XX. *On the Physiological Action of Vanadium.*

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I. INTRODUCTION.

THE investigation, of which the results are recorded in the following pages, was carried out in the Physiological Laboratory of the Owens College, at the suggestion and under the direction of Professor ARTHUR GAMGEE.

The elaborate investigations of ROSCOE had placed vanadium amongst the metals

whose chemical characters and relations have been rigidly investigated; they had shown that vanadium is to be ranked as a member of one of the most interesting families of elements, and yet not a single fact had been ascertained in reference to its physiological action. The hope that an elaborate examination of the physiological reactions of vanadium might cast some light upon the relations which may exist between the chemical and the physiological affinities of elements, and the fact that Professor ROSCOE offered to furnish any vanadium compound which might be required, acted as inducements to undertake this research.

Vanadium belongs to the group of pentad elements, which includes nitrogen, phosphorus, arsenic, antimony, and bismuth. It would obviously be out of place here to examine in detail the grounds upon which this relationship of vanadium has been based—as, for example, the analogies between the oxides of nitrogen and vanadium; the resemblance of phosphates, arseniates, and vanadates; the isomorphism of vanadinite and pyromorphite, &c.

A glance at the atomic weights of the chief members of the arsenic group of elements shows that vanadium has an atomic weight which places it between phosphorus and arsenic:—

N,	Nitrogen	14
P,	Phosphorus	31
V,	Vanadium	51·2
As,	Arsenic	75
Sb,	Antimony	122
Bi,	Bismuth	210

The fact that, in a family of which several members exert a highly poisonous action, a new metal could be found whose atomic weight was nearly the mean of that of the two members possessing the greatest toxicological interest appeared to render the research an important one; and the interest was enhanced by the fact that vanadium possesses an atomic weight very nearly the same as that of a poisonous metal not belonging to the arsenic group, but whose compounds bear some resemblance to those of vanadium, viz. chromium:—

Atomic weight of chromium . . .	52·2
„ vanadium . . .	51·2

Vanadium forms four series of compounds. First, a pentad series, of which vanadic oxide, V_2O_5, may be taken as a representative; this oxide forms soluble vanadates with the alkaline metals. Secondly, a series of hypovanadic compounds, represented by a tetrachloride, VCl_4, and by hypovanadic oxide, V_2O_4. Thirdly, a triad, vanadous series, of which may be taken as a representative the trichloride, VCl_3, analogous to the arsenic and antimony compounds, but, unlike them, non-volatile. Fourthly, a diad, hypovanadous series, represented by VCl_2 and V_2O_2 (hypovanadous oxide).

Although it appeared desirable to investigate bodies belonging to the various groups

of vanadium compounds, it was found expedient to restrict the investigation to the sodium compound of vanadic acid. The reasons for not examining the action of the lower oxides, or of the compounds analogous to them, were:—First, that definite solutions could not be obtained in such a condition as to admit of their being suitably introduced into the animal organism; this remark will be understood when it is stated that no useful results can be obtained from experiments in which a very alkaline or a very acid solution, capable of at once altering the chemical and physical properties of the blood, is introduced into that fluid. Second, that the lower oxides of vanadium are so extremely unstable as to render any experiments with them very difficult of interpretation. Fortunately we may, with reason, conclude that an elaborate investigation into the mode of action of any soluble vanadate will fairly represent the physiological action of the vanadium compounds generally; for although the lethal doses may be, and often are, different, the physiological properties of any of the inorganic compounds of a poisonous metal appear to be similar, whatever the nature of the compound.

The salt used in this research was the tribasic sodium vanadate (Na_3VO_4), obtained by fusing a mixture of three molecules of sodium carbonate with one molecule of vanadium pentoxide until no further evolution of carbonic acid occurred. The tribasic sodium vanadate resulting from this operation is a white crystalline mass, easily soluble in water. The solution employed throughout this research contained exactly five per cent. of V_2O_5. In order to avoid any accidental presence of sodium carbonate which might exert an injurious action on the blood of the animal experimented upon, a stream of CO_2 was passed through the concentrated solution of the sodium salt before it was diluted so as to have the required strength. The solutions employed were prepared from time to time in the Chemical Laboratory of the Owens College, under the supervision of Professor Roscoe.

In this paper the mode of action of vanadium on simple organisms and on animals of different classes will be described, and then the experiments which illustrate its more precise influence on the various functions of the body will be given in detail.

It was originally intended to institute in this memoir a comparison between the action of vanadium and that of the allied metals of the same family. However, we do not yet possess sufficiently elaborate accounts of the precise physiological action of these metals, so that further investigations are necessary before such a comparison can be usefully instituted. Such an investigation is now in progress in the Physiological Laboratory of the Owens College. A research which the author has lately carried out on the physiological action of chromium appears to prove most conclusively that this metal, whose atomic weight, as was just mentioned, is almost identical with that of vanadium, exerts an altogether different physiological action and possesses a less intense poisonous activity.

II. EFFECTS ON SIMPLE ORGANISMS.

A few preliminary experiments were undertaken to determine the effects of sodium vanadate upon *Bacteria*, germinating seed and fungi, and infusorians.

Experiment I.—December 12, 1873.

A ·5 per cent. solution of sodium vanadate does not prevent the development of *Bacteria*.

Exp. II.—May 14, 1874.

Mustard-seeds and lettuce-seeds were set to grow on pieces of flannel moistened with solutions of sodium vanadate of strengths varying from 1 per cent. to ·01 per cent. (the amount of V_2O_5 in the solutions being referred to in all cases), and compared with similar seeds set to grow on flannels moistened with distilled water.

When the experiments were at an end the vessels containing the flannels still moistened with the same solutions were allowed to stand for several days. Mould appeared in certain of the vessels only, viz. in those containing distilled water or solutions of the salt of vanadium of slight strength.

From these experiments it appears that germination is not prevented, although it may be slightly interfered with, by the presence of sodium vanadate in solutions of ·1 per cent. or less, but that it is totally prevented in solutions of 1 per cent.

The same remarks apply to fungi.

Exp. IV.—September 1874.

An infusion of cabbage-leaves was allowed to develop infusorians by being kept in a warm place.

Drops of the infusion were treated, while under observation beneath the microscope, with solutions of sodium vanadate.

From this experiment it appears that even dilute solutions of sodium vanadate (solutions containing ·01 per cent. of V_2O_5) cause an immediate disturbance of vital function in infusorians.

III. EFFECTS ON COMPLEX ORGANISMS.

A. General Action on the Animal System.

Certain preliminary experiments were made to determine the reactions between the vanadium salt used and some of the fluids and juices of the body with which it must come into contact in its passage through the system. The results were as follows:—

1st. Vanadate of soda does not affect the optical properties of blood.

2nd. No reduction of the vanadic salt takes place on treatment with peptones or saliva, or on treatment with starch-mucilage or fats.

These preliminaries having been settled, the effects of sodium vanadate upon the animal system were determined after the introduction of the poison by various ways.

i. *Action of the Poison when introduced into the System by subcutaneous injection.*

On Frogs.

Exp. VII.—December 3, 1873.

Weight 24 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected under the skin of the back.

h.	m.	
2	25.	Injection complete: frog very active.
3	0.	Normal to all appearance, and active.
3	10.	Not so active, but otherwise normal.
3	15.	Quieter.
3	20.	Still moves limbs freely; no signs of paralysis.
3	25.	Conscious; respiration has ceased.
3	35.	Quiet; moves on being irritated. Conscious; lower jaw has fallen. No breathing at the lungs.
3	40.	Lower jaw has sunk more; moves on being irritated; still not breathing.
3	55.	Cornea sensitive; attempts to move when stirred.
4	15.	Still capable of moving.
5	0.	On being stirred the frog makes vigorous efforts to leap, but does not seem able to grasp the table firmly enough, although its muscular contractions are sufficiently energetic.
5	50.	Nearly dead; does not retract its limbs after they have been spread out, as it did some time previously; still attempts to move a little when stimulated.
6	5.	No movement at all on being irritated.

The frog was then opened; the heart was contracting perfectly.

Liver very dark in colour.

Muscular and nervous irritability quite normal on applying electrical stimulation. On snipping through the cord the legs were observed to contract.

In this experiment it may be noticed that complete paralysis of voluntary muscles occurred in 3 hours 40 minutes after injection; that the poison began manifestly to act within 1 hour of injection; that the respiratory muscles were the first to cease acting; that consciousness remained for some hours after respiration had ceased; that the heart was not affected; that muscular and nervous irritability remained perfect on direct stimulation by induction-currents; and that the cord seemed capable of *conducting* stimuli.

Exp. VIII.—January 21, 1874.

Weight (a small English frog).

Dose 1 cub. centim. of a ·5 per cent. solution prepared from the ordinary 5 per cent. solution (*i. e.* 5 milligrammes V_2O_5), injected under the skin of the back.

Note.—A small amount was lost during injection.

In this experiment 5 milligrammes of V_2O_5 caused death in a frog within 36 hours. The noteworthy points are that a gradual and general paralysis occurred, that the intestinal tract was congested, and that it contained a greenish mucus.

Exp. IX.—February 20, 1874.

Weight 24·5 grms. (English frog).

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin of the back.

From this experiment we learn that paralysis appeared within 40 minutes of the time of injection, that the heart was so affected as to die on exposure sooner than an unpoisoned heart would probably have done, that the irritability of voluntary muscles and of motor nerves was unimpaired.

Exp. X.—February 20, 1874.

Weight 29 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin of the back.

Note.—A certain amount of the solution escaped during injection.

This experiment serves to corroborate the preceding.

Exp. XI.—May 27, 1874.

Weight 29 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin of the back.

This experiment shows that vanadium-poisoning causes paralysis of respiration, general paralysis of voluntary muscles, injury to the power of reflex activity, without affecting muscle, nerve, or *conducting-power* of cord directly.

On a Pigeon.

Exp. XII.—February 25, 1874.

The pigeon was healthy and rather young.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected under the skin of the breast.

h.	m.	
3	47.	Injection complete.
4	30.	Quiet, but otherwise normal.
5	15.	Discharge of fæces, green in colour.
6	10.	Further discharge of fæcal matter, which is now of a red colour and very watery, containing blood-corpuscles and epithelial cells.
6	30.	Further discharge of sanguineous fluid fæces.
9	48.	Sanguineous fæcal discharges have continued in the meantime.

Body sprawls; legs appear to be paralyzed, as also the whole body; gasping, beak open; eye insensitive.

The pigeon must have died soon after. The *post mortem* examination was not made until 10.30 the following morning.

Post mortem Examination.

On cutting through the skin over the throat dark maroon-coloured extravasations were noticed. Heart slightly distended.

Liver normal, or perhaps slightly congested.

Pancreas normal.

Œsophagus above the gizzard is filled with a green fluid matter and is also congested. Duodenum for 1 inch below the gizzard is much congested. The congestion then suddenly ceases (just where the pancreas is situated), but recommences about 2 inches lower down with great intensity. At this point the intestine becomes filled with brown mucous contents containing blood-corpuscles, epithelial cells, and granular bodies. The congestion becomes less marked as the intestine is traced towards the rectum, but increases again in the latter division of the alimentary tract. The crop is not markedly congested and is empty; the œsophagus below it is filled with green mucous contents.

Gizzard normal.

In this experiment we notice that the poison began manifestly to act within 2 hours 15 minutes of the time of injection; that the first symptoms were drowsiness, and an action on the alimentary canal as indicated by the sanguineous fluid fæces; that finally paralysis of motion occurred; that the alimentary canal was intensely congested in portions; that the lower portion was filled with brownish contents containing blood-corpuscles.

On Guineapigs.

Exp. XIII.—December 3, 1873.

Weight 632 grms.

Dose 2 cubic centims. of the 5 per cent. solution (100 milligrammes V_2O_5), injected under the skin of the back.

h. m.

2 25. Injection completed.

Quiet; seemed inclined to eat; but did not take the green food presented to it.

2 30. Appears quite normal and at ease.

2 45. Not quite so lively; does not stir when the hand is placed near it; manifests desire to hide itself beneath the hay in the observation-chamber.

2 50. Quiet, but otherwise normal.

3 0. Evinces great desire to hide itself under the hay or in a corner. Is indisposed

to stir when touched or moved. Walks with difficulty. Lies down on stomach. Appears paralytic. Frequent twitches, especially of the hind

h. m. legs and head.

3 10. Breathes by jerks. Spasmodic twitches of limbs.

3 15. Breathing not so rapid; frequent convulsions of legs and head and of the whole body.

Breathes in spasmodic gasps. Eyelids close only after repeated irritation of cornea.

3 25. Breathes in gasps; the convulsions have ceased.

3 30. Breathing shorter and more rapid. Is not so quiet as before. Cornea seems rather more sensitive. Breathing less violent.

3 40. Sensibility more perfect. Breathing rapid, but regular. Lies in normal position of health and not on its side as before. No convulsions have been noticed.

3 45. Breathing regular; attempts to move, but it is with difficulty, and a tendency to a return of the convulsive symptoms.

4 0. Breathing slight; occasional twitches.

4 15. Tries to move; the convulsive twitchings seem to be returning in strength.

5 0. Breathing irregular and at lengthened intervals.

On lifting the animal on to a table its fore and hind limbs became convulsed.

After lying for about 5 minutes, breathing at long intervals in feeble gasps, it died.

Post mortem Examination.

The blood coagulated normally.

The right heart distended. Ventricles contractile on irritation.

Liver apparently normal.

Stomach distended with food; exhibited punctiform, hæmorrhagic extravasations on the internal surface, chiefly at the vertebral aspect and cardiac end.

Duodenum normal.

Rectum perhaps slightly congested.

Blood taken from left ventricle diluted with water and placed before the slit of a spectroscope exhibited the normal oxyhæmoglobin bands. After standing two days the blood solution still appeared quite normal. On adding some of STOKES'S reagent the band of reduced, or oxygen-free, hæmoglobin appeared, and was again replaced by the two oxyhæmoglobin lines on shaking up the solution with air.

This experiment shows that 100 milligrammes (about) of V_2O_5 produced death in 2 hours 35 minutes; that symptoms appeared within 35 minutes of the time of injection; that the symptoms of poisoning were quiescence, paralysis, alternating with convulsions of the limbs and head; spasmodic respirations, the inspirations being shallow and rapid

(as in peritonitis); possibly an impairment of sensibility; *post mortem* appearances of congestion of the alimentary mucous membrane, with blood-extravasations. The blood was uninjured by the poison as far as its optical properties indicated.

Exp. XIV.—January 14, 1874.

Weight 595 grms.

Dose 2 cub. centims. of the 5 per cent. solution (100 milligrammes V_2O_5), injected under the skin.

This experiment shows that 100 milligrammes of V_2O_5 produced death in 3 hours 25 minutes; that symptoms of poisoning appeared within eight minutes of the time of injection; that the chief symptoms were drowsiness, a convulsive movement of the limbs, head, and body, with general weakness or inability to move easily; that sensation appeared unimpaired; and that respiration became difficult towards the close of the experiment. After death the alimentary canal appeared to have suffered slight but distinct congestion in portions, and the lungs were also congested.

Exp. XV.—January 21, 1874.

Weight 755 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected under the skin of the right shoulder.

h.	m.	
8	51.	Injection complete.
9	10.	Very uneasy; runs round box uttering slight cries. Twitches of head. Discharge of watery fæces.
10	0.	Belly very unduly swollen on the side on which the injection was made, due probably to tympanitis.
10	10.	Contrives to get into a corner and moans, twitching its head convulsively. Discharge of urine. No observation was made prior to injection as to the state of the pupils; but from a comparison with other animals they would seem to be dilated: they are quite sensitive to light.
10	25.	Hemiplegia of right side very marked.
10	30.	Respirations 132 per minute (22 in 10 seconds). (The heart-beats were so feeble that they could not easily be counted.)
10	45.	Cries when the abdomen is touched.
11	0.	Urine and fæces discharged; utters low cries. Can move quite well and normally.
11	25.	Evidently very uneasy; cries continually. Respirations 140 per minute (23·3 in 10 seconds).
12	0.	Still sensitive.
12	15.	Walks about normally.
12	35.	Respirations 132 per minute (22 in 10 seconds).

h. m.

3 0. The animal has exhibited no fresh symptoms; it is, however, now breathing more rapidly (33·3 in 10 seconds), as if much exhausted. It is quite sensitive.

3 45. Breathes very heavily, with a gurgling noise in the throat.

3 50. No paralysis, but great weakness and evident pain.

4 5. Breathing 76 per minute (12·6 in 10 seconds) and irregular.

4 45. Creeps along, evidently very weak.

5 10. Still sensitive; on touching the eyeball the lid moved languidly.

5 30. Gurgling noise in throat; struggles as if in great pain; drops of serous fluid exude from the nose; asphyxia. Eyes prominent. Gasps at intervals of 5–6 seconds. Heart has ceased to beat. Serous exudation from nose and mouth.

5 35. Dead.

Post mortem Examination.

Muscles contract on direct stimulation.

Blood dark-coloured, asphyxial.

6 5. Heart contracts on stimulation; right side distended.

General visceral congestion.

Liver pale, but otherwise normal.

Lungs congested, mottled with purple, the upper lobes more than the lower, and the left lung more than the right.

