without tenesmus, and rather with the association of effects of a sedative nature.

The *Anæsthetic Action* may be applied to the treatment of all nervous irritations. I have employed it with great advantage in various neuralgic affections and in irritable stomach. It probably acts by producing a local change in the nerves of the affected region, which interferes with their power of *receiving* or of *conducting* impressions. That it does not depend on any constitutional action of the kernel appears probable from the absence of any appreciable constitutional symptom.

An agent can remove painful impressions in only three ways,—1st, by an influence exerted on the tissues which cause the pain by their abnormal connexion with the sensitive nerve,—as in the swelling of inflammation; 2d, by an influence exerted on the organ which receives the impressions,—the cerebrum; and, 3d, by an influence exerted on the sentient nerve-fibre itself, or on its power of conducting sensation. We have no facts to support the first cause of the sedative action in the present instance, and it is extremely improbable; the second is disproved by the absence of cerebral symptoms; and every probability exists in favour of the last. I have employed both the tincture and the alcoholic extract, the former seeming to me the preferable form of application. Half a drachm to one drachm of the tincture, rubbed on the seat of suffering for fifteen minutes, will remove severe pain for an interval of about two hours, and an ultimate cure may be produced by repeating the application for a limited number of times. The following case will illustrate this action:—

CASE 6.—J. S., æt. 38. Married. Labourer and maltsman. 5th March 1862.—8 P.M. Afflicted with severe pain in the lumbar region, aggravated by movements. Pain commenced suddenly on the 1st March while patient was working, after a cold wetting. It was at first intermittent, but so severe during the paroxysm as to prevent him from working. The pain has become much worse during the last two days. It is now constant, though with occasional aggravations of severity, and has obliged the patient to remain in bed. He says he has not slept for two nights. When seen, patient was lying on his back, and appeared to avoid making the slightest movement. The pain was confined to the lumbar region, and was most severe on the right side.—One drachm of the tincture of Physostigma was ordered to be rubbed on the painful part for fifteen minutes.

7th March.—10 A.M. Patient is considerably better, can move a little, and

slept during the night. He says the pain was completely removed about half an hour after the application, but returned in a milder form in three hours. The same quantity was ordered to be rubbed in immediately, and this repeated at 7 P.M.

8 P.M.—Patient is sitting before the fire without the slightest pain.

The application was repeated once, and on the following day the patient returned to his work. In this case the epigastric sensation was produced by the external application.

I have employed this tincture as an anodyne in various other neuralgic affections. A slight degree of smarting is produced during the application, and a little redness generally remains, but this seems entirely dependent on the alcohol of the tincture. I have also administered it internally as a sedative in malignant disease of the uterus, and in neuralgia of the lower extremities caused by the pressure of a large uterine fibrous tumour, in both cases with marked relief, and without the disagreeable after-effects of opium.

The following case will illustrate the sedative action on the stomach :—

CASE 7.—Irritable stomach. I. M'G., æt. 19. Domestic servant. Has been unwell for a few days, with loss of appetite and a feeling of oppression in the epigastrium.

9th Nov.—9 P.M. To-day, immediately after breakfast, patient had severe vomiting, and this was repeated after very moderate meals at dinner and tea. Vomited matter consisted of almost unchanged food. Pulse 70. Tongue moist, with a little fur. Complains of great nausea.—Hab. Tinct. *Physostigmatis*, min. viij.

10th Nov.—10 A.M. Pulse 66, feeble and compressible. Nausea still complained of, but a little breakfast was retained. Patient experienced the epigastric sensation and eructation.—Repet. min. viij.

4 P.M.—Pulse 60, soft and irregular. Patient had a good appetite at 2 P.M., and took and retained her usual dinner. Nausea entirely absent. Complains of inability to work from weakness in the lower and upper extremities.—Omit. Tinct. Sickness and vomiting did not recur, and the weakness very soon disappeared.

Hypnotic Action.—*Physostigma* may in certain cases act as a hypnotic, though we have no proof of its possessing any specific or primary influence in producing sleep. Its action as an anodyne may account for the sleep in nearly all the cases where this ensued. The previous want of sleep had been due to the irritation of the pain, and by removing such irritation, the patient was allowed to repose. This was well illustrated in Case 6. It is also possible, however, that the sedative action on the heart may exert more direct influence in causing sleep, by producing that moderated activity of the circulation which invariably precedes and accompanies it.¹ In this way we may explain the sleep produced in Cases 1 and 2. In both of these the action has been to remove unnatural obstacles to the production of sleep; whether it can induce the same effect in a natural and healthy condition of the system is

¹ See Durham's paper in Guy's Hospital Reports.

a matter of doubt. In Professor Christison's experiment, sleep followed two hours after the dose had been taken; but this was of a most imperfect character, "the *mind being so active all the while that*" Dr Christison "was not conscious of having been asleep." In no experiment which I performed on myself did I observe the slightest tendency to drowsiness.

Topical.—A topical action which will prove of some service is the influence exerted on the pupils. The power which *Physostigma* possesses in contracting the pupils, when applied immediately to the eye, is very great; and the discovery of this is the more important as no substance was previously known to have such an action. In mydriasis, whether dependent on the over-action of belladonna, or as a symptom of amaurosis, especially the hydrocephalic variety; in the treatment of iritis, and of inflammations of neighbouring structures, where the prevention of adhesions may be more successfully secured by an alternation of contraction with dilatation than by dilatation alone; in all cases in which a change in the position of the iris is indicated, as in injuries of the eyeball, with displacement of the iris; as well as in many other cases which will suggest themselves to the ophthalmist, this agent deserves, at least, a trial. The local application is followed by no inflammatory symptoms, and should therefore be preferred to the usual stimulating applications which have been employed to produce contraction. I should recommend for this purpose the alcoholic extract, in the form of either the syrupy extract, or the more concentrated extract mixed with a definite proportion of water.

This preparation, however modified, must be always, to a certain extent, uncertain in the degree of its action, but this is no important objection, as the contraction of the pupil can be produced by a very minute portion of the syrupy extract. The only caution is to employ as small a quantity as possible. A preparation of unvarying strength will only be obtained when the active principle of *Physostigma* is discovered. For details of the symptoms produced by the local application to the conjunctiva, see Experiment 5, Actions on Man.

