of the impossibility of aerated blood being introduced through the arteries: in these cases, and under these circumstances alone, would we consider general bloodletting, as practised for puerperal convulsions, likely to have any beneficial effect.

Bunessan, Oban.

Article V.—On the Characters, Actions, and Therapeutical Uses of the Ordeal Bean of Calabar (Physostigma venenosum, Balfour). By Thomas R. Fraser, M.D., Assistant to the Professor of Materia Medica, Edinburgh University; late Resident Physician, Royal Infirmary, Edinburgh.

(Concluded from page 132.)

Section V.—Appendix.

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

A. Illustrating the Constitutional Effects.

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. Feces 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 The respirations were superseded by distinctly recurring spasmodic movements of the muscles of the thorax and abdomen, and, in seventeen minutes after the administration, these had entirely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 oesophagus. 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 pneumatic 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 minimis of syrpy 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 minimis of the syrpy 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 became 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—inmediate.**—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 feces, 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 feces 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—inmediate.**—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 mucous 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 sciotic nerves.

Remarks.—Experiments 10 and 11 were repeated with the like results, except that in Experiment 10 α, opisthotenos 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 was 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

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.
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, 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 parieties, 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 diarrhea 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 faccised. 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 faeces 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 faeces 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 vena cavae 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 feces were passed, and in an hour the pupils were slightly contracted. Very fluid feces 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 occurred 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 occurred 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 Physostigma 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 dyspnea. 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 still 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; threadly 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.

1. 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 suprorbital 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.

Part Second.

REVIEWS.

A Manual of Ophthalmoscopic Surgery. By Jabez Hogg, Assistant-Surgeon to the Royal Westminster Ophthalmic Hospital, etc., etc. Third Edition. Churchill and Sons: London: 1863.

The greater the number of exact observations made, whether in pathology or therapeutics, the more limited does the range of mere theory become.

If, to use Bacon's simile, we do seem to check the flight of genius and weary its bright wings by adding the lead of stern facts to its too nimble feet, we gain in certainty what we lose in speed; and the slow steady march, in which accuracy and attention make every step an acquisition, is preferable to the wing even of an archangel, which leaves no trace of its flight.

It was well observed by Pringle, more than half a century ago,