Stomach congested internally, especially near the smaller curvature and vertebral aspect, becoming less so towards the cardiac end, where, however, there is one piece of arborescent congestion apparent. There is another such patch on the abdominal aspect (internal surface) of the same viscus.

Œsophagus hardly congested.

Duodenum congested in patches internally at the free border, especially towards the lower end.

Great congestion of the free border of the small intestine, becoming more extensive as we descend. Towards its lower end the small intestine is filled with a brown opaque mucus.

Large intestine not nearly so much congested as small. Rectum partakes of the characters of the rest of the large intestine.

Bladder contracted and not congested.

Uterus slightly congested externally, but not so internally.

Kidney congested internally.

From this experiment we learn that 25 milligrammes of V_2O_5 produced death in $8\frac{3}{4}$ hours, and that symptoms of poisoning began to appear within 20 minutes. The symptoms were convulsive twitchings, partial and temporary paralysis, abdominal pain, rapid respiration. No importance can be attached to the apparent dilatation of the pupils, as it may have been due to the shade of the box. After death there were very

evident traces of great congestion of alimentary mucous membranes (especially at the free border of the small intestines) and of the lungs.

Exp. XVI.—February 18, 1874.

Weight 667 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes of V_2O_5), injected under the skin.

In this experiment 50 milligrammes of V_2O_5 produced death in 23 minutes from the time of injection. Symptoms began to appear within 10 minutes of injection. The symptoms were such as we have seen in preceding experiments, viz. indifference to surrounding circumstances, paralysis, especially of the hind limbs. The heart's vitality was not affected.

On Rabbits.

Exp. XVII.—January 23, 1874.

Weight 1373 grms.

Dose 4 cub. centims. of the 5 per cent. solution (200 milligrammes V_2O_5), injected under the skin of the right shoulder.

In this experiment 200 milligrammes of V_2O_5 produced death in a rabbit of 1373 grms. in 12 minutes. The poison produced death clearly by acting at once upon the nervous system, causing severe convulsions, and without inducing decided inflammation of the alimentary mucous membranes.

Exp. XVIII.—February 6, 1874.

Weight 1705 grms.

Dose ·5 cub. centim. of a 5 per cent. solution (25 milligrammes V_2O_5), injected under the skin.

From this experiment we learn that 25 milligrammes of V_2O_5 produced death in a rabbit of 1705 grms. in 49 minutes; that symptoms of poisoning set in within 30 minutes of injection. The symptoms agree with those of the previous experiment; and, coincident with the shallow and rapid respiration, there was a fall of 1°·5 C. in temperature. The temperature in the rectum remained constant for some time after death.

Exp. XIX.—February 11, 1874.

Weight 1449 grms.

Dose 1 cub. centim. of a ·25 per cent. solution prepared from the standard 5 per cent. solution (2·5 milligrammes V_2O_5), injected under the skin.

In this case a very small dose was injected; and no symptoms, distinctly attributable to poison, followed, except a slight indifference to external objects.

Exp. XX.—February 13, 1874.

Weight 1449 grms.

Dose 1 cub. centim. of a ·5 per cent. solution prepared as above (5 milligrammes V_2O_5), injected under the skin.

(This was the same rabbit as was used in the preceding experiment.)

In this experiment 5 milligrammes of V_2O_5 produced in a rabbit of 1449 grms. distinct symptoms of poisoning, but no fatal result. The symptoms were, as before, partial paralysis, paraplegia of the lower extremities, slight convulsions, excited respirations, drowsiness, and they appeared within 25 minutes of injection.

Exp. XXI.—February 18, 1874.

Weight 1392 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin of the belly.

Heart-beats in 10 seconds . 52
" " . 53
Respirations in 10 seconds . 22
" " . 24
} determined prior to injection.

h.	m.	s.	
12	37	0.	Injection complete.
12	39	30.	Weakness of posterior extremities.
12	40	0.	Almost complete paralysis of posterior extremity of body.
12	42	0.	General agitation, alternating with an appearance of somnolence.
12	44	0.	Breathing has almost ceased. Quivering over hind quarters. Heart exceedingly weak and slow.
12	46	30.	Twitching of head to one side. General convulsive movements of an opisthotonic character. Quivering, and dilatation of pupil.
12	47	0.	Cornea insensitive; pupil dilated. Jaws open once or twice in a gasping manner. Death.

Post mortem Examination.

Heart feebly pulsating; both ventricles moderately distended. Vena cava not much distended. Lungs somewhat pale. Lower part of small intestine normal. Duodenum and upper part of jejunum contained much glairy mucus, which in some places was frothing. Mucous membrane seems to be slightly swollen and congested.

In this experiment 250 milligrammes of V_2O_5 produced death in a rabbit of 1392 grms. in 10 minutes, the poison commencing to operate within $2\frac{1}{2}$ minutes of injection. The symptoms, as before, were paralysis of hinder extremities, convulsions, drowsiness, an affection of respiration and of the cardiac movements, and congestion of alimentary mucous membrane.

Exp. XXII.—March 5, 1874.

Weight 1386 grms.

Note.—The rabbit (doe) seems weak, and is suffering from some skin disease.

Dose 4 cub. centims. of 5 per cent. solution (200 milligrammes V_2O_5), injected under the skin.

Note.—The solution was afterwards discovered to be uncertain as to strength. The experiment is inserted for the general symptoms, which it exhibits very well.

Temperature in rectum . .	37°·4 C.	determined prior to injection.
Respirations in 10 seconds .	15	
„ „ .	16	
Heart-beats in 10 seconds .	40	

h.	m.	s.	
1	6	0.	Injection commenced.
1	8	0.	Injection complete.
1	11	0.	Runs about. Discharge of normal fæces. Respirations in 10 seconds, 20, and irregular.
1	14	0.	Heart-beats in 10 seconds, 30.
1	16	0.	Respirations in 10 seconds, 10.
1	17	30.	Rests head against side of box.
1	18	30.	Respirations in 10 seconds, 12·5.
1	19	30.	Respirations in 10 seconds, 14·6.
1	21	0.	Drowsy. Heart beats so feebly as to render counting impossible.
1	21	30.	Respirations in 10 seconds, 19.
1	22	30.	Respirations in 10 seconds, 17·3.
1	22	45.	Drowsy; lies down on side.
1	23	30.	Respirations in 10 seconds, 20. Evident uneasiness; sprawls out its hind legs. Closes eyes.
1	24	30.	Respirations in 10 seconds, 8 (about). Paraplegia; rocking of head; bending back of head.
1	25	0.	Attempts to lie on side; closes eyes, and lies with head low. Lies on its belly.
1	26	30.	Respirations in 10 seconds, 12.
1	27	0.	Opisthotonos; lies on side; pupil distended; cries.
1	28	0.	Cornea but slightly sensitive.
1	28	15.	Gasps; cornea insensitive to touch. Rabbit insensitive on pinching.
1	29	0.	Dead.
1	29	30.	Quivering of skin over hind legs.
1	32	0.	Pupil contracted; curious shaking of fore and hind limbs.
1	33	0.	Temperature in rectum 36°·6 C.

Post mortem Examination.

h. m.
1 37. Heart still beating (left auricle), 36 in 10 seconds.
Right heart distended; left heart contracted.
1 40. Right auricle beating; right ventricle beats on stimulation, but not so the left ventricle.
The pericardium contains a quantity of colourless effusion.
Temperature in rectum 36°·7 C.

From what was said at the beginning of this experiment the above results are valueless as regards the lethal dose. The symptoms of poisoning appeared in less than 15 minutes after injection, and were confirmatory of those stated in previous experiments. A rapid increase in the number of respirations per minute was one of the first signs of the action of the poison. When paraplegia became well marked the respirations sank suddenly from 20 in 10 seconds to 8 in 10 seconds and 12 in 10 seconds. The pulse sank and became very feeble, and the temperature sank (as in Exp. XVIII.) about ·8° C., and maintained that lower temperature for some time after death.

Exp. XXIII.—March 20, 1874.

Weight 2066 grms.
Dose 5 cub. centims. of a 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin. (A small amount was lost in injecting.)

In this experiment 250 milligrammes of V_2O_5 produced death in a rabbit of 2066 grms. in from 8 to 9 minutes. Symptoms of poisoning commenced to appear within from 2 to 3 minutes of injection, and were exactly confirmatory of those in the preceding experiment, viz. a marked increase in the number of respirations (which supervened more rapidly than in the preceding experiment), followed, when the nervous symptoms became very decided, by a sudden fall, a feebleness of heart-beat, and paralytic and convulsive symptoms.

Exp. XXIV.—May 6, 1874.

Weight 1280 grms.
Dose 5 cub. centims. of a 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin of the back.

In this experiment 250 milligrammes of V_2O_5 caused death in a rabbit of 1280 grms. in from 5 to 6 minutes. The symptoms developed within 2 minutes of injection, and exactly confirmed those of the preceding experiment.

Exp. XXV.—May 6, 1874.

Weight 1672 grms.
Dose 5 cub. centims. of a 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin of the back.

In this experiment 250 milligrammes of V_2O_5 caused death in a rabbit of 1672 grms.

in 10 minutes. Symptoms developed within 2 minutes of injection, and confirmed those of the preceding experiment.

On Dogs.

Exp. XXVI.—December 10, 1874.

The dog was a small, rough, young terrier; it had been used five days before in an experiment in which 100 milligrammes (?) of V_2O_5 had been injected (in the form of neutral sodium vanadate) into the right external jugular vein without producing death. It had apparently completely recovered.

Dose 10 cub. centims. of the 5 per cent. solution (500 milligrammes V_2O_5), injected under the skin of the back.

h.	m.	
11	50.	Injection complete; dog slightly sick.
12	5.	Much terrified; slight diarrhœa; vomits a stringy mucus; walks quite well.
12	20.	Vomited more mucus of a tenacious ropy nature.
12	50.	Salivated. Discharge of watery matter from rectum.
1	15.	Watery discharge *per rectum* continues, together with a quantity of light, loose fæces.
1	40.	Breathing irregular.
2	0.	Attempts to vomit ineffectually; breathing rather laboured and irregular; watery discharge from rectum continues.
2	40.	Again sick; vomited more stringy mucus. Discharge from rectum still continues.
3	25.	Symptoms as before; breathing irregular and laboured; watery discharge from rectum as before.
3	40.	No paralysis or convulsions have as yet been noticed; breathing heavy.
4	30.	Still salivated.
5	15.	Appears unable longer to support itself, and has fallen over on to its side; breathing short and irregular; quite conscious.
5	25.	Raised itself and sat up, but with great difficulty; sways about as if weak and unable to hold itself steadily upright.
5	30.	Lies down again; quite conscious.
6	0.	Region around the anus covered with a sanguineous watery matter which has issued from it during the afternoon.
6	30.	Quite conscious.
7	0.	Quite conscious.
7	10.	Breathes heavily and at short intervals.
8	0.	Conscious; breathing slight.
8	40.	Eyeball but slightly sensitive.
9	40.	Still breathing.
10	55.	Dead.

Post mortem Examination.

Blood very dark in colour; exhibits the normal hæmoglobin bands; coagulates firmly and normally.

Muscles irritable to tactile stimuli.

Heart not irritable; right side distended.

Liver normal; or, if any thing, darker than usual.

Stomach empty of food, but filled with a tenacious mucus; general congestion of mucous membrane, especially over the posterior surface, except near the pylorus, where it has the normal tint. On examination of the more highly congested regions we can make out that the arborescent injection is especially to be observed on the summits of the prominent rugæ, and is irregularly scattered over the mucous membrane bordering the alveoli.

At some points extravasations of blood of a very limited extent are to be seen.

Duodenum is in a state of intense congestion, covered with dark red mucus in which are seen under the microscope innumerable blood-corpuscles and epithelial cells.

The same appearances exhibited by the rest of the small intestine; undoubted extravasations of blood exist besides the congestion. A PEYER'S patch at the lower end of the ileum is undoubtedly enlarged; its borders are elevated, but, strangely enough, it is not so deeply injected as the adjacent mucous membrane.

Rectum undoubtedly injected.

Kidneys normal at the cortex, but slightly congested at the pyramids.

The blood yielded little or no serum after standing over night in the laboratory.

The intestine and liver, which were examined for vanadium in Dr. ROSCOE'S laboratory, were found to contain it. The following is the report of Mr. S. CARSON, who made the determination for us:—

"The intestines were cut up into small pieces and roasted in a platinum dish in a muffle-furnace until all the organic matter was burnt away. The ash left was moistened with a little pure HCl and warmed for some time on the water-bath. Water was then added; and after boiling for some time, the insoluble portion was filtered off and the filtrate (which had a distinct blue colour) examined for vanadium. It was evaporated to dryness and fused with a little KNO_3; the mass was again taken up by water, and a little oxalic acid added, which brought out the blue colour more distinctly. It was sought to estimate the vanadium in this solution by precipitating with $(NH_4)Cl$, but the quantity present was too small to admit of quantitative estimation.

"The liver was examined in the same way, and the blue colour due to vanadium was obtained on adding oxalic acid; but the coloration was not so dark as in the case of the intestines."

In this experiment 500 milligrammes of V_2O_5 caused death in a young and small dog in 11 hours 5 minutes, poisonous symptoms developing about 15 minutes after injection. The prominent symptoms were the vomiting of a thick, ropy mucus, salivation, and the almost continual discharge of at first a watery and afterwards a sanguinolent fluid *per rectum*. Respiration was irregular, and afterwards laboured and heavy. No nervous symptoms, such as were so characteristic in the case of rabbits, guineapigs, and frogs, were observed; and the animal was evidently conscious to the last. A *post mortem* examination disclosed evidences of an intense congestion of alimentary mucous membranes accompanied by distinct extravasations of blood. The blood coagulated normally, but yielded very little serum. Muscles retained their irritability to mechanical stimuli. Vanadium was discovered to be present in the tissues (not free from blood) of the liver and intestines.

Exp. XXVII.—February 20, 1874.

The dog used was a young English (black and tanned) terrier.

Dose 20 cub. centims. of the 5 per cent. solution was evaporated down carefully to a bulk convenient for subcutaneous injection. The dose equalled 1 grm. V_2O_5.

In this experiment 1 grm. of V_2O_5 caused death in a young and small dog in 7 hours 55 minutes, symptoms developing within 20 minutes of injection. The symptoms in the main confirm those of the preceding experiment, except that salivation did not occur here.

On Cats.

Exp. XXVIII.—December 12, 1873.

The cat was small and adult.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin of the back.

h. m.

2 20. Injection complete.

2 22. Vomits.

2 23. Discharge of fæces.

2 28. Again sick.

2 30. Great contractions of abdominal muscles and diarrhœa. Again sick.

2 35. Vomits a watery fluid.

2 37. Respirations about 15 in 10 seconds. Very much depressed; attempts to discharge fæces.

2 45. Respirations 16 in 10 seconds.

2 50. Salivation, the saliva being viscid. Respiration irregular, heavy, and chiefly abdominal.

h. m.
3 0. Very feeble; may be handled with impunity. Respirations rapid, and heart extremely feeble.

3 15. Rolls over two or three times, as if in pain; breathing very rapid and shallow. Rises, but cannot stand; lies on its side, stretches out its fore paws, and seizes with them the bars of its cage. Slight opisthotonos.

Right posterior extremity drawn forward. Great dyspnœa apparently. Moans.

3 20. On touching the cornea the eye was not closed. Dead.

Post mortem Examination.

Divested the animal of its skin.

Irritability of the pectoral muscles was noticed on touching them with the forceps. The heart was not contracting; the right side was distended with blood; on exciting the heart directly it contracted. The right ventricle was filled with a cherry-coloured blood, which took $3\frac{1}{2}$ minutes to coagulate.

3 47. The left side of the heart contains very little blood.

3 55. Œsophagus perfectly normal.

Trachea exhibits no marked congestion.

Lungs normal.

Abdominal viscera exhibit distinct general congestion.

Pancreas normal.

Stomach exhibits, on being opened, not the slightest congestion.

The whole of the small intestine is congested, the duodenum and jejunum being more distinctly so than the parts lower down. The congested intestines are covered with a viscid and transparent mucus. At points the intestinal mucous membrane appears to be the seat of ecchymosis. At the ileo-cæcal valve there is a patch of intense congestion and a small abrasion of mucous membrane, the abraded part being covered with mucus.

The cortical and pelvic parts of the kidney are quite normal; the pyramids, if any thing, are slightly congested.

Dr. Julius Dreschfeld confirmed the above observations.

The intestines of the cat were sent to Mr. S. Carson for examination. He reports:—"In the examination of the mucous membrane of the cat I did not succeed in finding any trace of vanadium."

In this experiment 250 milligrammes of V_2O_5 caused the death of a small adult cat in 1 hour, symptoms developing within 3 minutes of injection. The symptoms were partly confirmatory of those in the preceding experiments on dogs, viz. sickness, salivation, irregular respiration (which was noticeably rapid in this case), diarrhœa, great pain. In addition, nervous symptoms supervened analogous to those noticed in the case

of rabbits, &c. The *post mortem* appearances resembled exactly those in the cases of the dogs, but, owing to the rapidity of death, they were not so extensive or marked. Chemical examination of the intestines failed to show the presence of vanadium.