The only other external remedial use which I shall refer to, is in the treatment of various parasitic affections of the skin. This mode of application has not been thoroughly tested by me; but I can bear testimony to the great efficacy of the extract in killing the members of one species of parasitic animals. The infusion of the kernel is commonly employed by the natives of Calabar to remove lice from their persons. I obtained, through the ready instrumentality of a dispensary patient, some very large specimens of the *pediculus capitis*, and found that they were killed in five or six minutes after a small quantity of extract had been brought in contact with them.

Toxicology.—This department of the investigation is as yet almost untouched. The only case which can be referred to is one

which has been already mentioned as having occurred in Glasgow to two servant girls. They each ate, through curiosity, about five grains of the kernel. The symptoms which followed in one of those cases have been kindly narrated for me by Dr Maclaren of Glasgow. The woman "chewed and swallowed a piece about the size of a green pea. A very few minutes thereafter she felt sickish, and *had the feeling as if a ball were coming up to the throat*. She went out to the street on an errand, and felt stupid and giddy as she walked along, with a sensation of *a great feebleness over the whole body, rendering progression a matter of difficulty*. She did not vomit; but about an hour afterwards, being recommended to swallow a quantity of hot water, vomiting came on pretty freely. She went to bed and slept tolerably, but next morning, and for two days afterwards, she felt feeble and out of sorts."

This case is interesting, in so far as it gives an unbiassed account of the symptoms produced by a moderate quantity of the kernel. The emetic effect of the hot water had probably no influence in diminishing the action of the five or six grains which were taken, as it was not given for more than an hour afterwards. Coffee is peculiarly useful in getting rid of the languor and headache which are produced when somewhat large doses are taken. This was experienced by Dr Christison; and my own observation was invariably in support of his statement.

SECTION V.—APPENDIX.

Experiments with the KERNEL of Physostigma venenosum on the Lower Animals.

A. Illustrating the Constitutional Effects.

I. INTRODUCED THROUGH THE CELLULAR TISSUE.

EXPERIMENT 1.—A subcutaneous cavity was formed in the right flank of a full-grown white rabbit, and into this six grains of powdered kernel, made into an emulsion with half a drachm of water, were introduced.

No effect was produced for four minutes, when the posterior extremities began to drag. In another minute they were completely paralyzed, and almost immediately afterwards the anterior extremities yielded, and the rabbit lay stretched on the table. Fæces were passed, and a tremor commenced in the muscles of the neck. In eight minutes, the rabbit was lifted by the ears, and did not attempt to struggle, while the extremities hung down in a loose and flaccid manner. It remained on its side, or in almost any position into which it was arranged.

In twelve minutes, a few unsuccessful efforts were made to resume the normal position. The pupils were distinctly contracted. Muscular twitches succeeded each other over the whole body, but especially proceeding from the lower extremities, along the trunk to the neck. The respirations became noisy, and the inspiration was frequently accompanied with a general convulsive movement of the whole body. In fourteen minutes, the pupils were extremely contracted and immobile. The eyelids did not close on irritation of the conjunctiva. Respiratory movements became almost imperceptible. Irritation of the skin induced no reflex movement. The respirations were superseded by distinctly recurring spasmodic movements of the muscles of the thorax and

abdomen, and, in seventeen minutes after the administration, these had entirely ceased.

Autopsy—immediate.—The heart was found contracting sixty times per minute in a regular and rhythmical manner. The contractions continued, with perfect regularity, for fifteen minutes; the number then decreased till, at twenty minutes after death, they were forty per minute. In thirty minutes, the proper rhythm was lost, the left auricle first losing its contractility, then the right and left ventricles, and next forty minutes after death the right auricles. Irritation could produce contractions for fifteen minutes longer, or fifty-five minutes after death, and seventy-one minutes after the administration.

The large veins in the thorax were distended, and vermicular movements were distinctly evident in the intestines. The surface of the brain appeared injected with dark blood. No abnormality was detected in the spinal cord. Irritation of the phrenic and sciatic nerves produced a slight contraction of the diaphragm and muscles of the thigh. The lungs, liver, and kidneys were congested. The vessels of the abdomen were full of dark blood. On incising the heart, the right chambers were found to contain dark coagulated blood; in the left side a small quantity of blood of the same colour was seen. Frothy fluid was found in the pharynx and upper part of the larynx, but none in either the trachea or œsophagus. The whole digestive tract was examined, but nothing abnormal was seen. The stomach contained a semifluid material, and the lower part of the intestines was empty for a considerable distance above the rectum.

EXPERIMENT 2.—Seven grains of finely powdered kernel were made into an emulsion with one drachm of distilled water, and secured in a space in the subcutaneous cellular tissue of the left flank of a full-grown rabbit.

A few struggles occurred during the introduction, but these only lasted a few seconds, after which the rabbit became quite quiet. The first indication of any effect was shown by the animal stretching itself on the table, about four minutes after the introduction, the anterior extremities being extended forwards, and the posterior backwards. Immediately afterwards, a number of successive twitches occurred in the extremities, and the rabbit remained passively on its side. The muscular twitches soon extended to the neck, causing irregular movements of the head. In six minutes, the respirations became noisy, and evidently laboured, the inspirations being accompanied by movements of the extremities and trunk. The pupils were contracted, but mobile, and the eyelids closed on irritation. Sudden noise produced a distinct start.

In twelve minutes the pupils were contracted to the tenth of an inch. The inspirations became very laboured, and noisy, and frequent, but slight muscular spasms occurred. Glairy fluid escaped from the mouth, and tears from the eyes. In fifteen minutes, irritation of the conjunctiva did not produce contraction of the eyelids. The pupils were mere points. Reflex action could be caused to a very slight degree by some irritation of the extremities. The respirations occurred at very distinct intervals, and muscular spasms accompanied the inspirations. In sixteen minutes, respiration had almost entirely ceased, and had certainly done so in seventeen.

Autopsy—immediate.—The heart was found contracting with regularity, seventy per minute. This spontaneous action continued for twenty-five minutes, gradually, however, diminishing in strength and in the number of pulsations. Contraction of the heart could be renewed by gentle irritation for seventy minutes.

The brain and other organs had the appearances already described, with the exception of the lungs, which were peculiarly engorged, and presented the conditions of pneumonic condensation in the anterior portion of the inferior left lobe, and in nearly all the small middle lobe, and these portions sunk in water. The back of the tongue and all the veins of the thorax and abdomen were injected. Very little muscular irritation could be produced by stimulation, whether direct or through the nerves. The right side of the heart was

distended with venous blood; the left was nearly empty, but contained blood of a dark hue.

EXPERIMENT 3.—The skin was raised in the left flank of a large black and white female cat, the needle point of Wood's hypodermic syringe was inserted into the subcutaneous cellular tissue, and ten minims of a syrupy extract injected.

In two minutes, trembling occurred, and in three the cat fell. Fluid escaped from the mouth, the pupils contracted, and urine was voided. In five minutes, the respirations became hurried, noisy, and laboured. Reflex action could not be excited by severe stimulation, nor did the eyelids contract on irritation of the conjunctiva. The animal became perfectly flaccid; the only symptom of life was an occasional gasp, and this ceased entirely seven minutes after the administration.

Autopsy—immediate.—The pupils were observed to dilate. A very few contractions occurred in the muscles which were cut. The heart was perfectly quiet, and without the slightest action. No contraction could be produced by irritation of the phrenic and sciatic nerves. The stomach and intestines were full, and no vermicular action could be detected though carefully looked for. The brain appeared perfectly natural, the vessels being full without any engorgement, and no peculiarity was observed in the spinal cord. On removing the pericardium, irregular movements occurred in the heart, and a partial contraction could be produced by irritation fifteen minutes after death. The vessels of the thorax and abdomen were well filled, and could be readily distinguished by the colour of their contents. On incising the left ventricle, blood of the usual arterial hue escaped, and on incising the right, dark blood appeared. Both were allowed to run side by side, when the contrast was distinctly shown. The lungs, liver, spleen, and kidneys were normal. No change could be perceived in the mucous coat of the intestines. The gall-bladder was full.

The region of injection was found to be limited to the subcutaneous cellular tissue. It was of a red colour, and the characteristic odour of the extract was readily recognised.

II. INTRODUCED BY THE SEROUS TISSUE.

EXPERIMENT 4.—Five minims of syrupy extract were injected by Wood's hypodermic syringe into the cavity of the peritoneum of a rabbit five months old. Unsteadiness was produced in one minute, especially of the posterior extremities, which soon dragged powerless behind the animal. The anterior extremities were completely paralyzed in three minutes. At this time the pupils were contracted, the respirations were noisy, and fluid escaped from the mouth. Reflex excitability was completely lost in four minutes; and in four and a half minutes after the administration, all respiratory movements had ceased.

Autopsy—immediate.—Heart passive; contractions were excited by irritation and continued for seven minutes. Brain natural; spinal cord apparently healthy. Incision of the heart permitted blood to flow from both sides of the characteristic hues. The arterial and venous systems were normal, and their vessels full, with a little distention of the veins of the thorax. Stomach and intestines full. Bladder distended. Other organs normal. Nervous irritation produced a slight contraction of the diaphragm and muscles of the thigh. Pupils completely dilated. No inflammatory appearance could be detected in the peritoneum, but the odour of the extract was very evident.

EXPERIMENT 5.—The abdominal wall in a young rabbit of six months was cut through, and the peritoneum exposed. Four minims of the syrupy extract were injected into the peritoneal sac. The respirations were seventy-two per minute immediately before the operation.

In one minute, the respirations were eighty. In two minutes, the rabbit became unsteady. The pupils were very small, and the eyelids closed on irritation. Fluid escaped from the mouth. In four minutes, the respirations were laboured, noisy, and only thirty per minute. The animal soon fell

down, a few kicks occurred, and in five minutes it submitted to be laid in any position. Objects which were brought close to the eye produced no change in the position of the head, but a sudden noise caused a start. In six minutes, the eyelids could not be made to contract. A few muscular twitches, involving at once the muscles of the extremities, abdomen, thorax, and neck, succeeded each other. These were accompanied with feeble gasps, which gradually became weaker, and ceased entirely in seven minutes after the administration.

Autopsy—immediate.—The cut muscles contracted. The heart was acting regularly, seventy-eight per minute. This diminished gradually, but the spontaneous contraction of the right auricle continued till an hour and six minutes after death, while the contractility, as produced by physical impressions, did not cease until thirty minutes later. The vessels in the thorax and abdomen were distended. The brain was found injected with dark blood, and the vessels at the base of the cerebellum, and on the sides of the medulla oblongata, were full of venous blood. Vermicular action was well marked in the small intestines. The bladder, stomach, and gall-bladder were distended.

The lungs were dark and congested in various portions, but these did not sink in water. The right side of the heart was distended with dark blood, and a small quantity of the same colour was found in the left side.

No inflammatory change could be detected on the surface of the peritoneum. A frothy fluid was found in the fauces and upper portion of the larynx.

EXPERIMENT 6.—Two minims of the syrupy extract were injected into the left pleura of a kitten nine weeks old.

Almost immediately after, the respirations become noisy and hurried, and in one minute the animal fell down. The pupils rapidly contracted, and in three minutes the eyelids were not affected by irritation. The respirations became very infrequent, and ceased three and a half minutes after the administration.

Autopsy—immediate.—The pupils were observed to have again dilated before the cavity of the chest could be exposed. The heart was passive, and evidently distended; irritation could excite contractions for eleven minutes. On incision, the two sides were found to contain blood differing normally in colour. The viscera generally were healthy. The brain contained no unusual amount of blood, and the spinal cord was marked with a few injected points. The region of injection was confined to the pleural cavity, and had a red tinge, and a distinct odour of the extract.

III. INTRODUCED THROUGH THE DIGESTIVE SYSTEM.

EXPERIMENT 7.—Two grains of the extract, prepared as formerly mentioned, were formed into a small pill, with a little bread crumb. This was placed in the back of the pharynx of a full-grown, strong, and well-fed English terrier, and was observed to be swallowed.

No effect was produced for nine minutes, when fluid escaped from the mouth; the tongue was protruded and moved as if lapping; eructations were heard; and the gait became unsteady.

In twelve minutes, there was decided paralysis in the posterior extremities, and the respirations were hurried. Vomiting of a mucous substance, the passage of soft fæces, and a copious discharge of urine occurred simultaneously in seventeen minutes. The animal soon after fell on its haunches, and in a short time the anterior extremities became paralyzed, and it lay extended on its thorax and abdomen. When called by name, the head was turned. Common sensation and sight were unaffected. In twenty-five minutes, the pupils were considerably contracted, and at this time general muscular twitches occurred. In thirty-six minutes the dog again vomited a mucous and somewhat bilious-looking substance. This appeared to give some relief, as the animal rose up immediately, but, after standing in a very shaky manner for a few seconds, it again fell down. In forty minutes, vomiting recurred, and was followed by an unsuccessful effort to stand. The respiratory movements became feeble, and were attended by a loud stertor, in forty-three minutes. The dog remained in

any position. Muscular spasms became frequent; urine was voided, and extremely liquid fæces passed. The head was still turned when the dog was named, and distinct evidence of pain followed irritation. In forty-six minutes, the eyelids did not contract on irritation of the conjunctiva; and in fifty minutes after the administration all respiratory movements had ceased.