Exp. XXIX.—February 18, 1874.

Weight 1310 grms. A small cat.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin.

In this experiment 50 milligrammes of V_2O_5 caused the death of a small cat. As far as was observed, the symptoms were those of irritation of the alimentary mucous membranes, viz. vomiting, retching, and congestion of the interior of the stomach and intestines. The intestines, in their lower portion, contained much brown mucous fluid; and epithelium-cells, blood-, and mucus-corpuscles were found free in the stomach. The lungs were much congested and frothy.

ii. *Action of the Drug when introduced into the System by direct Injection into Blood-vessels.*

Only one experiment was performed with the express object of determining the effect of direct injection into the vascular system. In investigating the special action of vanadium upon circulation and respiration, however, frequent use was made of this mode of injection; and reference will be made, in the *Résumé* of the General Action of Vanadium (p. 518), to the experiments then performed.

Exp. XXX.—December 5, 1873.

The dog was a small rough terrier, rather young.

Dose 2 cub. centims. of a 5 per cent. solution (100 milligrammes V_2O_5), injected into the right external jugular vein.

Note.—Some of the solution was lost during injection.

In this experiment (less than) 100 milligrammes of V_2O_5 were insufficient to cause death in a small young dog when directly injected into a vein. The only symptom attributable to vanadium-poisoning was the drowsiness which followed on injection. On comparing this experiment with Experiment XXVI., in which 500 milligrammes of V_2O_5 injected subcutaneously produced death in about 11 hours, it seems probable that a considerable quantity of the solution was lost in this experiment during injection.

For further observations of the action of vanadium on the system, when injected directly into blood-vessels, see Experiments XLII. to LX. (on Circulation and on Respiration).

iii. *Action of the Poison when introduced into the System by Injection into the Alimentary Canal.*

Exp. XXXI.—June 10, 1875.

Rabbit.—Weight 2430 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected by means of a catheter into the stomach.

h. m.

11 45. Injection complete. Very quiet.

12 10. Sudden convulsions (opisthotonos ?). Lies out on belly. Respiration rapid and shallow.

On touching the leg of the rabbit the latter got up and walked.

12 20. Temperature in rectum 38°·9 C. (The temperature prior to injection was 40°·2.)

12 30. Very quiet.

12 55. Lies out at length with legs spread out; gets up when its legs are touched.

1 10. Respiration not so rapid. Quiet.

1 50. Temperature in rectum 38° C.

Very slight watery rectal discharge. Very quiet. Respiration deeper and more regular (14 in 10 seconds).

3 0. Still lies with legs spread out behind; can move them quite normally, however. Respiration has normal characters (15 in 10 seconds). Temperature 38° C.

No further rectal discharge has taken place; the region around the anus, however, is moist.

4 0. Very quiet. Respiration as above (16 in 10 seconds). Rocks head as if weak. Sluggish movements of the eyelids on touching the cornea.

4 10. Discharge of urine. Rabbit leans against the side of the box, as if weak. Respiration seems weaker.

4 15. Respiration 12·5 in 10 seconds.

4 25. Respiration 10–11 in 10 seconds.

Leans in a corner of the box, as if weak. Region about the anus moist with brownish fluid.

4 45. Temperature 38°·3 C.

5 30. Rabbit evidently very weak. No fresh symptoms. Respiration 11 in 10 seconds.

On being irritated it moves to another part of the box quite normally.

6 0. Symptoms as before.

7 45. Symptoms as before in general; rabbit weaker. Temperature 35° C.

9 0. Symptoms as before; region about anus moist with brownish or yellowish fluid.

h. m.
10 45. Symptoms as before in general; weaker. Respiration 12 in 10 seconds. Region about anus moist as before. Temperature 34° C.

12 35. As before. Moves spontaneously.

1 0. I had left the laboratory for half an hour. On returning at this hour I found the rabbit lying on the floor at some distance from its box, quite dead and stiff, with fore and hind legs spread out forwards and backwards respectively, as if it had had stretching-convulsions. The rabbit was certainly too weak to leap out of its box on to the table and thence to the floor; it must therefore have been projected from its box, which was narrow and 18 inches high, on to the floor during the death-struggles.

Post mortem Examination.

Heart is not acting: filled with venous blood. Stomach not very full; contents of the usual green colour. Mucous membrane intensely and extensively congested, except at the pyloric end. A few spots of extravasation.

Intestine everywhere more or less congested, filled with a greyish mucus; the vermiform appendage filled with much dark, fluid, and very fæcal matter. The mucous membrane of the intestine exhibits everywhere numerous, but not thickly set, large, thickened spots ($\frac{1}{8}$ inch in diameter and less), with a yellow centre and intensely red periphery, which do not seem to be confined to any border in particular.

Kidney seems normal.

Lungs not congested.

Liver firm, greyish internally, and, so far as can be made out, very slightly fatty.

From this experiment we gather that the effects of large doses of sodium vanadate *per œsophageum* resemble those of small doses when subcutaneously injected. Respiration becomes rapid and shallow at first, but quickly falls again to the normal. At the same time the temperature falls about 1° C., and never again attains its previous height. Convulsions occurred only once, at the beginning of the experiment. The stretching-out of the hind legs may have been due to imperfect paralysis, but at no time was paralysis complete. Death must have been accompanied by severe convulsive struggles, and was preceded by great weakness and depression of temperature. The great alimentary congestion and the presence in quantities of viscid intestinal contents indicate the chief action of the poison. Death occurred in 13 hours after injection.

Exp. XXXII.—June 10, 1875.

Rabbit.—Weight 2720 grms.

Dose 3 cub. centims. of the 5 per cent. solution (150 milligrammes V_2O_5), injected *per rectum*.

The rabbit had quite recovered by the next day.

In this experiment the only symptom of poisoning was a rapidity of respiration, unaccompanied by any fall in temperature attributable to vanadium.

Exp. XXXIII.—September 15, 1874.

Rabbit.—Weight 1670 grms.

Dose 3 cub. centims. of the 5 per cent. solution (150 milligrammes V_2O_5), injected into the stomach.

In this experiment the dose of 3 cub. centims. was simply injected into the stomach instead of into the rectum. There was no marked respiratory symptom, the rabbit appearing throughout to be quite normal. The rabbit recovered.

No effect was produced by the injection of 150 milligrammes V_2O_5 into the stomach.

Exp. XXXIV.—September 16, 1874.

Guineapig.—Weight 630 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected into the stomach.

h.	m.	s.	
11	38	0.	Injection complete.
11	40	0.	Movements as of vomiting. Retching: seems quiet and ill. Moves spontaneously.
11	41	30.	Retching; defecates; retches; vomits a dark green tenacious fluid, which oozes from nostrils as well as mouth.
11	47	0.	Moves about unsteadily; jerks forward at each respiration, as if weak; moves unsteadily; lies down, as if weak.
11	50	0.	Unsteady. On moving the head shakes, as if the animal were very weak or "nervous." Moves about.
11	52	0.	Gasps; vomits again; very weak apparently. Crawls along very unsteadily.
11	54	0.	Gasps; vomits.
11	55	0.	Gasps; moves about uneasily; jerks its head; crawls along uneasily; jerks its head, as if hiccoughing.
11	59	0.	Twitches head and hind limbs.
12	0	0.	Spasmodic jerks of head and body.
12	2	0.	Turns over on to its side; deep gasps; eye but slightly sensitive.
12	4	0.	Gasps at long intervals. Hind legs quite flaccid and apparently insensible; gasps shallower; eye insensitive.
12	5	0.	Dead.

Post mortem Examination.

Muscles irritable on striking.

Lungs congested at the back.

Liver appears normal.

Congestion of abdominal viscera.

Normal peristaltic action of the intestines.

Stomach filled with bright green contents. Walls much congested, especially near the cardiac end and lesser curvature.

Duodenum filled with bright green contents. The mucous membrane is covered with a thick yellowish tenacious matter, which hides a deep congestion beneath.

Jejunum contains a darker green substance, and is also much congested in its mucous membrane.

Ileum presents the same appearance as the jejunum.

Rectum not congested.

Kidney not congested.

Œsophagus not congested.

In this experiment 250 milligrammes of V_2O_5 caused death in a guineapig within 27 minutes. Death was preceded by the vomiting of a greenish fluid, an unsteadiness of gait and great apparent weakness, a gasping respiration, and convulsive twitches of head and hind limbs. A *post mortem* examination disclosed a congestion of the lungs (Is this due to the action of vanadate of sodium?) and intestinal mucous membranes, as well as the presence in the alimentary canal of green contents.

Exp. XXXV.—September 17, 1874.

Guineapig.—Weight 505 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected into the stomach.

In this experiment the animal died in less than a day after injection. The symptoms were trembling and an excessive discharge of urine. The urine was tested by shaking it up with ether containing hydrogen peroxide, which causes with vanadic acid a red coloration; it contained no vanadic acid in such amount as to be capable of detection. The *post mortem* appearances indicated gastric congestion.

Exp. XXXVI.—September 18, 1874.

Guineapig.—Weight 463 grms.

Dose 2 cub. centims. of the 5 per cent. solution (100 milligrammes V_2O_5), injected into the stomach.

Sept. 19.—The guineapig had died in the night.

In this experiment the guineapig died in less than a day after injection. The only symptom noticed during the five hours of observation immediately after injection was an excessive secretion of urine.

Lethal Dose.

From the preceding experiments on rabbits the minimum lethal dose of vanadic pentoxide in the form of sodium vanadate was determined for those animals.

In Exp. XX. a rabbit weighing 1449 grammes had sodium vanadate subcutaneously injected containing 5 milligrammes V_2O_5. The rabbit recovered; that is to say, 3·45 milligrammes V_2O_5 per kilogramme of rabbit are insufficient to cause death.

In Exp. XVIII. a rabbit weighing 1705 grammes was injected subcutaneously with a similar solution containing 25 milligrammes V_2O_5. The rabbit died; therefore 14·66 milligrammes V_2O_5 per kilogramme of rabbit are sufficient to cause death.

A rabbit was taken weighing 2720 grammes (it was the same rabbit as had recovered four days previously from the injection *per rectum* of 150 milligrammes V_2O_5; see Exp. XXXII.). A solution of sodium vanadate was prepared containing 25 milligrammes V_2O_5, *i. e.* 9·18 milligrammes per kilogramme of rabbit, and injected subcutaneously. Marked symptoms of poisoning occurred—rapid respiration, sluggishness, rocking of head, partial paralysis and weakness, which lasted for about an hour and a half; after which the rabbit became rapidly normal, and completely recovered.

It was deemed unnecessary, in the case of a body like vanadium, to sacrifice more rabbits in order to fix with greater exactness the lethal dose. The minimum lethal dose, therefore, lies between 14·66 milligrammes and 9·18 milligrammes of V_2O_5 per kilogramme of rabbit.

Résumé of the General Action of Vanadium.

A review of the experiments on the general action of sodium vanadate on the animal economy displays two well-marked modes of action, by either of which, or by both combined, the poison may produce death. The first, an action on the nervous system, takes in frogs the form of gradual paralysis, first of respiration, and afterwards of motion generally; and in pigeons, guineapigs, rabbits, and cats, of drowsiness, or indifference to external circumstances, together with partial paralysis and convulsions affecting some or all of the muscles of the body. The second, an action on the alimentary mucous membrane, exists in frogs only in cases of slow poisoning, and is evidenced by congestion of the interior of the alimentary canal. In pigeons, in which, when the dose of the salt has been small, it precedes the nervous symptoms by some hours, it is evidenced by the discharge of sanguinolent fluid fæces during life, and after death by the congested condition of the alimentary mucous membrane and the quantity of mucous contents of the intestine. In guineapigs, in which, on the contrary, the nervous symptoms are more important, congestion of the alimentary tract (which is especially noticeable when the dose of poison has been small) sufficiently attests the presence of intestinal mischief. In rabbits, again, the nervous affection is more prominent, and in the majority of cases is clearly the proximate cause of death. But in their case, as in that of guineapigs, signs of congestion in the intestines, and the presence in them of quantities of glairy fluid after poisoning, prove the existence of irritation. In the case of dogs the doses

administered, although relatively large, failed to produce any nervous symptoms whatever; and the intense gastric and intestinal congestion and blood-extravasations, together with the evident signs of great abdominal pain, vomiting, and watery or sanguinolent rectal discharges, during life, gave unmistakable indication of the cause of death. In cats, which are killed by much smaller doses of V_2O_5 than dogs, nervous symptoms (convulsions) occurred, in addition to the signs of intestinal irritation, which were similar, though, owing to the rapidity of death, not so marked as in dogs.

Besides those above mentioned, indications of disorder in other portions of the animal system were noticeable. Thus, in guineapigs and rabbits, one of the earliest symptoms of poisoning was that respiration became rapid and shallow; and when steps were taken for exact observations, it was found in rabbits (1) that this alteration in the character of the respirations was accompanied by a fall of about 1° C. in temperature, and (2) that as soon as the nervous symptoms became well marked the number of respirations per minute sank at once.

Drowsiness or indifference to external circumstances was noticed in all cases of vanadium-poisoning, and it often supervened extremely rapidly after introduction of the drug. Consciousness did not seem in any case to be impaired, as far as it was possible to judge. Sensibility to pain also seemed perfect. The cord and brain were not congested.

Congestion of the lungs was observed to follow in some guineapigs and one cat, but not in rabbits or dogs.

Muscular and nervous irritability remained for many hours in all cases where indications of it were sought, and appeared normal.

In rabbits the pulse was noticed to be slow and feeble. The hearts of frogs continued to beat for a long time after paralysis of motion was complete, and the hearts of rabbits &c. were always irritable, if not contracting, for some time after death.

When injected into the stomach the general symptoms were similar in kind to those mentioned above; in addition, great prostration followed in rabbits, and, in guineapigs, vomiting when the dose was large, and excessive secretion of urine when it was small.

The minimum lethal dose for rabbits, when injected under the skin, lies between 14·66 and 9·18 milligrammes of V_2O_5 per kilogramme.

B. Special action on various functions of the Animal Body.

i. *Special Action of the Poison on the function of Muscular Tissue (after local application).*

On Voluntary Muscle.

Exp. XXXVII.—June 4, 1874.

1 h. 35 m. Decapitated a small toad. Cut off the legs at the knee, leaving the feet

attached. Laid bare the muscles down to where the feet commence. Irritated the muscles of both by means of an interrupted current (the secondary coil being at a distance of 20 centims. from the primary) and produced distinct movements in both. Placed one in a capsule filled with a ·5 per cent. solution NaCl, and the other in a 2 per cent. solution of V_2O_5 in the form of sodium vanadate. The leg in the vanadium solution appeared to stiffen a little.

Each leg was tested at intervals during the succeeding hours, by stimulating with induced (interrupted) currents, with the following results:—

Time.	Leg in Vanadium solution.	Leg in NaCl solution.
h. m.		
1 45	Moves with secondary coil at 16–17.	Moves with secondary coil at 20–21.
2 0	,, ,, 13.	,, ,, 20.
2 25	,, ,, 12.	,, ,, 20.
3 30	,, ,, 6–5.	,, ,, 20–23.
4 5	Slight movements with secondary coil at 0.	,, ,, 20–21.
4 50	No movements at all; leg stiffening.	,, ,, 20.
6 50	Leg stiff as if from rigor mortis.	,, ,, 20–23.
8 0	.....	Movements not so brisk. Leg quite flexible; distinct movements with secondary coil at 8.

Exp. XXXVIII.—June 1875.

The gastrocnemii of two frogs were prepared in the same manner as in the preceding experiment. They were all tested, and the minimum stimulus in the case of each was found to be when the secondary coil was at 18.

The gastrocnemii of frog (α) were placed, one in a ·5 per cent. solution NaCl, and the other in a 1 per cent. solution V_2O_5 (sodium vanadate); those of frog (β) were placed, one in a ·5 per cent. solution and the other in a ·05 per cent. solution of V_2O_5 (sodium vanadate). On immersion into each of these liquids, muscular twitches were observed to follow in the legs, and in the legs in the 1 per cent. and ·5 per cent. solutions there were tetanic extensions. These muscular movements ceased in all cases after 20 minutes.

The muscles were tested by electrical stimuli at intervals, and within 2 hours 10 minutes all the muscles which had been immersed in solutions of the vanadium salt died, viz. that placed in the 1 per cent. solution within 1 hour 20 minutes, that placed in the ·5 per cent. solution within 2 hours 10 minutes, and that placed in the ·05 per cent. solution within 1 hour 38 minutes, the muscle placed in salt solution remaining sensibly normal.

From the preceding experiments we learn that solutions of vanadate of soda, even when very dilute, rapidly cause death when directly applied to muscle.

On Involuntary Muscle.

Exp. XXXIX.—June 1875.

Three frogs were taken and decapitated. The hearts of all were exposed, and the number of beats in 10 seconds counted. One heart was cut out of the body (including the sinus venosus) and placed in a ·5 per cent. solution of NaCl; another was prepared in the same manner, and placed in a solution of sodium vanadate of strength equivalent to a ·5 per cent. solution of V_2O_5. The third was not cut out of the body, but immersed together with the whole upper half of the body in a solution of strength equivalent to ·05 per cent. solution of V_2O_5, the pericardium having been previously cut away. The heart immersed in ·5 per cent. solution of the salt of vanadium ceased to beat and failed to contract on application of a powerful stimulus (electrical) within 25 minutes of immersion; that placed in ·05 per cent. solution within 40 minutes; while the heart which was placed in salt solution ceased to beat after 1 hour 45 minutes, and failed to respond to stimulation after 2 hours 12 minutes.