Autopsy—immediate.—The cut muscles contracted vigorously. The heart was found acting regularly, eighty-six per minute. It retained this spontaneous action for seventeen minutes, and contractions could be excited till forty minutes after death. The vessels of the thorax were distended with black blood, and this was distinctly perceptible in the aorta. The vermicular action of the intestines was very evident, and continued for ten minutes. The substance of the brain was injected with dark blood; its external surface was covered with vessels containing black blood, and a quantity of serum escaped when it was exposed. No change was detected in the medulla oblongata or spinalis. The lungs were dark and congested in various places. They floated in water; but when one particularly engorged portion was detached, it was found to sink in water. The liver, kidneys, and spleen were very much engorged. No change could be detected in the mucous membrane of the digestive system. The stomach was empty, and the large intestines for a considerable distance above the rectum were also empty. Frothy mucus was found in the pharynx and larynx. Irritation of the phrenic and sciatic did not produce contractions in the diaphragm and muscles of the thigh.

EXPERIMENT 8.—Five and a half grains of the fine powder of the kernel were made into pills, and swallowed by a buck rabbit eight months old.

A slight degree of paralysis was seen in the posterior regions in ten minutes, and, soon after, they yielded, the anterior portion of the trunk remaining supported by the fore-limbs.

In fifteen minutes, the fore-legs gave way. Fæces were passed. In twenty minutes, the respirations became noisy, reflex action was unimpaired, and the pupils contracted. In thirty minutes, the rabbit submitted to be placed in any position. In thirty-five minutes, the respirations became extremely noisy and accompanied with muscular spasm. Fæces and urine were passed, and reflex action could not be induced by puncturing the skin. General, but slight, muscular spasms now occurred frequently; the eyelids did not contract when the eyeball was pricked, and the respiratory stertor ceased. In forty minutes, a general spasmodic contraction of the muscles occurred; and, in forty-one minutes, all respiratory movement had ceased.

Autopsy—immediate.—The cut muscles contracted. The heart was acting seventy-two per minute, and this ratio gradually diminished till it ceased, thirteen minutes after death. The brain was rather darker than usual, and no change could be perceived in the spinal cord. The cerebro-spinal fluid was in abnormal abundance. The large veins were distended. The right chambers of the heart were engorged with black blood; the left ventricle was empty, but a little black blood was found in the left auricle. A considerable quantity of fluid was present in the abdomen, and the vermicular action of the intestines was well marked. All the viscera contained an abnormal excess of blood of a dark colour. The muscular system was extremely flaccid, but contractions could be caused by irritation of the nerves.

Remarks.—This experiment formed one of a series undertaken to discover the smallest dose which could produce death in a full-grown rabbit. A number of rabbits, as nearly as possible equal in age and weight, were selected, and a series of doses was given, commencing with four grains, and increasing at the rate of a quarter of a grain. Five and a half grains, as in the present instance, was the smallest quantity of the kernel which produced death.

EXPERIMENT 9.—Ten grains of a very fine powder of the kernel were suspended in two drachms of distilled water, and injected into the rectum of a full-grown rabbit. (The rectum had been previously emptied by injecting warm water.)

The first symptom observed was contraction of the pupils, five minutes after

the administration. About the same time, the rabbit appeared languid, and in ten minutes fell, and remained in any position. In twelve minutes, the eyeball was touched, without closure of the eyelids, and no symptoms of pain followed severe pricking of the trunk or extremities. Fluid escaped from the mouth, and the respirations became very noisy, laboured, and accompanied by spasmodic actions of the extremities, trunk, and head. The respirations gradually became weaker, and ceased entirely in twenty minutes.

Autopsy—immediate.—The heart was found contracting fifty-two per minute. This action gradually diminished, and spontaneous contraction ceased in the right auricle, fourteen minutes after death. In five minutes, the contractions were forty-four; in ten minutes, fifteen; and in twelve minutes, four. Irritation could produce contractions one hour longer, or seventy-four minutes after death. Both chambers of the heart contained black blood. Vermicular movements were observed in the intestines, *only at the upper portion*. The brain and other organs were enlarged with venous blood.

EXPERIMENT 10.—A small quantity of syrupy extract, sufficient to cover the extreme point of a penknife, was placed on the back part of the tongue of a sparrow. The bird was immediately set free, and allowed to fly in a room.

In two minutes it had alighted, and gasping movements of the jaws were observed. With this exception, nothing occurred for fifteen minutes, when a gelatinous-looking substance was vomited. The legs soon failed, and, after flying about for a few seconds, the bird fell on the right side. In fifteen minutes, the respirations were very irregular, and accompanied by spasmodic contractions of the wings and legs. In twenty minutes, one such of unusual severity occurred, after which no respiratory movement took place.

Autopsy—immediate.—The heart was contracting ninety per minute, and continued to act for eighteen minutes. Its cavities contained dark blood. The veins of the thorax and abdomen were injected.

EXPERIMENT 11.—About twice the quantity of extract that was employed in the previous experiment was applied to the tongue of a sparrow. The bird was liberated, and flew away.

In one minute the wings were evidently paralyzed to a slight extent, and in two minutes ineffectual attempts were made to fly. The respirations became hurried, and in four minutes the bird fell on its side and vomited. A slight muscular spasm, or rather a feeble tremor, occurred; and, in five and a half minutes, respiration had entirely ceased.

Autopsy—immediate.—The heart had ceased to contract, and no action could be produced by irritation with the point of a scalpel. Its chambers were distended, and contained blood of normally different colours. No muscular contraction could be produced by irritation of the phrenic and sciatic nerves.

Remarks.—Experiments 10 and 11 were repeated with the like results, except that in Experiment 10 *a*, opisthotonos occurred.

EXPERIMENT 12.—Five minims of tincture of physostigma, mixed with a little water, were poured into the throat of a full-grown sea-gull.

No effect was produced for four minutes, when, in rapid succession, the bird trembled violently, subsided on the thorax and abdomen, fell on its side, and, after a few irregular gasps, ceased to respire, four and a half minutes after the administration.

Autopsy—immediate.—The heart contracted very feebly and slowly for two minutes. Irritation could produce a slight contraction for twenty-two minutes after death. The heart's chambers contained blood differing normally in colour. The right side of the heart and the large veins were distended.

IV. INTRODUCED BY THE CIRCULATORY SYSTEM.

EXPERIMENT 13.—Five minims of a syrupy extract were injected into the left femoral vein of a full-grown rabbit, in a direction *from* the heart, or centrifugally. The rabbit almost immediately fell, and remained quite motionless, excepting a few occasional kicks with the posterior extremities.

In thirty seconds, the eyelids did not close on irritation, and reflex action

could not be produced. Respirations ceased in forty-two seconds after the administration.

Autopsy—immediate.—Heart distended and passive. Colour of contained blood, normal. Vermicular action could not be discovered in the intestines.

V. INTRODUCED BY THE RESPIRATORY SYSTEM.¹

EXPERIMENT 14.—Five minims of syrupy extract were injected into the right thorax of a young rabbit, by means of Wood's hypodermic syringe. This was done in such a manner that the pleura was punctured, and the pulmonary structure reached.

The rabbit was perfectly quiet for seventy-five seconds, when it endeavoured to jump away and stumbled. In one minute and a half the fore-legs yielded, and the animal fell; and, immediately afterwards, the posterior extremities were paralyzed, and it lay extended in a flaccid condition. The pupils became contracted. Irritation of the eyelids or eyeball did not produce closure of the eye. A few jerks occurred in the hind-limbs. General muscular quivering accompanied, and could scarcely be distinguished from, the respiratory movements, and these ceased in two minutes after the administration.

Autopsy—immediate.—The heart was passive, distended, and contained red blood in the left chambers, and dark blood in the right. The vermicular action of the intestines was very slight. Feeble contractions followed irritation of the phrenic and sciatic nerves. The other various organs and viscera were normal.

EXPERIMENT 15.—The trachea of a full-grown rabbit was exposed, and cut open a short way above the sternum. Five minims of syrupy extract were allowed to run down the trachea towards the lungs, in a gentle stream, from the needle point of Wood's syringe.

As soon as the rabbit was liberated, it ran a few steps, then stumbled, and, in forty-two seconds, fell down. The pupils contracted, and irritation of the eyeball did not produce winking. A few gasps and slight muscular tremors occurred, and in two minutes all respiratory movement had ceased.

Autopsy—immediate.—The heart was passive. Irritation could produce a slight, wavy, muscular action for ten minutes. When incised, black blood was found in the right side, and scarlet in the left. The vermicular action of the intestines was extremely indistinct. The stomach and bladder were distended. The arterial and venous systems appeared normal, and their vessels filled without distention.

No inflammatory change was discovered in the trachea or bronchi, but a distinct odour of the extract could be perceived over a great portion of both lungs. There was no congestion of the pulmonary texture.

VI. INTRODUCED BY THE NERVOUS SYSTEM.

EXPERIMENT 16.—The cranium of a full-grown guinea-pig was exposed, and, from the internal portions of both parietal bones, small portions of bone were removed with scissors. The exposed dura mater was cut through, the surface of the brain uncovered, and a horizontal slice removed with a sharp knife. A considerable amount of bleeding occurred, which was controlled by the application of cold. No nervous phenomena followed this operation. Fifteen minutes afterwards, six minims of syrupy extract were placed on the comparatively clean surface of the brain.

The first symptom observed was paralysis of the posterior extremities; in twelve minutes, they began to spread, the guinea-pig being still active. In fifteen minutes, a quantity of greenish, grumous-looking matter issued from the mouth,

¹ The results obtained under this section were those following introduction through a variety of channels. Excepting one experiment, the method followed was forcibly to puncture the thoracic wall and the pleura with the needle point of Wood's syringe, and through this to inject a syrupy extract. In this way, however, a passage was afforded for the poison to enter the system, not only through the respiratory, but also through the circulatory apparatus.

which was afterwards examined microscopically, and found to be similar to a substance found in the stomach. This was accompanied by a condition of tension of the abdominal parietes, and a drawing together of the limbs, giving the idea of straining. In twenty minutes, fæces were passed, and, shortly after, urine was voided. Hearing and sight were unaffected, and the contraction of the pupils very slight.

The paralysis of the extremities became gradually greater, and in one hour the guinea-pig could employ only the fore-limbs, and stagger from one place to another. Fæces and urine were passed at intervals, the former being almost liquid. A discharge took place from the eyes of a milky fluid. The respirations were noisy and laboured, and accompanied by a distinct spasm of the extremities.

In one hour and fifteen minutes, pinching produced cries of distress, but no reflex movements. In one hour and thirty minutes, the posterior extremities had yielded, and the animal was supported on the pelvis and anterior extremities. Severe spasms occurred twice, during which the animal fell on the side, but immediately recovered itself.

The respirations were at this time very laboured. From this stage the symptoms diminished, and in two hours the animal could walk about, and the diarrhœa had ceased.

Eight hours afterwards the guinea-pig was found dead.

Autopsy.—Ten hours after the administration.

Great serous congestion in the chest. Right and left sides of the heart contained dark and partially coagulated blood. Lungs congested; two small portions sank in water. A quantity of frothy mucus was found in the pharynx and covering the rima glottidis. Brain congested, and distinct signs of inflammation in the immediate neighbourhood of the injured portion. No odour of the extract was perceived. The spinal cord was very slightly congested in its cortical substance. The organs generally were dark and congested, and the vessels contained loosely coagulated blood.

Remarks.—This experiment does not show that death was produced by application to the *nerve-substance*, for these results may have been caused by the absorption of the extract by the cut and exposed bloodvessels.

B. *Illustrating the Topical Effects.*

I. WHEN APPLIED TO MUSCULAR TISSUE.

EXPERIMENT 17.—A full-grown buck rabbit was rendered unconscious by chloroform, and the biceps muscle of the right anterior extremity exposed, and carefully dissected from the surrounding structures, its origin and insertion being untouched. All the soft structures of the limb (except the biceps) were dissected from the humerus, and a ligature was tightly applied at the upper portion of this mass, and a second at the lower. The intermediate portion was cut away. A little thin gutta-percha parchment was then used to isolate the biceps as much as possible. The exposed muscle quivered in successive portions after being exposed.

The musculo-cutaneous nerve was pinched with forceps, the biceps contracted, and the elbow was flexed. The biceps was then painted over with the syrupy extract. In four minutes, all quivering of the muscular bundles had ceased, and, in eight minutes, irritation of the nerve-extremity, or of the muscular substance by pinching, pricking, and the action of the alkalies, acids, and a hot wire, produced no effect. The opposite leg was at this time thrown into energetic action by moderate irritation. The animal died in thirty minutes, with symptoms and appearances of death by asphyxia.