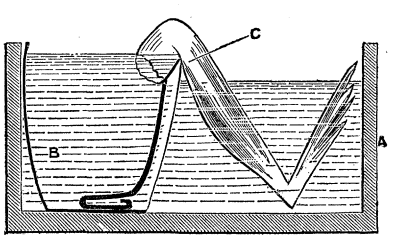
The results of this experiment are similar to those on voluntary muscle; extremely dilute solutions of sodium vanadate quickly cause death of muscular tissue when directly applied.

ii. *Special Action of the Poison on the function of Nervous Tissue (after local application).*

Exp. XL.—June 1874.

The legs of a frog were taken, and the sciatic nerve of each divided as high up as possible in the abdomen. The thigh was cut away above the knee, leaving the knee-joint intact. The nerves were tested, as a preliminary, by means of an interrupted current. Each leg moved when the secondary coil was 30 centims. from the primary. The arrangement drawn in the following diagram had been previously prepared for the reception of each leg:—

Fig. 1.



A is a glass capsule containing a ·5 per cent. solution of NaCl.
B is a crucible containing, in the case of one leg, a ·5 per cent. solution of NaCl, and in the case of the other a 2 per cent. solution of V_2O_5 in the form of sodium vanadate.
C shows the arrangement of the frog's limb and the nerve, the purpose of which is evident.

Helmholtz's arrangement of the induction-coil (interrupted currents) was used in stimulating the nerves from time to time, the minimum stimulus needed to produce contraction of muscles being in each case registered.

As before, the numbers represent the distance in centimetres between the two coils.

Time.	Leg whose nerve was immersed in NaCl solution.	Leg whose nerve was immersed in V_2O_5 solution.
h. m.		
4 30	Nerve immersed.	Nerve immersed.
4 50	Moves when the distance is 28–30.	Moves when the distance is 27.
5 0	,, ,, 27.	,, ,, 27.
5 15	,, ,, 25.	,, ,, 25.
5 30	,, ,, 24.	,, ,, 17.
5 45	,, ,, 23.	Twitches with distance 16.
6 7	,, ,, 21.	,, ,, 11.
6 40	,, ,, 21–22.	,, ,, 6.
8 0	,, ,, 19–20.	No movement at all with the secondary coil at 0.

Exp. XLI.—June 1875.

The above experiment was repeated exactly, except that the strength of the vanadium solution was equal to ·05 per cent. V_2O_5. At intervals during the experiment the muscles of both legs were tested by direct stimulation, and found to be normal as to their irritability throughout.

Helmholtz's arrangement was not used. With the preliminary stimulation, while still in the body, both legs moved when stimulated with the secondary coil at 31–32 centims. Within 2 hours 40 minutes the nerve immersed in the ·05 per cent. solution of vanadium salt ceased to induce contraction in the attached muscles on application of electrical stimuli; while, on the other hand, the nerve immersed in the salt solution remained sensibly normal for more than 10 hours 45 minutes, when observations were discontinued.

The direct application of very dilute solutions of sodium vanadate rapidly causes death in nervous tissue.

Résumé of the action of Vanadium upon Muscle and Nerve on direct application.

Direct application of vanadium solutions to muscular and nervous tissues is rapidly fatal to them.

iii. *Special Action of the Poison on the Function of Circulation.*

The following experiments were undertaken with a view to detect the causes of the disturbance of circulation, by determining the special parts of the circulatory system affected by vanadium. In the experiments the blood-pressure was recorded by means of a mercurial kymographion, continuous tracings being often taken during the whole time occupied by the experiment. The rate of rotation of the cylinder was checked by means of an electro-magnetic marker, the circuit being made and broken by Ludwig's Stromunterbrecher.

Both injection under the skin and injection into veins were made use of.

Exp. XLII.—March 4, 1874.

Rabbit.—Weight 1343 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin. The kymographic cannula was inserted into a carotid artery.

The rabbit died in 19 minutes 35 seconds after injection, and exhibited the usual general symptoms (see Experiments on pp. 505–508).

Note.—The solution was afterwards discovered to be under strength; hence the relatively long time the rabbit took to die.

Owing to the slight excursions of the pen at each heart-beat, it was impossible to obtain from the tracing of the experiment a series of numbers indicating rapidity of pulse.

From the record of the experiment we learn that, after the momentary rise due to the insertion of the injecting-syringe and the commencement of injection, the blood-pressure exhibited a succession of alternate rises and falls, gradually, however, attaining a lower and lower level until the death of the rabbit 19 minutes 35 seconds after injection. This alteration in the blood-pressure, as is shown by the tracing taken at the time, took place very regularly, and was only occasionally accompanied by struggles.

Exp. XLIII.—March 30, 1874.

Rabbit.—Weight 1834 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

The method of experiment resembled that of the foregoing. The rabbit died 10 minutes 30 seconds after injection. In this experiment, also, it was impossible to count the pulse from the kymographic tracing.

We learn that vanadium-poisoning causes the blood-pressure to fall from the moment of injection until death, that there are occasions on which the blood-pressure reasserts itself for a time, by a gradual rise, followed immediately by a gradual fall, and that once or twice the blood-pressure rose and fell in a jerky manner to a height of 15 or 20 millims. (having previously stood at about 45 millims.).

In the following experiment the attempt was made to prolong life by artificial respiration.

Exp. XLIV.—March 31, 1874.

Rabbit.—Weight 2075 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

The kymograph was connected with the right carotid artery.

The rabbit died within 22 minutes from the time of injection, artificial respiration being of no avail to prolong life.

From this experiment we learn that the blood-pressure declined steadily until the death of the rabbit, with the exception that once or twice it tended to regain its former level, the rise being accompanied sometimes by violent movements of the muscles.

On one occasion the rise and the muscular movements were both violent and sudden and simultaneous; but previously the convulsions or muscular movements preceded by about 15 seconds the rise, which was slow and accompanied by as gradual a fall. Although the record of the pulse is not very exact, as the rate of rotation of the cylinder was not checked, we can make out a decline in the number of heart-beats per 10 seconds, which is almost constant. The pulse, moreover, became at first much more marked as well as slower.

Exp. XLV.—May 13, 1874.

Rabbit (male).—Weight 1958 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
h. m. s.			Kymographic cannula in left carotid artery; tracheal cannula fixed for simultaneous respiration-tracing (see p. 537).
1 41 0	128	38	Normals prior to injection; respiration-curves are shown; Excursion of pen at each pulse=2 millims.
1 47 0	113	41	Injection finished; excursion of pen much less (=1 millim.) at each pulse and irregular.
1 49 0	116	39	Irregular pulse; composed of alternate long and short beats.
1 49 30	98	30–33	
1 50 0	...	29–30	Pulsations irregular; irregularities in line of blood-pressure due to struggles; respiration-curves have disappeared.
1 52 30	96·5	36–38	Pulsations regular but slight.
1 53 45	84	23	
1 54 30	90		
1 54 45	94	33–34	Pulse irregular and feeble.
1 55 0	90		
1 56 30	83	27–28	
1 58 0	...	30	Pulse alternately long and short.
1 58 30	77	20	Pulse marked; excursion of pen=2–3 millims.
2 0 0	74	28	Pulse regular but feeble.
2 1 30	62	19–20	Pulse deeper but regular.
2 2 30	67	22	
2 3 30	50	15	
2 6 0	36·5	22–16	
2 8 30	32	17	Pulse feeble but regular.
2 9 30	36·5	15	
2 10 30	38	13	Pulse feeble but regular. At this point a clot formed in the cannula and was removed.
2 12 45	62	18	The line indicating mean blood-pressure now commenced to describe long, sweeping curves; pulse deep and regular.
2 12 50	66		
2 13 0	52		
2 13 10	62		
2 13 20	48	20	Pulse deep and regular; sweeping curves of B. P. line.
2 13 30	53		
2 14 0	30	10	Pulsations deep, irregular and jerky.

TABLE (*continued*).

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
h. m. s.			
2 14 30	42	20	Pulse regular and feeble; sweeping curves of B. P. line.
2 14 50	34	28	Sweeping curves of B. P. line.
2 15 30	71	29	Pulse regular and deeper; sweeping curves of B. P. line.
2 16 20	42	18–19	Pulse regular; sweeping curves of B. P. line.
2 16 30	50	23	Sweeping curves of B. P. line.
2 17 0	38	18	
2 18 0	42	33	
2 18 30	57	29	
2 19 0	32	19–23	Pulse irregular; struggles. Sweeping curves of B. P. line.
2 20 0	36	33	Pulse regular. Sweeping curves of B. P. line.
2 20 30	56	31	Sweeping curves of B. P. line.
2 21 10	29	23	
2 22 0	7	...	Pulse cannot be counted; gasps: dead.

This experiment, which was a very successful one, and deserves much weight, confirms the results of the preceding. From it we learn that under the action of vanadium-poisoning the blood-pressure commences to sink, and never again regains its former height; that this decline is at first pretty regular and constant; that, after a time, a series of rises and falls succeeds, during which the blood-pressure gradually traces on the rotating cylinder long, sweeping curves, which are not only not due to, but are altogether unaccompanied by, struggles or convulsions, thus showing that the muscular movements, which in preceding experiments coincided with similar rises and falls, were not, in all probability, the cause of them. In this experiment the rate of rotation of the cylinder was checked by the electro-magnetic marker, in consequence of which a full and accurate list of numbers denoting the rapidity of heart-beats was obtained. From this we gather that there is a decline in the rapidity of the heart as well as of the pressure of the blood, which commences almost as soon as injection is complete. This decline is also marked by periods during which the heart tends to its original rapidity of motion, without, however, at any time reaching it. It may be noticed that the variations in blood-pressure and in pulse are not always coincident.

In the following experiments injection took place into veins.

Exp. XLVI.—June 8, 1874.

Rabbit.—Weight 2180 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected into the right external jugular vein.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
h. m. s.			
2 25 0	...	...	Kymographic cannula inserted into left femoral artery; cannula inserted into vein for injection.
2 25 0	100	35–40	Normals prior to injection. The respiration-curves are well shown.
2 30 0	97	35	Commence to inject. Respiration-curves well shown.
2 30 15	97	35	A sudden rise of B. P. to the extent of 10 millims. here took place without any alteration of pulse or respiration-curves.
2 30 20	106		
2 30 38	70	33	The B. P. now sank below the normal, and respiration-curves disappeared.
2 30 55	72	29	
2 31 0	...	11	Injection complete. The character of the pulse changed completely, becoming deeper, less regular, and less frequent. B. P. falling regularly.
2 31 45	35	11	The pulse is very irregular, shallow, and long.
2 32 40	24	12	The pulse is so undecided and irregular as to render counting difficult.
2 33 0	...	...	A sudden and irregular rise in B. P. from 22 millims. to 30 millims., followed by a less sudden fall to 22 millims., occurred at this point.
2 33 15	24	15	Pulse alternately long and short. Respiration 7–10 in 10 seconds and deep.
2 34 15	18	13–14	Respiration slight; eye insensitive; heart-beats long, regular, and dicrotic.
2 35 15	12	14	Pulse long and very irregular. Rabbit has been struggling. Respiration seems to have ceased.
2 36 30	10·5	14	Respiration resumed in a series of gasps.
2 38 30	8	...	Heart has ceased to beat; death.

In this experiment, in which vanadium was injected directly into a vein, the general symptoms are like those after injection under the skin, except that they supervene much more rapidly. Within 20 seconds after injection was commenced the blood-pressure rose rapidly from 97 to 106 millims., respiration-curves remaining normal. Within 38 seconds of the commencement of injection the blood-pressure had fallen below the normal, and respiration-curves were no longer to be seen, although the pulse was normal, except that it was slightly slower. From the time that injection was complete (1 minute after its commencement) the blood-pressure sank rapidly and almost constantly until the rabbit died, $7\frac{1}{2}$ minutes afterwards. During injection the pulse appeared normal but somewhat slower; but immediately after injection its characters changed very suddenly indeed, its rapidity sank from 29 to 11 in 10 seconds, and it became at first deep and regular, and afterwards slight and irregular. About 5 minutes before death it picked up slightly. During the experiment the rabbit exhibited some struggles of a convulsive character, which were not, however, accompanied by any marked disturbance of blood-pressure.

Exp. XLVII.—June 15, 1874.

Rabbit.—Weight 2430 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected into the right external jugular vein.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
			Kymographic cannula inserted into left carotid artery. Cannula in vein for injection. Cannula in trachea for simultaneous respiration tracing (see p. 538).
h. m. s.			
12 10 5	116	49	Normals prior to injection.
12 11 30	117	45	Normals prior to injection. Respiration-curves well shown.
12 14 55	117	49	Commenced to inject. About 10 seconds after the B. P. commenced to rise.
12 15 10	128	47	Injection complete. Pulse changed suddenly.
12 15 15	..	22	The B. P. sank more quickly than it rose; it sank to 70 millims., and afterwards began to rise again, reaching a height of 95 millims., owing to the rabbit's struggles. Respiration-curves disappeared.
12 15 20	70	..	
12 15 25	95	14	
12 15 40	48	12	Pulse regular and deep.
12 16 15	36	12	
12 16 45	31	14	Pulse shallower.
12 16 55	..	..	The B. P. rose several times very suddenly, owing to the struggles of the rabbit. Twice it attained a height of 61 millims.
	61		
12 17 40	31		
12 18 20	..	10–14	The rabbit began again to struggle; it appeared to be convulsed, exhibiting tonic spasms of the lower limbs. The eye became insensitive and the pupil dilated. The B. P. rose and fell irregularly.
12 18 45	22	5–6	The B. P. became steady and the pulse regular, long, and shallow.
12 20 20	..	10	Respiration in gasps; pulse very feeble.
12 21 30	14	..	Heart ceased to beat.
12 22 0	9	..	Dead.

In this experiment, with the exception of certain disturbances occasioned by the struggles of the animal, the variations in the character of the blood-pressure and the pulse resemble exactly those in the preceding one.

In the next two experiments it was desired to see the effects of poisoning by vanadium after section of both nervi vagi.

Exp. XLVIII.—February 19, 1874.

Rabbit.—Weight 1761 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
h. m. s.			
4 21 0	112	50–57	Normals after insertion of cannula into left carotid artery for kymographic tracing and exposure of both nervi vagi. Respiration-curves are well shown; pulse small.
4 22 0	106	..	Both vagi divided; respiration-curves shown; pulse small.
4 22 15	136		
4 22 30	120	52	
4 23 0	..	50–60	
4 28 38	112	60	Injection commenced.
4 29 0	116	62	Injection complete. Respiration-curves shown.
4 30 30	102	30	No respiration-curves; pulse small; long sweeping curves described by the kymographic pen.
4 30 40	120	28	Pulse dicrotic; long sweeping curves of blood-pressure line as above.
4 30 55	93		
4 31 0	116		
4 31 15	86	50	Respiration-curves pretty well shown; long sweeping curves of line of blood-pressure.
4 31 30	105		
4 31 40	82		
4 33 0	72	26	No respiration-curves.
4 34 10	50	30	
4 35 0	56	32	Respiration-curves shown.
4 36 0	48	31	Long sweeping curves, as above.
4 36 20	40		
4 36 25	50	..	Struggles of rabbit, and irregular rises and falls of blood-pressure.
4 37 0	62	32	Pulse regular.
4 37 25	42	32	Pulse very faint. At this point there occurred numerous irregular rises and falls of blood-pressure coincident with respiration. Pulse cannot be counted.
4 38 0	62	32	Pulse regular.
4 38 20	38	..	Pulse slight but regular.
4 44 0	28	..	A delay had been occasioned by winding up the clockwork of the revolving cylinder, which had run out. Convulsions.
4 44 15	23	..	Opisthotonic convulsions; pulse cannot be counted; blood-pressure very irregular, exhibiting sudden rises and falls.
4 45 0	0	..	Dead.

The symptoms exhibited by this rabbit resemble in general those of the rabbit in Experiment XLV., where the same dose was injected in a similar manner without previous section of the vagi. Here, as there, the blood-pressure commenced to sink after poisoning; but at intervals it tended to regain its former height (even exceeding it at one moment) by gradual rises succeeded by gradual falls, the results of which are recorded on the recording cylinder as long, sweeping curves. The oscillations of blood-pressure, normally coincident with respiration, disappeared and reappeared several times in this experiment—a circumstance which was not noticed in Experiment XLV. In addition to these regular variations of blood-pressure, there occurred several jerky irregularities,

due, apparently, in most cases, to struggles or convulsions. With respect to the pulse the comparison of the two experiments holds good also, when we take into consideration that the rapidity is, *in general*, greater in the case of the rabbit with divided vagi. Section of the vagi in rabbits does not at once cause the pulse to increase in rapidity. Bearing in mind, therefore, the fact that the full effect of division would occur *after* the injection of vanadium, we can see that there was a gradual decline of rapidity, marked, as we have noticed in preceding cases, by short periods of acceleration. For the rest, the animal exhibited the usual convulsions prior to death.