II. WHEN APPLIED TO NERVE SUBSTANCE.

EXPERIMENT 18.—The great sciatic nerve was exposed in its course from the pelvis to the knee in a large frog. A small portion, about the fourth of an inch, was separated from the surrounding tissues by gutta-percha parchment.

It was found that muscular contraction could be produced by irritation of the nerve in any part of its course. The exposed portion was then painted over with the syrupy extract.

In twelve minutes, an irritant applied to the nerve *above* the isolated portion produced no muscular contraction, while a similar irritant applied *below* this portion was followed by contraction. The frog died in thirty minutes, probably because of the extract escaping from the edges of the isolating material into the surrounding structures.

III. WHEN APPLIED TO THE HEART.

EXPERIMENT 19.—The spinous processes and laminae of the first two cervical vertebrae were exposed in a young rabbit. By bending the neck forwards, a sufficient space was obtained between the first and second vertebrae to admit a small probe. This was passed into the spinal canal, about a quarter of an inch upwards and downwards: the respiratory centre was thus destroyed, and the animal instantly killed.

The chest was opened, and the heart was found beating slowly and irregularly. In four minutes afterwards, when the cardiac action had regained its proper rhythm, five minims of the syrupy extract were injected into the right auricle, through the muscular wall, by Wood's syringe. The action of the heart instantly ceased. Irritation could, however, produce a laboured contraction for ten minutes. No blood escaped when the needle point was withdrawn. The heart's chambers were incised, and found filled with blood of different colours.

EXPERIMENT 20.—A young rabbit, five months old, was killed as described in Experiment 19, and the heart exposed. In four minutes the contractions were eighty per minute, and at this time the entire cardiac surface was painted with the syrupy extract. In one minute, the contractions had entirely ceased; but, half a minute afterwards, the left ventricle spontaneously resumed its action, and, in two minutes after the application, the whole heart was contracting at the rate of seventy-six per minute.

The application was thrice repeated with similar results, a longer interval occurring latterly between the suspension and recovery of the cardiac contractility.

Remarks.—These experiments were repeated on frogs, with the heart removed from the body and empty, and the results were the same.

IV. WHEN APPLIED TO THE ALIMENTARY CANAL.

EXPERIMENT 21.—The vermicular action of the intestines was very active in the rabbit employed for Experiment 19, and could be increased by direct stimulation of the gut. A portion of the small intestine, about two inches long, was separated from the mesentery, and isolated with gutta-percha parchment. This was covered with syrupy extract by a camel's-hair brush.

The vermicular action immediately ceased in the separated portion, and it became evidently flaccid. Irritation produced no effect. It was distinctly observed that, when a contraction ran along the intestine towards this portion, it stopped at the margin where the extract had been applied, appeared to *skip over* it, and was resumed at the other extremity of the healthy intestine. The power of contraction was not recovered by the painted portion. This experiment has been frequently repeated with the same result.

V. WHEN APPLIED TO THE SKIN.

EXPERIMENT 22.—A Corrigan's cautery was placed in boiling water for twenty minutes, and immediately applied to the cutis—previously shaved—at the right flank of a full-grown rabbit. It was kept in contact for six minutes. Four hours afterwards a blister had formed, and, by removing the cuticle, the dermis was exposed. This was covered with twelve minims of syrupy extract. The rabbit was secured in such a manner that this extract could not be removed. It was examined, at various intervals, for four hours without any

change being observed. The rabbit continued in perfect health for two days, when it was employed in another experiment.

EXPERIMENT 23.—(a) A little syrupy extract was painted over the whole length of a large earthworm. It immediately began to wriggle in the dish where it had been placed. In six minutes, progression had ceased, the only movement being a waving motion of one end. This ceased in ten minutes, slimy mucus was voided, and the worm lay contracted and swollen. Reflex excitability was also lost, and in fifteen minutes the worm was dead.

(b) A large earthworm was painted, on the posterior half, with the syrupy extract. It wriggled about for a short time, the movement being equally shared by all parts. In six minutes, the posterior half, or painted portion, was nearly motionless, and in ten minutes it was perfectly passive and contracted. The anterior half continued active for five minutes longer, and was quite passive in seventeen minutes after the application.

(c) The anterior half of a large earthworm was painted with the syrupy extract. In five minutes, an evident diminution had occurred in the movements of this part. In ten minutes, it was perfectly motionless.

The posterior half was not completely paralyzed for thirty-five minutes.

VI. WHEN APPLIED TO MUCOUS MEMBRANES.

(a) *Nasal*.—EXPERIMENT 24.—A fine camel's-hair brush, dipped in the syrupy extract, was passed thrice into the left nostril of a full-grown rabbit, care being taken that the brush should not convey a sufficient quantity to allow any to escape into the pharynx. In four minutes, a copious mucous discharge flowed from both nostrils, but in larger quantity from the left. In six minutes, the pupils were contracted. In ten minutes, the rabbit fell down, and remained in any position given to it. The respiration was noisy. It was dead in twenty minutes after the application.

In the examination, the phenomena already detailed, as resulting from death by asphyxia, were seen. The whole mucous membrane of the left nostril was red and tumefied. No abnormal appearance was formed in the right nostril.

(b) *Auditory Membrane*.—Death was also produced by asphyxia, by injecting into the auditory canal of a rabbit and of a mongrel dog ten minims of the syrupy extract. The same result was produced by an infusion of eight grains of the kernel in four drachms of water.

(c) *Conjunctiva*.—See EXPERIMENT 25.

VII. WHEN APPLIED TO THE EYE.

EXPERIMENT 25.—The left eyeball of a full-grown rabbit was painted over with syrupy extract. This appeared to cause no uneasiness until two minutes, when the lachrymal secretion escaped in considerable quantity, and the eyelids were semi-closed.

In three minutes, the left pupil was distinctly contracted, and in five minutes it was reduced to the one-sixth of an inch. In fifteen minutes, the contraction was extreme, but the iris was mobile. No change was observed in the right pupil. A large quantity of very liquid fæces was passed and urine freely voided. In twenty minutes, a slight degree of contraction could be perceived in the right pupil, but this did not increase. No distinct evidences were seen of muscular paralysis. When lifted by the ears, the rabbit struggled violently. *It was observed, that during these struggles the contraction of the left pupil was diminished and the right became slightly dilated.* In forty-five minutes, liquid fæces was again passed, and afterwards the contraction of the left pupil was the only remaining symptom. This diminished in two hours, but it continued very apparent for eight hours, and had disappeared in ten hours after the application. The rabbit recovered completely.