Exp. XLIX.—June 24, 1875.

Rabbit.—Weight 1315 grms.

Dose ·75 cub. centim. of the 5 per cent. solution (37·5 milligrammes V_2O_5), injected into the right external jugular vein.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
			Both vagi exposed; kymographic cannula inserted into the left carotid artery; cannula inserted into the right external jugular vein for injection.
h. m. s.			
4 45 0	101	..	Normal blood-pressure.
4 47 10	101	42	Normals prior to injection. Respiration-curves pretty well shown.
4 47 20	..	43	Left vagus divided. Blood-pressure rises. Respiration-curves well shown.
4 47 35	108		
4 47 40	..	48	Right vagus divided; blood-pressure rises.
4 48 0	142	41	Rabbit struggles and cries; irregularities of blood-pressure follow. Noise in throat of rabbit, due to paralysis of laryngeal muscles. Respirations 4 in 10 seconds.
4 49 10	{ 118 / 108 }	48	
4 50 5	105	53	Injection commenced. Within 7 seconds of commencement the blood-pressure began to rise, reaching a maximum of 113 millims.
4 50 10	..	49	
4 50 15	113	46	
4 50 20	..	..	Injection complete. The blood-pressure fell suddenly, but rose again to 82 millims. The pulse changed suddenly in character, becoming at first shallow and rapid, then deep and irregular; the respiration-curves disappeared.
4 50 30	{ 70 / 82 }	24	
4 51 0	..	27	Pulse rather more regular.
4 51 15	56	23	Respiration-curves have reappeared, and seem normal. Pulse seems composed of alternately short and long beats.
4 51 20	..	..	The rabbit here commenced to struggle, and continued to do so for two minutes, causing great disturbance in the blood-pressure and obscuring the pulse; respiration-curves have disappeared again.
4 53 10	24	10–11	Pulse very irregular. Further struggles, forcing the blood-pressure up.
4 54 30	18	11–12	Pulse more regular. Eye insensitive.
4 55 40	12	10	Respirations seem to have ceased.
4 59 0	6	3–4	Pulse remarkably shallow and long.
4 59 40	5	4	Death.

A comparison of this experiment with one (say Exp. XLVI.) in which the conditions

were similar, except that the vagi remained intact (and the dose was slightly larger on account of the size of the rabbit), will show an almost exact similarity of symptoms. The slight divergence is, simply, that the general rapidity of pulse after injection in the experiment where the vagi were divided was greater than in the other—a circumstance which is explained by a consideration of the inhibitory functions of the vagus.

In the next three experiments the object was to discover the effects of poisoning by vanadium upon animals whose cords had been divided.

Exp. L.—June 23, 1874.

Rabbit.—Weight 2370 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected into the left external jugular vein.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
			Tracheotomy: inserted metal tracheal tube; chloroform administered; cord exposed high in the neck; cannula inserted into vein for injection; kymographic cannula inserted into the left femoral artery.
h. m. s.			
5 2 0	..	..	·75 cub. centim. of 1 per cent. solution of curare injected into the vein; artificial respiration set up.
5 9 0	76		
5 12 0	74	54	Heart-beats are shallow and rapid.
5 12 45	108	51	On raising the rabbit's head with the purpose of dividing the cord, the blood-pressure went up suddenly, but fell again immediately.
5 12 50	78		
5 12 55	..	..	Commenced to divide the cord.
5 13 0	128	30	On inserting the knife the blood-pressure rose at once.
5 13 5	..	..	Division of cord complete.
5 13 30	..	46	After another slight rise the blood-pressure continued to descend until it stood steadily at about 22 millims.
5 14 30	24		
5 16 10	22	34	The pulse, which had become imperceptible soon after section, now became more vigorous.
5 16 40	22	37	Injection of vanadate commenced.
5 16 55	22	26	Injection complete; the pulse suddenly became less rapid and longer.
5 17 10	28	24	The blood-pressure rose with a steady sweep, the pulse meanwhile becoming much more marked but less rapid.
5 17 30	35	18	
5 17 45	38	19	
5 18 0	38	18–19	From this point the blood-pressure declined gradually until the rabbit died, the pulse becoming very faint—too faint to be counted.
5 18 15	30	18	
5 18 30	25		
5 18 45	22		
5 19 10	20		

In this experiment the effects of poisoning by vanadium upon the circulation appear to have been (1) to cause a steady rise of blood-pressure from 22 millims. to 38 millims., which took about 1 minute to develop, followed by a steady fall, death supervening when the pressure had attained its previous level; (2) to cause a decline, first of all in

rapidity, and afterwards in vigour, of the pulse, which developed first suddenly (from 37 per 10 seconds to 26 per 10 seconds in the space of 15 seconds), but afterwards more gradually.

Exp. LI.—June 23, 1874.

Rabbit.—Weight 2465 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected into the right external jugular vein.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
h. m. s.			Preparations as in Exp. L.
3 5 0	..	..	·75 cub. centim. of a 1 per cent. solution of curare injected into the vein. Artificial respiration commenced.
3 21 20	109	50	
3 22 22	..	..	Commenced to divide cord.
3 22 28	160	34	Rise due to insertion of knife into cord.
3 22 32	..	..	Division of cord complete.
3 22 35	132	45	Blood-pressure began to fall, but rose again (owing to irritation by bleeding?) to 146 millims.
3 22 55	146		
3 25 30	52	40	Blood-pressure again fell suddenly, and continued at 52 millims.
3 27 0	46	26	The pulse began to get slower.
3 27 20	40	..	The heart ceased to beat somewhat suddenly, and the blood-pressure sank to 25 millims. at once.
3 27 32	25		
3 28 0	..	7–12	The heart recommenced to beat with slow but vigorous contractions, and quickly regained rapidity; the blood-pressure rose rapidly and exceeded, at first, its previous level.
3 28 30	75	30	
3 29 55	48	26	The blood-pressure settled at last at about 48 millims.; the pulse did not regain its former rapidity.
3 30 23	48	26	Commenced to inject the vanadate.
3 30 35	48	23	Injection complete.
3 30 45	48	20	The pulse became less frequent and the pressure sank slightly.
3 30 55	46	14	
3 31 5	..	..	The heart seemed to stop suddenly, and the blood-pressure at once sank to 30 millims.
3 31 20	30		
3 31 50	..	8–13	The heart began again just as it had done at $3^h\ 28^m$, and the pressure rose to 95 millims.
3 32 5	95	23	
3 32 10	..	14	The pulse again became slow, and the blood-pressure fell to 65 millims.
3 32 20	65		
3 32 30	70	20	The pulse quickened a little, and the blood-pressure rose. From this point the blood-pressure sank quite regularly until death supervened. The pulse became too faint to count.
3 33 10	46		
3 34 50	22		

In this experiment the symptoms were complicated by a sudden and momentary stoppage of the heart's action immediately after injection (at $3^h\ 31^m\ 5^s$), which is not, probably, to be attributed to the action of vanadium, as an exactly similar stoppage had taken place before injection (at $3^h\ 27^m\ 20^s$). With this exception the symptoms resemble those of the preceding experiment.

Exp. LII.—July 1, 1874.

Rabbit.—Weight 1810 grms.

Dose ·75 cub. centim. of the 5 per cent. solution (37·5 milligrammes V_2O_5), injected into the right external jugular vein.

Time.	Mean B. P.	Pulse in 10 seconds.	Remarks.
h. m. s.			Preparation as in Exp. L., without the loss of any blood.
3 44 0	96	45	Pulse regular; respiration-curves are well shown.
3 46 30	..	42	·75 cub. centim. of a 1 per cent. solution of curare injected into the vein.
3 49 30	102	42	Artificial respiration commenced; pulse stronger.
3 56 0	..	46	More curare injected.
4 0 0	..	..	On raising head to divide cord the blood-pressure rose and fell several times.
4 1 0	110	..	Rise due to insertion of knife into cord.
4 1 20	124	..	Cord divided: blood-pressure first rose and then fell, until it stood steadily at 36 millimetres. Pulse of normal depth.
4 6 0	36	30–33	
4 12 30	34	30	Injection of vanadate commenced. About 5 seconds after commencement the blood-pressure began to rise, and reached 71 millimetres by the time injection was completed.
4 12 50	71	28	
4 13 10	64	27	Blood-pressure fell gradually, the pulse becoming less frequent and fainter.
4 13 30	54	26	
4 13 50	62	24	Blood-pressure rose gradually, the pulse still sinking in rapidity and becoming fainter.
4 14 0	60	24	Blood-pressure declined again, and continued to do so until the death of the rabbit, the pulse becoming too faint to be counted.
4 14 30	48		
4 15 0	30	..	Death.

The symptoms of this experiment resemble in general those of Exp. L. Injection of the poison caused a gradual rise of blood-pressure, followed in succession by a fall, another rise, and another fall, which continued until the death of the rabbit. The pulse became gradually slower and fainter from the moment of injection.

In the following experiment the object was to observe directly the action of vanadium upon the heart after its introduction into the circulation. In order to do this, all the extracardiac circulatory nervous centres were removed in a frog by division of the cord below the atlanto-occipital articulation and destruction of the nervous organs above; and the heart was then fully exposed to view.

Exp. LIII.—June 30, 1875.

Frog.—Of large size.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes $V_2 O_5$), injected into the abdominal vein.

Time.	Pulse in 10 seconds.	Remarks.
h. m. s.		
4 5 0	..	Divided the cord at the atlanto-occipital articulation, and destroyed the brain.
4 45 0	..	Tied the frog down on its back: inserted cannula into the abdominal vein for injection. Exposed the heart, avoiding all bleeding.
	9–10	Heart-beats counted directly.
4 50 0	..	Injected about ·25 cub. centim. of the solution. Ventricle seems much dilated and very purple.
	9	Heart-beats not so vigorous.
4 52 0	9–10	Heart-beats rather more vigorous.
4 54 0	..	Rest of solution injected. Ventricle seems very purple: beats less vigorously.
	9–10	Reflex action quite normal on pinching.
4 57 0	7–7·5	Ventricle becomes purple and distended: heart-beats less vigorous.
	7	
4 59 30	7	Heart-beats less vigorous. Ventricle much dilated and purple.
5 4 0	6	Ventricle seems unable to contract so as to drive out the whole of the contained blood.
5 5 30	6–7	
5 8 0	5	
5 10 0	5	
5 11 0	5	
5 21 0	5–5·5	Heart-beats more vigorous.
5 30 0	4–5	
5 33 0	5	Reflex action slight on pinching.
5 38 30	5	Heart-beats weaker.
5 50 0	5	
5 55 0	5	
5 59 0	5	Reflex activity has quite disappeared.
8 30 0	..	The heart went on beating for a long time, exhibiting no other symptoms than a gradually increasing languor. At $8^h 30^m$ it was left for the night, beating, but very slowly.

From this experiment we learn that the effect upon the heart of vanadium, when injected directly into blood-vessels, is to cause a diminution in the rapidity and the vigour of its beats.

Résumé of the Action of Vanadium upon the Circulation.

In the preceding experiments the solution containing vanadium was injected either underneath the skin or directly into veins. The results in the latter case were exactly similar in kind to those in the former; but they took place with extreme rapidity, owing to the more concentrated action of the poison.

A consideration of the experiments shows that the influence of vanadium upon the

circulation is threefold. In the first place, there is a diminution of blood-pressure, which, however, is not quite continuous, but is marked by intervals in which there is a tendency to regain the former height; these alternate rises and falls take place with considerable regularity. In the second place, there is a disappearance of respiration-curves; and in the third place, there is irregularity and diminution in rapidity of the pulse, which, like the fall of blood-pressure, is not quite regular. In the case of injection into veins there was scarcely time, owing to the rapidity of death, for the development of the marked fluctuations noticed when injection was hypodermic.

The disappearance of respiration-curves can only be due to some alteration of the vasomotor centre, whose oscillations of activity are the cause of them. The marked fall of blood-pressure might be due to one or more of the following circumstances:—1, paralysis of the vasomotor centre; 2, peripheral irritation of depressor nerves; 3, relaxation of arterial tonus due to other causes than vasomotor paralysis; 4, weakening of the heart's action. The alteration of the pulse may be caused by:—1, some action upon the vagi; 2, poisoning of intracardiac centres; 3, poisoning of muscular substance of heart; 4, diminution of blood-pressure. As previous division of the vagi does not seem in the least to alter the circulatory effects of poisoning by vanadium (Experiments XLVIII. & XLIX.), it is clear that none of these effects can be attributed to an action on the vagi. It is, moreover, evident, from experiments detailed elsewhere in this paper, that there is no poisoning of the muscular substance of the heart itself. Further, the fact that vanadium does not paralyze unstriped muscles in other regions of the body (as in the intestines) renders it probable that there is no direct action upon the muscular walls of the arteries. We may therefore at once eliminate both these possibilities from the question. It will be seen on comparison that the fluctuations in blood-pressure and in pulse are only sometimes coincident; neither will, therefore, serve as sufficient explanation of the other, although the effects may be partially due to their interaction. There remains, therefore, the vasomotor system of nerves, with the depressors and the intracardiac nervous mechanism, to which we must look for the chief explanation of the phenomena under consideration. From the experiments in which the cord was divided in the neck, we gather that the effects of vanadium-poisoning upon the pulse occurred as usual, while the diminution and fluctuations in blood-pressure were no longer visible, being indeed replaced by a rise. As in those experiments the vasomotor centre, the accelerators, and the vagus centre and terminations were eliminated (the vagus terminations by means of the curare which was injected), we are driven to the conclusion (1) that the depression and fluctuations of blood-pressure are for the most part due to some action of the poison on the vasomotor centre, and (2) that the irregularities of heart-beats are caused by an affection of intracardiac ganglia. The former conclusion is strongly confirmed by the disappearance of respiration-curves, which must be due to vasomotor mischief, and by the fact that other centres in the cord are acted on by vanadium. Hence it seemed hardly necessary to perform any special experiments after elimination of the depressors. The latter conclusion is fully borne out by

Experiment LIII. on a frog, where the usual diminution followed in a heart which was directly observed after the removal of all extracardiac nervous influences.

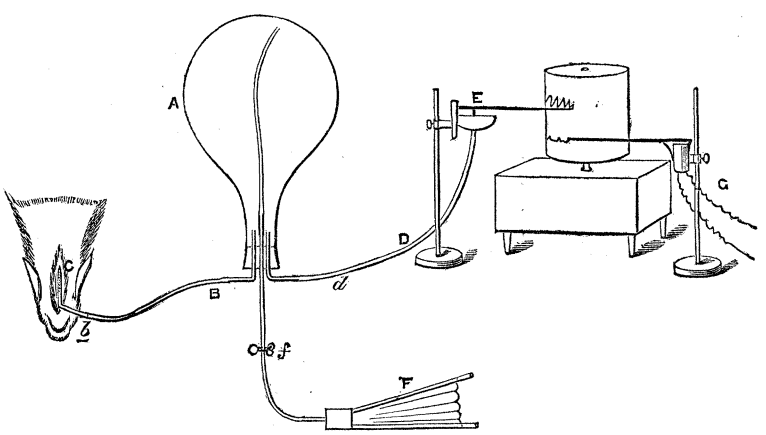
The rise of blood-pressure which follows injection into the veins of rabbits whose cord had been cut is considered to be due to the greater vigour of the heart which was noticed.

IV. SPECIAL ACTION OF THE POISON ON THE FUNCTION OF RESPIRATION.

The following experiments were performed in order to determine the special action of poisoning by vanadium upon the respiratory function.

In the experiments the depth and frequency of the respirations were recorded upon a rotating cylinder, the rate of rotation of which was checked by means of LUDWIG'S Stromunterbrecher and a magnetic marker, in the manner illustrated by the following diagram:—

Fig. 2.



A is a large bolt-head, of capacity equal to $16\frac{1}{2}$ litres, stopped by means of an india-rubber cork fitted with three glass tubes. One of the glass tubes is connected, by means of the caoutchouc tube B, with the glass cannula inserted into the rabbit's trachea, C. Another is connected, by means of the tube D, with a MAREY'S tympanum and pen (E), arranged so as to write upon a SÉCRETAN'S cylinder. The third glass tube is connected on the one side with a flexible tube descending to the bottom of the bolt-head, and on the other with a pair of bellows (F). The object of the pair of bellows is to enable the operator to remove completely all traces of respiratory carbonic acid, and thus to avoid the fallacies introduced by its presence.

After every few minutes in the course of an experiment the tube D was occluded at *d* by means of a clip, the tube B was disconnected at *b*, and the clip at *f* was removed. A few blasts from the bellows then sufficed to thoroughly clear the bolt-head of all the products of respiration; after which the previous conditions were resumed, and the

experiment proceeded with. G is the electro-magnetic pen connected with LUDWIG'S Stromunterbrecher.

Both injection under the skin and injection into veins were made use of.

Exp. LIV.—May 6, 1874.

Rabbit.—Weight 1760 grms.

Dose* about 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

Time.	Respirations in 10 seconds.	Remarks.
h. m. s.		
12 15 0	..	Tracheotomy: insertion of glass cannula into trachea.
12 18 0	10	Normal prior to injection.
12 19 0	10	Do. do.
12 22 40	..	Injection commenced.
..	11	
12 26 30	12	
12 27 0	..	Injection complete.
12 29 0	11	
12 30 0	12·5	
12 33 0	15	
12 35 0	17	Respiration shallow.
12 40 0	23	Do. very shallow.
12 42 0	22	Do. do.
12 44 20	17	Do. do.
12 46 0	20	Do. do.
12 50 0	16	Still shallower than before.
12 52 0	13	Respiration deeper and less regular.
12 55 0	10	
1 0 30	17	Very shallow.
1 4 30	15	Do.
1 9 0	13	Do. Eye sensitive.
1 14 30	13	Do.
1 20 0	11	Do.
1 23 0	3	Gasps. Short, shallow inspirations, followed by longer exspirations. Eye insensitive. Twitching of abdominal muscles. Pupil dilated. Dead.

A post mortem examination made at $1^h\ 30^m$ showed that the right and left auricles were beating, that the ventricles also were irritable, and that the right side of the heart was much distended.

From this experiment we learn that injection of vanadate of sodium under the skin causes increase of rapidity, and diminution of depth, of respiration; that the symptoms commenced to develop almost immediately after injection, and had become most marked 20 minutes after injection; that the symptoms abated somewhat, but afterwards became violent again; and that death was accompanied, if not immediately caused, by asphyxia.

* A little of the solution was lost during injection.

Exp. LV.—May 11, 1874.

Rabbit.—Weight 2000 grms.

Dose about 4 cub. centims. of the 5 per cent. solution (200 milligrammes V_2O_5), injected under the skin.

The rabbit died 30 minutes 30 seconds after injection. Artificial respiration, which was commenced immediately on the cessation of natural breathing, again failed to prolong or restore life (see Exp. XLIV.).

In this experiment the symptoms were in general like those of the preceding one; there was, however, no fluctuation in the intensity of the symptoms.

Exp. LVI.—May 13, 1874.

Rabbit.—Weight 1958 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

Time.	Respirations in 10 seconds.	Remarks.
h. m. s.		Tracheotomy. Insertion of glass cannula into trachea; exposure of carotid artery for simultaneous blood-pressure tracing. (See Exp. XLV.)
1 41 0	14–15	Normals prior to injection.
1 45 0	..	Injection commenced.
1 47 0	..	Injection finished.
1 47 20	15	
1 49 30	17–18	
1 53 0	18	
1 55 0	18	
1 58 30	17	
2 0 30	20	Very shallow.
2 3 0	19	Very shallow. Eye sensitive.
2 9 0	13–14	Very shallow indeed.
2 9 30	11	Slightly deeper.
2 10 30	9	Slightly deeper.
2 12 15	12	Deeper, but not of normal depth. Eye slightly sensitive.
2 12 45	10	
2 13 15	8	Very deep—deeper than normal. Abdominal muscles convulsed.
2 15 15	12	Shallower.
2 16 0	8–9	
2 16 15	..	Struggles, which render respiration deep, irregular, and less frequent.
2 18 30	10	Moderately deep.
2 19 0	8–9	
2 20 0	9	
2 20 30	9	Moderately deep.
2 21 0	7	
2 22 0	..	Death supervened suddenly, preceded by a few shallow gasps.

This experiment agrees exactly with the preceding one.

Exp. LVII.—May 19, 1874.

Rabbit.—Weight 1347 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

The rabbit died within 15 minutes after injection.

This experiment agrees with the preceding, except that the symptoms came on with remarkable rapidity; possibly the injection-syringe punctured some considerable vein (see the experiments on direct injection).

In the following two experiments injection took place directly into a vein.

Exp. LVIII.—June 15, 1874.

Rabbit.—Weight 2430 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected into the right external jugular vein.

Time.	Respirations in 10 seconds.	Remarks.
		Tracheotomy. Insertion of glass cannula into trachea; exposure of carotid artery for simultaneous blood-pressure tracing. Insertion of cannula into vein for injection.
h. m. s.		
12 13 0	10	Normal prior to injection.
12 15 0	9	Injection commenced. Respiration not so deep.
12 15 15	17	Injection finished. Respiration very shallow indeed.
12 15 30	39	Extremely shallow. Rabbit commenced to struggle, rendering respiration irregular and deeper.
12 16 15	12	About normal depth.
12 16 30	12	Rather shallower.
12 18 45	9	Very irregular in depth, owing to the almost incessant and violent struggles of the rabbit. Convulsions and tonic spasms of the lower limbs.
12 19 0	..	Eye insensitive; pupil largely dilated.
12 20 0	3	A succession of shallow gasps. Dead.

The cord and brain were exposed the whole length, and appeared to be quite normal.

In this experiment the general symptoms were the same as in the case of hypodermic injection, except that they were much more rapid. Within 15 seconds of the commencement of injection respiration was becoming much more rapid and shallow, and the maximum of rapidity and shallowness was attained within 30 seconds of the commencement. From this point respiration declined until death, which occurred amid a succession of gasps.

Exp. LIX.—June 15, 1874.

Rabbit.—Weight 1184 grms.

Dose 1 cub. centim.* of the 5 per cent. solution (250 milligrammes V_2O_5), injected into the right external jugular vein.

The rabbit died within 4 minutes 45 seconds after injection.

The symptoms in this case were substantially the same as in the preceding experiment.

In the next experiment an attempt was made to discover the effect of poisoning by vanadium upon respiration after section of the vagi.

Exp. LX.—May 11, 1874.

Rabbit.—Weight 1235 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

Time.	Respirations in 10 seconds.	Remarks.
h. m. s.		Nervi vagi exposed. Tracheotomy. Insertion of glass cannula into the trachea.
2 45 0	8–10	Normal respirations, somewhat irregular.
2 51 0	..	Vagi divided.
2 53 30	6–7	Respirations after section of vagi deeper than before. Struggles of rabbit.
2 56 0	..	Injection commenced.
2 57 15	..	Injection complete.
2 58 0	8	Rather shallower.
3 0 0	6–7	Slightly deeper. } Struggles of rabbit.
3 0 30	8	Slightly deeper.
3 1 0	9–10	Rather deeper.
3 2 0	9	Much shallower.
3 3 0	3–5	Very irregular and more like gasps.
3 5 0	..	Short, sharp gasps at long intervals. Pupil insensitive and much dilated.
3 7 0	..	Dead.

In this experiment the injection of vanadate of sodium beneath the skin of a rabbit whose vagi had been divided previously caused a distinct shallowness and increase in rapidity of respiration, as in the case of rabbits whose vagi were intact; but the alterations were not, proportionally, so great in the former as in the latter case.

Résumé of the Action of Vanadium upon Respiration.

From the experiments just detailed we learn that the action of vanadium, in the form of sodium vanadate, upon respiration is to cause coincidently increased rapidity and diminished depth, which proceed regularly until the period of the greatest intensity of

* A small quantity escaped during injection.

the symptoms is reached, after which the characters of respiration again become normal. Respiration then declines until death, the decline being gradual in some cases, but marked in others by periods of increased vigour and frequency. Death seems to be proximately caused by failure in respiration. There are, therefore, (1) a stimulation and (2) a depression of respiration, which may result either from some lesion of the respiratory centre in the medulla, or from some affection of the afferent respiratory nerve—the vagus. As the usual respiratory symptoms seem to follow after section of both nervi vagi, we must assume the disturbance of respiration caused by vanadium to be centric.

V. SPECIAL ACTION OF THE POISON ON THE FUNCTIONS OF THE MUSCULAR AND NERVOUS SYSTEMS.

In the following experiments frogs were the animals chiefly used, the common *Rana temporaria* being caught from time to time in the neighbouring ponds for the purpose. The minimum stimulus required to produce movement in a muscle was the test made use of. A Du Bois-Reymond's induction-machine was used in stimulation, the coils being gradually approximated until the feeblest contraction occurred, and the distance between them then noted. Interrupted currents were generally used, but single induction-shocks were sometimes resorted to.

The next seven experiments were devised to show the action of vanadium upon the motor and sensory powers of the nervous system and upon muscles.

Exp. LXI.—May 19, 1874.

Frog.—Weight 25 grms.

Dose 1 cub. centim. of the 5 per cent. solution (5 milligrammes V_2O_5), injected under the skin.

h. m.

1 45. The femoral artery of right leg exposed and ligatured a little way above the middle of the thigh. Injection complete; lively; jumps about.

1 50. Lies down, with ligatured leg spread out.

1 52. Drags ligatured limb.

2 23. Lies quiet; moves spontaneously.

2 30. Both legs lie spread out. On touching the ligatured leg the frog kicked twice with the other.

On pinching the non-ligatured leg both legs were moved, but not so vigorously as before.

On pinching the right arm both legs moved, but the ligatured one first.

3 30. Quite dead. Rigor mortis appears to have commenced.

Exposed the sciatics of both legs quickly.

1 Leclanché's element. Interrupted currents.

Non-poisoned limb.	Distance between primary and secondary coils.		Poisoned limb.
Just moves.	25	25	Just moves.

In this experiment no difference in the behaviour of the non-poisoned and of the poisoned legs could be detected, either in the case of voluntary stimuli before death, or of electrical stimuli after death.

Exp. LXII.—May 19, 1874.

Frog.—Weight 28 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected subcutaneously.

The frog was arranged as in the preceding case, the nerves being tested, as before, as soon as reflex activity had ceased.

In this experiment the motor and sensory nerves of both poisoned and non-poisoned limbs were affected in exactly the same way as indicated by the movements which followed on pinching both legs. The nerves (motor) of both limbs responded equally easily to electrical stimuli after death.

Exp. LXIII.—May 19, 1874.

Frog.—Weight 28 grms.

Dose 1 cub. centim. (about) of the 5 per cent. solution (about 50 milligrammes V_2O_5), injected subcutaneously.

h. m.

4 50. The femoral artery of the right leg was tied close up to the pelvis.

Injection of vanadium solution complete. Quite active.

5 10. Moves on being irritated; also spontaneously, but with a dragging movement.

The frog was noticed at intervals during the next two hours, and exhibited the same phenomena as the last two had done, *i. e.* there did not appear to be any difference in behaviour between the poisoned and non-poisoned limbs.

7 7. Dead to all appearance.

Exposed sciatic nerves quickly. On cutting the skin of the left (poisoned) leg to expose the sciatic nerve, a slight reflex movement took place. Single induction-shock.

Non-poisoned limb.	Distance between coils.		Poisoned limb.
Just moved.	23	21	Just moved.

The muscles were then directly stimulated with single shocks.

Non-poisoned limb.	Distance between coils.		Poisoned limb.
Just moved.	12	12	Just moved.

And again with an interrupted current.

Just moved.	10	10	Just moved.

This experiment serves to confirm the results of the preceding one, and shows, further, that the muscles of the poisoned and non-poisoned legs were equally little affected.

Exp. LXIV.—May 20, 1874.

Frog.—Weight 23 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin.

In this case the whole thigh, except the sciatic nerve, was compressed firmly by a ligature.

Rather more than half an hour after respiration had ceased, but before paralysis was general, the frog was decapitated, and the sciatic nerves tested as in the preceding cases.

This experiment confirms the results of the preceding ones, showing that the non-poisoned and the poisoned muscles and nerves are equally irritable.

Exp. LXV.—May 22, 1874.

Frog (α).—Weight 29 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected under the skin.

Frog (β).—Weight 29 grms.

Dose ·5 cub. centim. pure water injected under the skin.

Time.	Frog (α).	Frog (β).
h. m.		
3 30	Injection complete.	Injection complete. Active.
3 45	Very quiet; eyes closed. Moves on being touched. Respiration appears to have ceased.	Quite active.
4 0	Lower jaw hanging.	
	Decapitated.	Decapitated.
4 5	Sciatic of right leg exposed.	Sciatic nerve exposed.
	Movements when the distance between coils is 30.	Movements occur when the distance between coils is 32–35.
	Muscles of right leg irritated directly. Movements occur when the distance is 18.	Muscles of leg directly irritated. Movements occur when the distance is 16–17.
	Inserted the electrodes into the cord. Movements of legs when distance is 20.	Inserted electrodes into the cord. Movements of legs when distance is 24.

The battery consisted of one LECLANCHÉ'S element. Currents interrupted.

This experiment (a modification of the preceding) practically confirms the results previously obtained, the difference in irritability between the two frogs being merely such as might be due to differences in idiosyncracy, or due to the deficient aëration of the blood in frog (α), owing to early cessation of respiration, and not such as ought to be attributed to a direct action of the poison on muscle or nerve.

Exp. LXVI.—May 25, 1874.

Guineapig (α).—Weight 310 grms.

Dose 3 cub. centims. of the 5 per cent. solution (150 milligrammes V_2O_5), injected under the skin.

Guineapig (β).—Weight 400 grms.

Time.	Guineapig (α).	Guineapig (β).
h. m.		
4 20	Injection complete. Runs about basket.	
4 25	Lies on side. Eyeballs sensitive.	
4 26	Convulsions of hind legs. Clonic spasms. Moves on pinching.	
4 28	Gasps and retches; passes urine. Eyeball insensitive. Dead.	Bled to death [guineapig (α) was not bled].
4 29	Gasped.	
4 35	Cord exposed; electrodes inserted. Very slight movements of dorsal muscles with the secondary coil at 0. The sciatic nerve and the muscles gave good contractions on stimulation.	Cord exposed; electrodes inserted. Active movements of dorsal muscles with secondary coil at 8–10. The sciatic nerve and the muscles gave good contractions on stimulation.

A battery of one LECLANCHÉ'S element was used. Currents interrupted.

This experiment loses value from the circumstance that one animal was bled while the other was not. As regards the (sciatic) nerves and muscles, it confirms the experiments on frogs; but, as regards the cord, it seems to show that poisoning by vanadium interferes with the *conductivity* of the cord. But this observation, in the case of a *warm-blooded* animal, must be regarded as having little weight when it opposes observations to the contrary effect in experiments on *cold-blooded* animals.

Exp. LXVII.—May 26, 1874.

Rabbit (α).—Weight 900 grms.

Dose 2 cub. centims. of the 5 per cent. solution (100 milligrammes V_2O_5), injected under the skin.

Rabbit (β).—Weight 890 grms.

Rabbit (α).

h. m.

1 15. Injection complete.

1 16. Quiet.

1 17. Drags hind legs.

1 20. Turns over on to back; drags hind legs. Breathes very quickly.

1 21. Moves on being pinched.

1 22. Gave a little chloroform preparatory to bleeding. Cries, struggles on being chloroformed.

1 23. Bled to death from the neck. Proceedings were taken to test the irritability of cord &c. See below.

Rabbit (β).

2 10. Chloroformed, and bled to death from the neck. The cord &c. of this rabbit were then tested.

The results in both cases are tabulated side by side, for convenience of comparison.

Rabbit (α).	Rabbit (β).
Cord exposed about middle of back. Movements of dorsal muscles with secondary coil at 8.	Cord exposed about middle of back. Movements of dorsal muscles with secondary coil at 8.
Sciatic nerve of right leg induced contractions in the limb on stimulating with secondary coil at 8–10.	Sciatic nerve of left leg was found to be quite irritable.
The electrodes were inserted between two lumbar vertebræ. The legs contracted on passing a current; but, unfortunately, the distance between the coils was not noticed.	The electrodes were inserted just above the sacrum. Contractions of the legs occurred on passing a current with the secondary coil at 8.

A battery of one LECLANCHÉ'S element was used. Currents interrupted.

This experiment may be said to confirm exactly the phenomena in the case of frogs. The conditions of the poisoned and unpoisoned animals were rendered equal in this case, unlike that of the preceding experiment.

In the following three experiments attention was more particularly given to all those phenomena in which *sensory* nerves played a part, the special object being to determine whether sensory nerves were acted on by the poison or not.

Exp. LXVIII.—June 1, 1874.

Frog.—Weight 36 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin.

h. m.

3 30. The right femoral artery has been tied. Injection complete.

3 42. Breathing slight. Abdomen pinched up and contracted. Voluntary movements.

h. m.

3 56. Lies in a curious posture, with its arms folded beneath it. Membranæ nictitantes half closed. Lower jaw beginning to droop. On being turned over on to its back it does not attempt to recover. No throat-movements of respiration.

On pinching each foot the corresponding leg moves, and to an equal extent in each case.

4 0. Moves spontaneously towards a dark corner of the bell-jar.

4 3. On stirring the bell-jar the frog respired, and jumped.

4 10. On pinching either foot it moved *both* legs with equal vigour. The frog leaped away after having its *poisoned* leg pinched. Lies on belly.

4 12. Spontaneous movements.

The frog was taken from the bell-jar and both feet immersed in a 2 per cent. solution of H_2SO_4; both legs moved, but the *poisoned* one first by a second or two. A 4 per cent. solution of H_2SO_4 was taken, and at

4 32. The frog's feet were immersed in it: no movements occurred after they had remained in for 50 seconds.

4 34. No movements occur on pinching all over the body and limbs.

4 40. Decapitated. Irritated the exposed end of the cord; movements in the arms and lower jaw (which had been allowed to remain) with the secondary coil at 8.