In another experiment, in which a larger quantity of extract was employed, the muscular prostration was more marked, and the contraction of the pupil continued for twenty-four hours.

C. *Modified Actions.*

I. WITH BOILED KERNEL.

EXPERIMENT 26.—Twenty grains of powdered kernel were boiled for two hours with distilled water, and placed in a cavity in the subcutaneous cellular texture of a rabbit. A few struggles followed the introduction; the breathing became rapid; and the rabbit fell down in four minutes. The pupils contracted; very feeble struggles occurred when the rabbit was lifted; and it remained in any position. In six minutes, the reflex function of the eyelids was lost, and in seven the respirations had ceased.

Autopsy—immediate.—The pupil dilated during the opening of the chest. The heart was found passive and distended. All its chambers contained blood, and the difference in colour between the right and left sides was strongly marked. The vermicular action of the intestines was very feeble. The sciatic and phrenic nerves were pricked without any effect. No congestion was seen of any viscus. The mesenteric arteries and veins were distinctly different in colour. The abdominal aorta and venæ cavæ contained blood of normal colours. The stomach and bladder were full. Rigor mortis began in one hour. No redness nor any other morbid appearance was found in the region of application.

II. WITH THE BEAN BOILED ENTIRE.

EXPERIMENT 27.—An entire bean, weighing seventy-two grains, was boiled in distilled water for four hours. The kernel was then separated from the spermoderm, and found to be of a brownish colour. One cotyledon, weighing probably twenty-eight grains (the other having been dried and found to be of this weight), was made into an emulsion, and introduced into the right flank of a full-grown rabbit.

No effects were observed till twenty minutes, when the rabbit began to move its jaws, and to grind its teeth as in chewing. In fifty minutes fluid fæces were passed, and in an hour the pupils were slightly contracted. Very fluid fæces and urine were now frequently, almost incessantly, voided for two hours longer, when these symptoms diminished, and entirely disappeared in five hours after the administration. No effects remained six hours afterwards.

III. WITH STRYCHNIA AND PHYSOSTIGMA.

EXPERIMENT 28.—Three-tenths of a grain of strychnia were sprinkled on a recent wound in the left flank of a mongrel dog. The animal stumbled and fell in four minutes, and the muscles of the extremities and trunk became rigid. In five minutes, the pupils were dilated and spasms rapidly succeeded each other.

Five minims of syrupy extract were injected into the subcutaneous cellular texture of the wounded flank (left), near the place of the application of the strychnia.

Almost immediately afterwards the spasms ceased in the left limb, and in a short time in the right also. In three minutes after this injection, reflex action could not be excited in the posterior extremities. The pupils remained dilated, and clonic spasms frequently recurred in the anterior extremities and trunk. In seven minutes, the eyelids closed, and, when opened, the pupils were found pointing upwards and outwards. No muscular action recurred in the posterior extremities, but slight spasms were observed in all other regions. The animal died twenty minutes after the administration of strychnia.

Autopsy—immediate.—On opening the thorax several bloodvessels were cut, and very dark blood escaped. The cut muscles contracted vigorously. The heart was acting with regularity and force. The vessels of the thorax were injected with dark blood. Irritation of the phrenic nerves produced contraction of the diaphragm, but no action could be caused by pinching the great sciatic on either side.

IV. WITH ARTIFICIAL RESPIRATION.

EXPERIMENT 29.—Five minims of syrupy extract were injected into the cellular tissue in the left flank of a kitten one month old. Artificial respiration was performed for fifteen minutes. This did not appear in the slightest degree to modify the action. The animal was flaccid in three minutes, and the pupils contracted. On exposing the heart, it was found passive and distended.

*Experiments with the KERNEL of the *Phyosostigma venenosum* on Man.*

A. *Illustrating the Constitutional Effects.*

EXPERIMENT 1.—I ate six grains of finely-powdered kernel, two hours after taking food. The pulse had been examined at different times, within the previous fifteen minutes, and found to average 68 per minute.

In six minutes, the pulse was 74 per min., and no sensation of other symptoms were experienced. In nineteen minutes, the pulse was 72, and a slight degree of a peculiar sensation was experienced at the epigastrium. In fifteen minutes, the pulse was 76. In twenty minutes, the pulse was 75. Epigastric sensation more marked. In twenty-five minutes, the pulse was 77. In thirty minutes, the pulse was 72. Sensation continues to occur at intervals, but still slight. In thirty-five minutes, the pulse was 69. In forty minutes, the pulse was 66. Epigastric sensation recurred. In forty-five minutes, the pulse was 68. In fifty minutes, the pulse was 64. A slight degree of giddiness. The epigastric sensation is much increased. It now resembles the somewhat painful sensation which is produced when large pieces of food are suddenly swallowed, and recurs at intervals. It is at first slightly indicated by a sensation in the thorax, near the upper part of the sternum. This extends downwards, becoming more and more intense, until it reaches the epigastrium, when it is almost painful, and eructation usually occurs. There is a distinct escape of gas, and this is followed by a reversal of the direction of the pain from the lower sternum to the throat, so that eructation occurs in the middle of this sensation. The sensation or the eructation may take place independently of each other, and each at times is very slight. In fifty-five minutes, the pulse was 65; full and regular. Frequent renewal of the sensation and eructation. In sixty minutes, the pulse was 62; rather feeble. Dimness of vision and dizziness. In sixty-five minutes, the pulse was 62. Increase of head symptoms, with a little perspiration. In seventy minutes, the pulse was 60; very small and wiry, but regular. Nausea. No recurrence of the epigastric sensation since fifty minutes. In seventy-five minutes, the pulse was 62. Copious perspiration all over the body. Unable to continue reading, especially because of the dizziness. Experienced slight difficulty in walking. In eighty minutes, the pulse was 60; very thready and difficult to count. In eighty-five minutes, the pulse was 60. In ninety minutes, the pulse was 58. Respiration accompanied with a little difficulty, and with a slight degree of dyspnoea. In ninety-five minutes, the pulse was 59; very feeble, and with occasional intermissions. In one hundred minutes, the pulse was 56. Eructation without the epigastric sensation. Considerable nausea and dizziness. In one hundred and five minutes, the pulse was 56; thready and intermittent. In one hundred and ten minutes, the pulse was 58. Head symptoms greatly diminished. Dizziness and nausea lessened. Great difficulty in walking. Respirations require an effort. In two hours, the pulse was 60. In two hours and five minutes, the pulse was 59. In two hours and ten minutes, the pulse was 60; rather fuller. In two hours and twenty minutes, the pulse was 58. Felt sick, and accordingly lay down in bed. Was conscious of having remained awake for some time in a dreamy state. Next morning, felt uncomfortable, had a bad appetite, and experienced a slight degree of dizziness during the day.