4 44. Passed the electrodes down behind the cord for about $\frac{1}{2}$ an inch (with care, so as not to injure the cord); movements followed, on passing a current, when the secondary coil stood at 9.

4 50. Removed the back of the 5th (or 6th) vertebra as carefully as possible; inserted the electrodes into the cord: movements followed with the secondary coil at 11.

4 53. Removed the back of the vertebral arch next below, and inserted the electrodes into the cord; movements followed in the abdominal and thigh-muscles with the secondary coil at 11.

4 55. Removed the back of the arch next below; extension of *both* legs occurred on passing a current with the secondary coil at 11.

5 0. Both sciatics exposed and placed on the electrodes below (as well as above) the level of the ligature on the right femoral artery; equal movements of *both* calves followed with the secondary coil at 21.

5 4. The muscles of both legs were irritated directly, and about equal extent of movement occurred in both poisoned and non-poisoned leg with the secondary coil at 10.5.

From this experiment we deduce the following:—At a time when the vanadium salt had undoubtedly commenced to produce nervous symptoms no indications of any affection of sensory nerves in the poisoned limb could be detected; at least, the indications given by the poisoned limb were exactly such as were given by the non-poisoned limb. There was, however, distinct impairment of reflex excitability, as shown by the

strength of acid necessary to produce even a sluggish reflex action; but this impairment was not due to any affection of the afferent or efferent nerves in the leg, and for the reason, given above, that both legs behaved alike. On stimulating the nerves after decapitation (complete paralysis having previously occurred), it was noticed that, although the whole frog appeared somewhat less responsive than usual, no difference could be detected between the poisoned and non-poisoned limbs.

Exp. LXIX.—June 1, 1874.

Frog.—Weight 31 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected under the skin.

In this experiment, instead of the femoral artery being ligatured, the whole of the structures of the thigh, excepting the sciatic nerve, were compressed by a thread. In other respects it was a repetition of the preceding experiment, and serves to confirm its results.

Exp. LXX.—June 1, 1874.

Frog.—Weight 30 grms.

Dose 1·5 cub. centim. of the 5 per cent. solution (75 milligrammes V_2O_5), injected under the skin of the back.

In this experiment the right femoral artery was tied prior to injection. The frog was examined, as in the preceding cases, after the poison had begun to manifest itself, and with generally confirmatory results.

In the experiments next succeeding the object was to discover the effect of vanadium-poisoning upon the general functions of the cord as a conductor and as a centre of ordinary reflex action. The action of vanadium upon some of the special centres contained in the spinal cord is found in the notes of experiments on circulation and respiration.

Exp. LXXI.—May 27, 1874.

Frog.—Weight 29 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected subcutaneously.

h. m.

2 33. Injection complete.

2 47. Respiration very slight.

2 50. Throat does not move at all.

2 53. Reflex action follows, on immersing the toes in a 1 per cent. solution of H_2SO_4, in 5 seconds. On being plunged into water it has great difficulty in keeping its head above the surface.

3 3. Reflex action occurred instantaneously on touching the frog's skin with strong acetic acid.

3 33. Abdominal muscles curiously pinched in; sits upright; moves eyelids, but not vigorously, on the cornea being touched; a solution of H_2SO_4 distinctly acid

to taste produces reflex movements, on dipping the frog's toes into it, in from 4 to 5 seconds. A healthy frog, treated in the same manner, contracted its legs after its toes had been immersed in the acid for 2 seconds.

h. m.

4 15. The same acid solution induces reflex movements in 10 secends.

4 25. Decapitated, and irritated the end of the exposed cord; movements resulted in the leg-muscles as soon as the secondary coil stood at 8.

4 30. A healthy frog had been decapitated and allowed to recover from the shock of the operation; its cord was now irritated in the same way; movements resulted when the secondary coil stood at 11.

4 30. On again testing the reflex irritability of the poisoned frog in the manner above indicated and with the same solution of acid, no indications were obtained, even after the feet had been immersed for 100 seconds.

This experiment indicates a general impairment of the power of reflex action, while the function of the cord as a conductor of stimuli remained intact to all intents, the apparent difference in the degree of irritability of the cord in the normal and in the poisoned frog being most probably due to the deficient aëration in the latter case, a circumstance only indirectly attributable to the poison.

Exp. LXXII.—May 27, 1874.

Frog.—Weight 23 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected subcutaneously.

h. m.

2 40. Injection complete.

2 55. Respiration seems almost to have ceased; the frog lies quite flat on its belly as if weak. Reflex action, after immersing the toes in a ·1 per cent. solution of H_2SO_4, in 25 seconds.

On being put into a large beaker of water, the frog sank immediately and did not attempt to swim. It can jump quite well, however.

3 0. Reflex actions induced by strong acetic acid after 5 seconds.

3 5. Lies quiet: moves of its own will.

3 7. On touching the cornea the eyelid did not move until after some time. Sluggish movements result on pinching the leg, also on gently rubbing the thigh with the point of a lead pencil.

3 20. On touching the cornea with the points of the electrode of a secondary coil through which strong interrupted currents were passing, distinct movements of the eyelids were observed.

3 30. On lifting up the bell-jar under which the animal had been lying, the frog moved spontaneously. Pinching induces sluggish reflex actions.

A solution of H_2SO_4 (distinctly acid to taste) caused contractions of a reflex character in 5 seconds.

h. m.
3 36. Reflex activity tested as above; movements occurred after immersion for 10 seconds.
3 42. Reflex actions occurred after an immersion of 20 seconds.
3 47. On exposing the cord high up in the back and irritating, distinct movements occurred when the secondary coil was at 17.

In this experiment reflex action was distinctly impaired; but it may be remarked that voluntary movements occurred long after that impairment had distinctly begun; *i. e.* long after reflex irritability had begun to disappear, the cord was capable of *conducting* impressions from the brain.

The remaining experiments on the functions of the cord were tabulated in order to show clearly the diminution in reflex irritability. In all cases the frogs had their cords cut at the atlanto-occipital articulation, and the parts above the points of section destroyed, in order to get rid of their influence. In testing reflex irritability dilute H_2SO_4 was used as a stimulus, the frog being suspended by the head in such a manner as to allow the toes (or feet) to dip below the surface of the acid; the seconds were counted which intervened between immersion and the occurrence of contraction, and taken to indicate the degree of irritability. The frogs in experiments LXXIII., LXXIV., and LXXVI. were poisoned by the injection of sodium vanadate in solution under the skin; the frog in experiment LXXVII. was similarly injected with pure water, and its reflex irritability used as a standard. Experiment LXXIII. is given in detail to illustrate the method; but its results were exactly confirmed by the succeeding experiments, as will be gathered from the brief notes attached to the latter.

Exp. LXXIII.—June 2, 1874.

Frog.—Weight 34 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected under the skin.

h. m.
June 1. 7 30 P.M. Cord of frog divided and brain destroyed.

June 2:—

Time.	Remarks.	Strength of acid per cent.	Number of seconds between immersion and contraction.	Mean number of seconds.
h. m.				
11 45 A.M.	Normal reflex actions	2	2	
11 50	„ „ „	1	1	
	„ „ „	1	1	
11 52	„ „ „	1	1	
11 55	„ „ „	·5	3	
	„ „ „	·5	2	1·2
12 10	Injection complete.			
12 10	Tips of toes immersed	·5	8	
			4	
			4	
			6	
12 15	„ „ „	·5	4	
			10	6

TABLE (*continued*).

Time.	Remarks.	Strength of acid per cent.	Number of seconds between immersion and contraction.	Mean number of seconds.
h. m.				
12 20 A.M.	Tips of toes immersed	·5	3	
			5	
			3	
			4	
			5	4
12 25	„ „ „	·5	5	
			6	
			5	
			4	
			4	
			5	5
12 35	„ „ „	·5	10	
			7	
			5	
			9	
			5	
			6	
			7	
			7	7
12 49	Only slight movement occurred	·5	11	
to	Marked contraction.		10	
12 52			13	
			11	
			10	
			15	
			11	11·5
12 57	No movement at all	·5	100	
	„ „ „	....	100	
1 2	„ „ „	1	60	
1 5	The acid was allowed to cover more of the feet; contraction occurred	1	5	
			4	
			6	
			6	
	Slight movement	....	17	
	No movement at all	....	60	
1 10	Heart exposed and found to be beating, though languidly.			
1 15	After immersing the whole foot in acid, twitches were observed	1	7	
	Again twitches of calf-muscles occurred	1	50	
	No movement at all	1	150	
	Cord exposed in middle of back, and excited; contractions with secondary coil at 15.			
	Decapitated; irritated exposed end of cord; contraction with secondary coil at 10 to 12.			

Exp. LXXIV.—June 2, 1874.

Frog.—Weight 27 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected subcutaneously.

h. m.

June 1. 7 30 P.M. Cord cut and brain destroyed.

June 2. 4 7 P.M. Injection complete and experiment commenced.

In rather more than an hour reflex activity had ceased.

Exp. LXXVI.—June 3, 1875.

Frog.—Weight 35 grms.

Dose ·5 cub. centim. of the 5 per cent. solution (25 milligrammes V_2O_5), injected under skin.

h. m.

12 30. Cord divided and brain destroyed.

3 40. Injection complete.

In rather more than an hour reflex activity had ceased.

Exp. LXXVII.—June 3, 1874.

Note.—This experiment was made to serve as a standard for the preceding.

Frog.—Weight 25 grms.

Dose ·5 cub. centim. pure water injected subcutaneously.

h. m.

12 30. Cord divided and brain destroyed.

3 35. Experiment commenced.

Reflex activity diminished very slowly.

7 0. Fair reflex movements on pinching or irritating the skin with acid.

Left for the night in a moist chamber. The next day all reflex power seemed to be absent.

It may be noticed that in these experiments, as the parts above the atlanto-occipital articulation were destroyed, the cord alone is concerned in the reflex acts, inhibition of reflex power by the optic lobe (SETCHENOW) being no longer possible.

The Tables based on these experiments, and figured on Plate 45. figs. 1 & 2, show at once the action of vanadium upon the reflex function as compared with the effects of gradual death in a frog under conditions exactly similar, except that it was not poisoned.

With regard to the *conducting* power of the cord for electrical stimuli, these experiments confirm preceding ones in indicating that vanadium does not affect it at all.

The following experiments were undertaken in order to examine more minutely the effects of vanadium upon the contractility of muscle.

Exp. LXXVIII.—June 1875.

Three frogs were taken, two of which were poisoned by the subcutaneous injection of about 1 cub. centim. of a 5 per cent. solution of vanadate of soda (=50 milligrammes V_2O_5).

When paralysis had completely occurred in one frog, it and the non-poisoned frog were decapitated, and the gastrocnemii of each arranged in a PFLÜGER'S myographion, for recording the length of contraction under different loads. The muscles were directly

stimulated with single induction-shocks from a DU BOIS-REYMOND'S machine, the opening shock being used. The battery consisted of a single DANIELL'S element. The maximum stimulus was ascertained in the usual manner, and employed to produce contractions.

The second frog was allowed to remain until five hours had elapsed from the time of injection, and more than three from the occurrence of complete motor paralysis.

The curves obtained by taking the weights of the load as abscissæ and the length of contraction as ordinates were found to be sensibly the same in the case of poisoned and non-poisoned muscles, as is shown in fig. 4, Plate 46.

The experiment was repeated with similar results.

Exp. LXXIX.—June 1875.

In this experiment preparations were made for recording upon a revolving surface the contraction of muscles when directly stimulated.

The arrangements for stimulation resembled exactly those in the preceding experiment.

Three frogs were again taken, and two poisoned by the subcutaneous injection of 1 cub. centim. of a 5 per cent. solution of sodium vanadate (=50 milligrammes V_2O_5). They were allowed to remain until four hours after injection and two hours after complete motor paralysis. They were then arranged in a myograph and weighted with 10 grammes.

Both opening and closing of the primary current were made use of.

The normal frog was decapitated, and allowed to remain for two hours before being tested. The curve of its contraction was then obtained in the above-mentioned manner. Rotation of the revolving surface was checked and time recorded by means of the vibration of a tuning-fork vibrating 100 times per second.

The curves obtained in the cases of poisoned and of non-poisoned muscles were sensibly the same, as is shown in fig. 3, Plate 45.

The experiment was repeated with similar results.

The preceding two experiments are considered to show that vanadium in the form of sodium vanadate does not affect muscular tissue when introduced into the circulation of living animals.

It has been shown in a previous part of this research that the disturbance of circulation and respiration which follow poisoning by vanadium are mainly due to an action of the poison upon their respective centres in the cord. It seems, therefore, of interest to give here, among the experiments relating to the nervous system, some which show the simultaneous action of the poison upon circulation and respiration.

Exp. LXXX.—May 13, 1874.

Rabbit (buck).—Weight 1958 grms.

Dose 5 cub. centims. of the 5 per cent. solution (250 milligrammes V_2O_5), injected under the skin.

Note.—The half of this experiment which refers to the circulation has already been given on p. 524 (Exp. XLV.) with full explanatory remarks; similarly the half referring to the respiration is found on p. 537 (Exp. LVI.).

From the data furnished by those experiments a Table (fig. 5, Plate 46) has been constructed illustrating the simultaneous effects of the poison upon the vasomotor and respiratory centres. The chief points of interest are:—(1) that the line of mean blood-pressure sinks from beginning to end, while the line indicating the rapidity of respiration first of all rises and afterwards sinks; and (2) the numerous irregularities, especially near the termination, indicating the successive revivals of functional activity on the part of those centres.

Exp. LXXXI.—June 15, 1874.

Rabbit.—Weight 2430 grms.

Dose 1 cub. centim. of the 5 per cent. solution (50 milligrammes V_2O_5), injected into right external jugular vein.

Note.—The half of this experiment which refers to the circulation has already been given on p. 527 (Exp. XLVII.) with full explanatory remarks; similarly the half referring to respiration is found on p. 538 (Exp. LVIII.).

The results of this experiment are tabulated in the manner adopted in the last experiment (fig. 6, Plate 46). The remarks there made apply to this Table also, except that the initial increase in rapidity of respiration is in this case more marked; and when once the rapidity has commenced to diminish it does not, as in the preceding experiment, ever increase again. This may, however, have been due to an error in the method of observation (see note to fig. 6, Plate 46).

Résumé of the Action of Vanadium upon the Muscular and Nervous Systems.

In the account of the general action of vanadium upon the animal economy it was noticed that in nearly all animals, when the dose was large, one of the most important symptoms of poisoning was the occurrence of convulsions and paralysis of motion.

The experiments which have just been detailed furnish the explanation of those phenomena.

Frogs were the animals chiefly used. As, however, paralysis was the only form which

the nervous symptoms of poisoning took in them, the conclusions drawn apply primarily to those symptoms.

Paralysis of voluntary motion may result from disorder of one or more of four sets of organs. It may be caused by some affection of the motorial end-plates of nerves in muscles, as in the case of poisoning by curare; it may result from some interruption in the conducting apparatus by which impulse to contraction is conveyed from the centre to the muscle, as in the case of lesions of the cord or trunks of nerves due to mechanical or other causes; it may be attributable to some alteration in the central nerve-cell from which the impulse to contraction (proximately) originates; or it may be due to loss of irritability of muscular tissue, as in the case of poisoning by sulphocyanides. In paralysis of reflex motion (which occurs in frogs, but not in other animals) the motor apparatus itself is not necessarily implicated, as such paralysis may be due to an affection of any one of the analogous parts of the afferent system, viz. peripheral organ (of sense), centripetal nerve-fibre, or central cell in which the impulse conveyed from the periphery is reflected. When, however, paralysis of reflex action is accompanied by paralysis of voluntary motion (as in the case of frogs poisoned by vanadium), it is clear that, whether the afferent apparatus be affected or not, there is some disorder of the other series of organs to which reference was made.

In order to obtain the necessary data, comparative experiments of the following nature were carried on:—The femoral artery of one limb of a frog was ligatured, in order to prevent the passage of the vanadium solution, which was injected hypodermically, to the tissues of the leg. Under these circumstances, in which the nerve-trunks and motorial and sensory end-organs were kept from the influence of the poison, it was found that as the poison began to take effect no difference in behaviour between the two legs could be detected. Up to the same moment the same stimulation applied to the skin produced the same amount of motion, and at the same time paralysis of motion occurred in both limbs and all over the body. When paralysis was complete, and the nerves above and below the point of ligature were tested, the same degree of stimulation (practically) was needed to excite the muscles of each leg to contraction, and on comparison with normal frogs it was seen to be just so much as was required to excite the muscles in their case. In the same way no difference was discernible in the behaviour of the muscles of the two legs and of healthy frogs. In all cases similar degrees of stimulation produced the same amount of contraction. Paralysis was therefore not due to any alteration, in the case of reflex activity, of conducting fibres or peripheral organs of either afferent or efferent systems; or, in the case of voluntary motion, of conducting fibres, motorial end-organs, or muscular tissue.

In other comparative experiments two frogs were taken of about the same weight, and one of them was poisoned by injecting vanadium solution underneath the skin of the back. As soon as paralysis of motion was effected both frogs were decapitated, and the cords of each stimulated. The slight differences which were sometimes observed in the degree of stimulus needed to induce contraction were only such as might be attri-

butable to the defect of aëration in the poisoned frog due to the early cessation of respiration. Paralysis was therefore not due to any defect of conducting-power in the cord.