EXPERIMENT 2.—Three calculations of the pulse, within fifteen minutes, gave an average of 74 beats per minute. Eight grains of the powdered kernel were then carefully chewed and swallowed.

In three minutes, the pulse was 76. In five minutes, the pulse was 70, and the epigastric sensation, accompanied with eructation, occurred. In ten minutes, the pulse was 72. In fifteen minutes, the pulse was 66, with slight sensations in epigastrium. In twenty minutes, the pulse was 66. Sensations more intense, and accompanied with eructation. It was supposed that a degree of muscular weakness was experienced, and this was tested with a dumb-bell, which in ordinary circumstances could be readily lifted. It was found a great burden, and I experienced the greatest difficulty in extending my arm with it. While going through this little exercise, a steady erect posture was with difficulty maintained. In thirty minutes, the pulse was 68; soft and compressible. The epigastric sensations recur, without eructation. In thirty-five minutes, the pulse was 62. In forty-five minutes, the pulse was 64. In fifty-five minutes, the pulse was 58, and very feeble. Sensations occur at the epigastrium in quick succession. In one hour and five minutes, the pulse was 60. In one hour and fifteen minutes, the pulse was 57. In one hour and twenty-five minutes, the pulse was 54; soft, compressible, and with occasional intromissions. In one hour and thirty-five minutes, the pulse was 57. Dizziness experienced. Drank a cup of coffee. In two hours, the pulse was 63; rather stronger. In two hours and ten minutes, the pulse was 58. Dizziness gone. Muscular weakness still experienced. The pulse continued to range between 60 and 65, until three hours from the commencement of the experiment, when the observations were discontinued.

EXPERIMENT 3.—Ten grains of the powdered kernel were eaten. In three minutes, violent epigastric sensations occurred, and in six, eructation. Muscular weakness was distinctly indicated, in ten minutes, by the tests employed in the preceding experiment. No change was observed in the frequency of the pulse for twenty minutes, when it began to diminish in frequency and strength. General lassitude and dizziness became so great at this time that reading had to be discontinued. The pulse soon afterwards could not be counted.

In walking down stairs to my bedroom great dizziness and dimness of vision were experienced. The progression and gait were very unsteady, and I can remember having encountered the wall and handrails, more than once, on the way. Went to bed immediately, undressing with some difficulty, and on a chair, and soon fell asleep. This was about nine o'clock in the evening. Next morning, I rose at seven, took a bath in the sea, and felt quite well all day.

Remarks.—The above was written in the forenoon of the day following the experiment, when the particulars were fresh in my memory. In Experiments 1 and 2 the note paper was with me, and every thing written down as it was observed.

EXPERIMENT 4.—Pulse averaged 70 per minute. Ten minims of tincture of physostigma, diluted with half a drachm of distilled water, were drunk. In five minutes, the epigastric sensation was perceived, and the pulse was 76. In one hour, the pulse was 63; thready and feeble. In one hour and a-half the pulse was 54. It continued between 52 and 60 for one hour longer,—two hours and a-half after administration. In four hours, the pulse was 68; strong and full. All symptoms had entirely disappeared.

B. *Illustrating the Topical Effects.*

I. ON THE EYE.

EXPERIMENT 5.—A small drop of a syrupy extract was placed on the point of a thin probe, and applied to the conjunctiva over the left eye-ball. A copious discharge of tears immediately occurred.

In five minutes, the left pupil was a little contracted, and very evidently so in eight minutes, the left being one-half the size of the right. In ten minutes, the left pupil was the one-sixteenth of an inch in diameter. Vision with this eye was imperfect, the visual distance being lessened, but the iris was

mobile. A slightly painful sensation was now experienced in the supra-orbital region of the left side, and a sensation of heat in the left eyeball. In thirty minutes, no change had occurred in the right pupil; the left was a mere speck. Vision with the left eye was almost lost; there was a little redness, and tenderness on exposure to the light. In one hour and a-half, all disagreeable sensations had gone, the dimness of vision was less marked, but the extreme contraction of the pupil continued. In four hours, the dimness of vision disappeared; but the contraction of the left pupil continued unchanged for twenty-four hours. It gradually diminished after this, but very slowly, as the symptom continued for five days.

EXPERIMENT 6.—A small quantity of the extract was applied to the outer surface of both eyelids of the right eye, avoiding, as far as possible, any contact with the conjunctiva.

In six minutes, the right pupil was contracted, and effects were caused exactly similar to those described in Experiment 5, with the exception that a marked immobility was produced in the eyelids, accompanied with a disagreeable sensation of dryness. A slight degree of inversion of the upper eyelid was also produced when the eye was being closed. These symptoms disappeared in three days.

II. ON THE SKIN.

EXPERIMENT 7.—A test-tube, containing an ounce of tincture, was applied for twenty-five minutes, with its mouth in contact with the skin at the point of the index-finger of the left hand. No change was produced in the tactile or common sensibility of the finger.

EXPERIMENT 8.—A small piece of flannel was soaked in tincture of physostigma, and with this a portion of the back of the hand, over the first and second metatarsal bones, was rubbed for fifteen minutes. A drachm and a-half of tincture was altogether used. The common sensibility in this region was almost entirely destroyed. Pricking with a needle-point produced very little sensation, and the region could be defined by a succession of pricks from the unaffected skin.

This experiment was repeated with the extract and the result was the same.

I have much pleasure in taking this opportunity to acknowledge my obligations to Professor Balfour, for his kind liberality in supplying me with the greater quantity of the bean employed in this investigation. The remainder was sent to me by the Rev. John Baillie of Old Calabar, to whom, as well as to the Messrs S. H. Edgerley, Hugh Goldie, and Geo. Thomson, I am indebted for the promptness of their replies to my inquiries regarding the employment of this ordeal at Calabar, and for the valuable information they have collected for me. My sincere thanks are also due to Dr Charles Wilson, for many suggestions in preparing this paper for the press.