The preceding results were verified, as far as was possible, in the case of young mammals.

The cause of paralysis, therefore, presumably affects the initial cells concerned in the origination or transmission of nervous impressions.

The experiments on the reflex activity of frogs, both with and without the presence of brain (and SETCHENOW's inhibitory centres in the optic lobes), show a diminution of irritability, which must be attributed to centric disturbance, since afferent and efferent nerves are unaffected.

It is only necessary to allude here to the action of vanadium upon the special centres of the cord. It acts upon the vasomotor centre in such a manner as, in course of time, to release the arterial tonus, and it first excites, and afterwards depresses, the respiratory centre, as is shown in figs. 5 & 6, Plate 46. It may be noticed that the effects of poisoning by vanadium do not increase with regularity. In the case of the reflex, as of the circulatory and respiratory centres, there occur brief, but very well-marked, periods during which functional activity is almost fully resumed before finally succumbing to the poison. This is well shown in figs. 1, 2, 5, & 6, Plates 45 & 46.

With regard to sensibility, no indications were noticed of any defect, either in the experiments on the general effects of poisoning or in the comparative experiments mentioned above.

No cerebral symptoms were seen, except the sluggishness which occurred in all cases of poisoning; and in other respects the animals experimented upon (except frogs, in which the occurrence of general paralysis rendered it impossible to judge) remained apparently conscious until death.

Special experiments were undertaken to discover whether vanadium (an intense irritant poison) was not also a muscle-poison. No indications of its being a muscle-poison could be detected. (See figs. 3 & 4, Plates 45 & 46.)

IV. CONCLUSION.

From the experiments and observations described in this paper it results:—

1. That vanadium is a metal possessed of intense poisonous activity.
2. That it manifests this poisonous activity when a soluble salt (a vanadate) is introduced into the system by the stomach, by subcutaneous injection, or by direct injection into veins.
3. That it interferes with the vital functions of simple organisms.
4. That it destroys the irritability of muscular and nervous tissues when directly applied to them, even in very dilute solutions.
5. That when introduced into the system by the stomach, or subcutaneously, it produces congestive and inflammatory changes in the alimentary mucous membranes.
6. That it exerts no direct action on the blood.

7. That when introduced into the system subcutaneously, it does not affect the irritability of muscle and nerve.
8. That it depresses the temperature of animals poisoned by it.
9. That it slows and finally weakens the action of the heart by acting upon its intrinsic nervous mechanism.
10. That it lowers the blood-pressure by acting
    (*a*) Upon the vasomotor centre.
    (*b*) Upon the heart.
11. That it first quickens, then slows, and ultimately arrests the movements of respiration by acting on the respiratory centre.
12. That it causes convulsions and partial paralysis in higher animals, and in frogs complete paralysis of voluntary and reflex activity, which is of spinal origin.

In conclusion, the author begs cordially to thank Professor ARTHUR GAMGEE for the kindness he has manifested towards him while engaged in this research, and Professor ROSCOE, for his liberality in supplying and supervising the preparation of the necessary reagents.

EXPLANATION OF PLATES 45 & 46.

Figs. 1 & 2 are Tables founded upon Experiments LXXIII.–LXXVII., the results of which they present in a comparable form.

The continuous lines in both figures are curves built upon data obtained from frogs poisoned by subcutaneous injection of vanadate of sodium, while the dotted lines are curves similarly obtained from frogs injected under the skin with distilled water. The method of experiment and the nature of the data are stated on pp. 548–550. (Details of Experiment LXXV. were omitted from the text as unnecessary to the comparison at that stage. The curve of the experiment is, however, retained here for the sake of exactness; for the experiments of fig. 1 were all under conditions which differed slightly from the conditions in the experiments of fig. 2, as may be gathered from the text.)

In the Tables the time is divided into fractions (minutes), which form abscissæ, while the ordinates represent the degrees of irritability. The latter are calculated from the number of seconds intervening between immersion into the acid and contraction. The number 15 was taken arbitrarily as an index of perfect reflex power, indicating instantaneous response to stimulation by the acid. As the number of seconds between immersion and contraction was found by looking at the second-hand of a watch, without any automatic register, all contractions occurring within 1 second of immersion are accounted "instantaneous." Decline of reflex power was manifested by the successively increasing number of seconds intervening between stimulation and response.

The descent of the dotted curve in fig. 2, after the 140th minute, is supposititious, not ascertained, as reflex power departed during the night (see Exp. LXXVII. p. 550); but the descent is probably overestimated, *i. e.* reflex activity declined less rapidly than the diagram indicates.

Fig. 3. Curves of muscular contraction in the cases of a normal frog (b, b') and of two frogs poisoned by subcutaneous injection of vanadate of sodium (a, a' and c, c'), to illustrate Exp. LXXIX., where the method of obtaining them is described.

a, a', with muscles of poisoned frog 4 hours after poisoning. Maximum stimulus was employed (secondary coil close up to primary).

	Making.	Breaking.
Time of whole contraction	·11 second.	·11 second.
Time of latent period	·015 „	·0075 „
Time of maximum contraction	·0725 „	·07 „

b, b', with muscles of normal frog 2 hours after decapitation. Maximum stimulus was employed (secondary coil close up to primary).

	Making.	Breaking.
Time of whole contraction	·105 second.	·105 second.
Time of latent period	·0075 „	·005 „
Time of maximum contraction	·0625 „	·065 „

c, c', with muscles of poisoned frog 4 hours after poisoning. Maximum stimulus was employed (secondary coil close up to primary).

	Making.	Breaking.
Time of whole contraction	·115 second.	·1125 second.
Time of latent period	·0125 „	·01 „
Time of maximum contraction	·08 „	·065 „

Fig. 4. Curves of muscular work in the cases of a normal frog (b) and of two frogs poisoned by subcutaneous injection of vanadate of sodium (a and c), to illustrate Exp. LXXVIII., where the method of obtaining them is described.

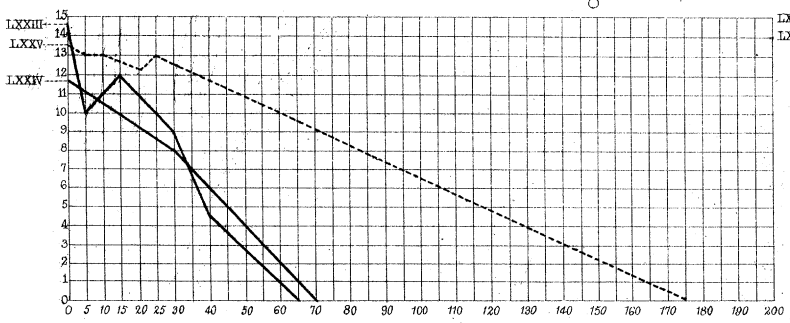
a, with muscle of poisoned frog $1\frac{1}{2}$ hour after poisoning, when paralysis of motion was fully developed. Maximum stimulus was employed (secondary coil 5 centims. from primary).

b, with muscle of normal frog soon after decapitation. Maximum stimulus was employed (secondary coil 5·5 centims. from primary).

c, with muscle of poisoned frog 5 hours after injection of poison, and 3 hours after paralysis of motion was fully developed. Maximum stimulus was employed (secondary coil close up to primary).

Fig. 5. To illustrate Exp. LXXX. The continuous line represents the variation in blood-pressure, the *outside* vertical column of figures at each end of the Table indicating the blood-pressure in millims. of mercury, while the times are given by the row of figures (=minutes) along the bottom of the Table. The dotted line traces the variation in *rapidity* of respiration, the *inside* vertical column of figures at the left end of the Table giving the number of respirations in 10 seconds, while the times, as before, are given by the figures at the foot.

Fig. 6. To illustrate Exp. LXXXI. The explanation of the preceding figure applies to this also.—*Note.* The rise of blood-pressure indicated by the (*) was accompanied by struggles; at the same moment the rabbit's trachea happened to be disconnected from the apparatus for registering respiration (see p. 535); hence it is impossible to say whether or not an increase in rapidity of breathing occurred which should have been recorded at (×).



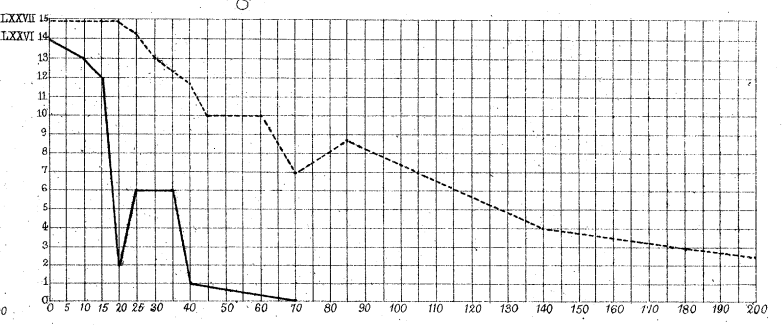
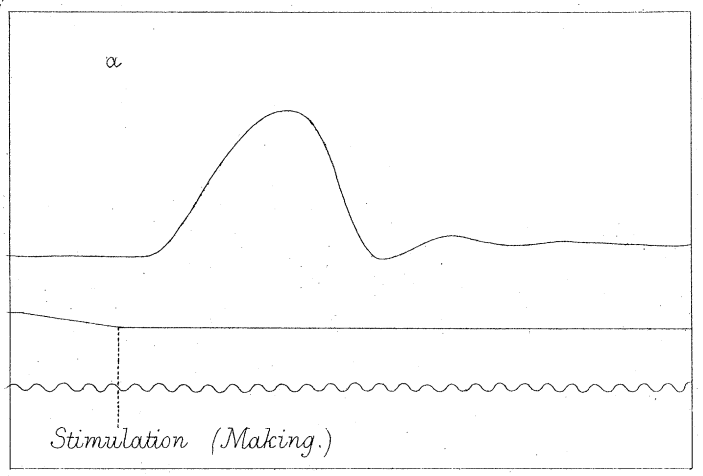
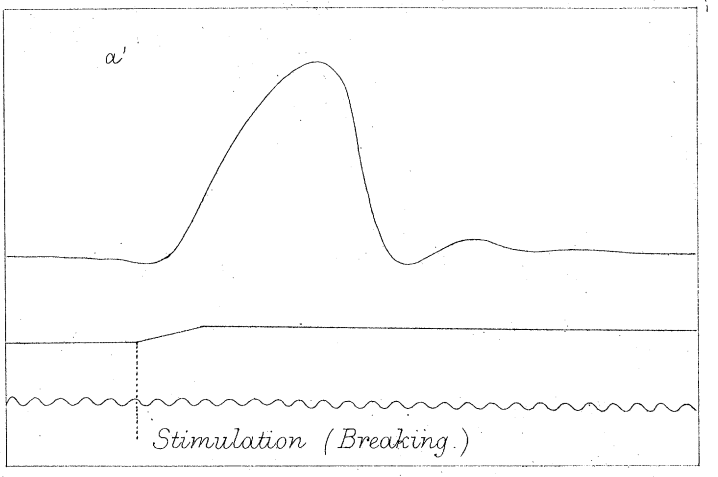
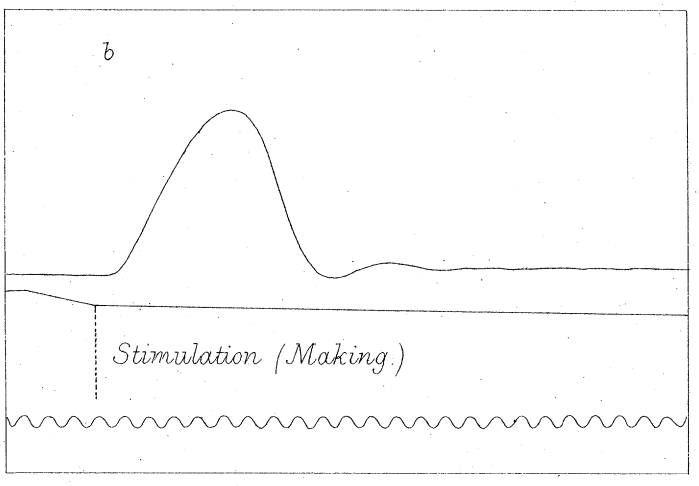
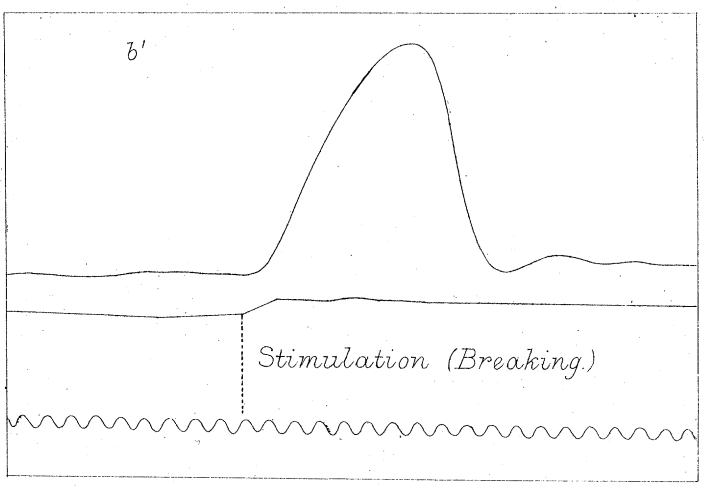


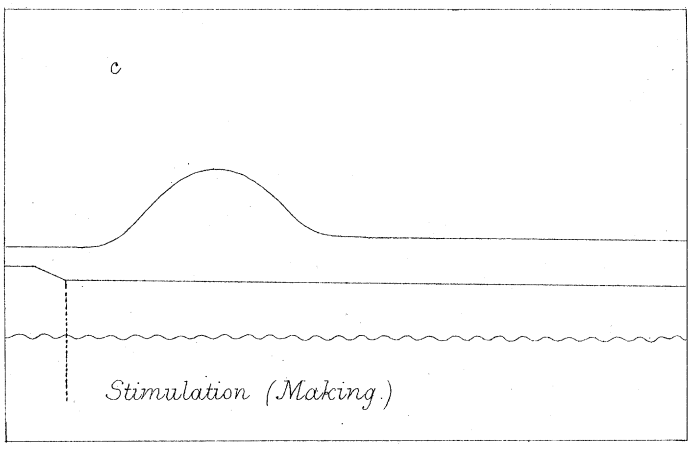
Fig. 3.











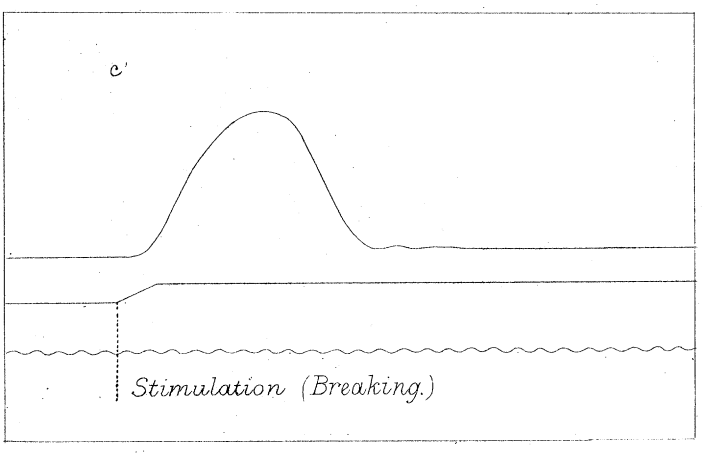


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Fig. 4.

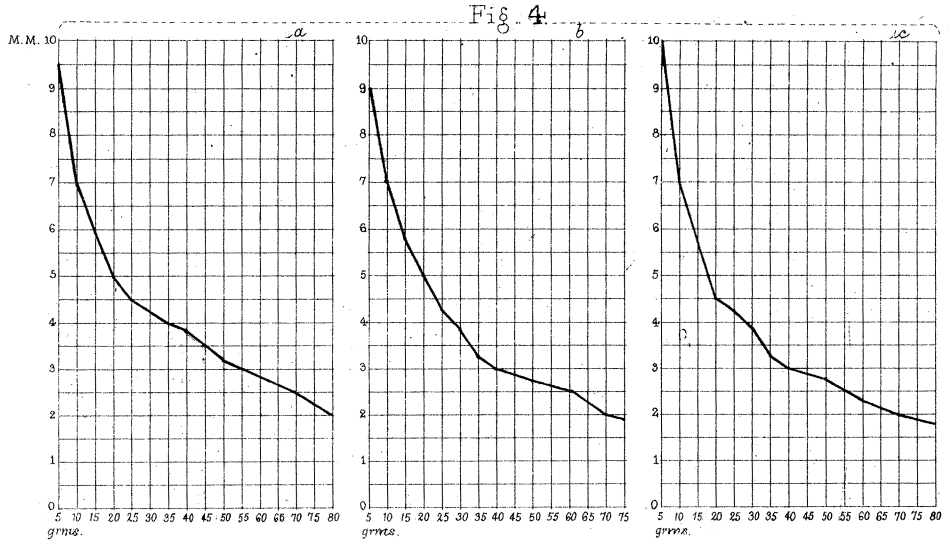


Fig. 5.

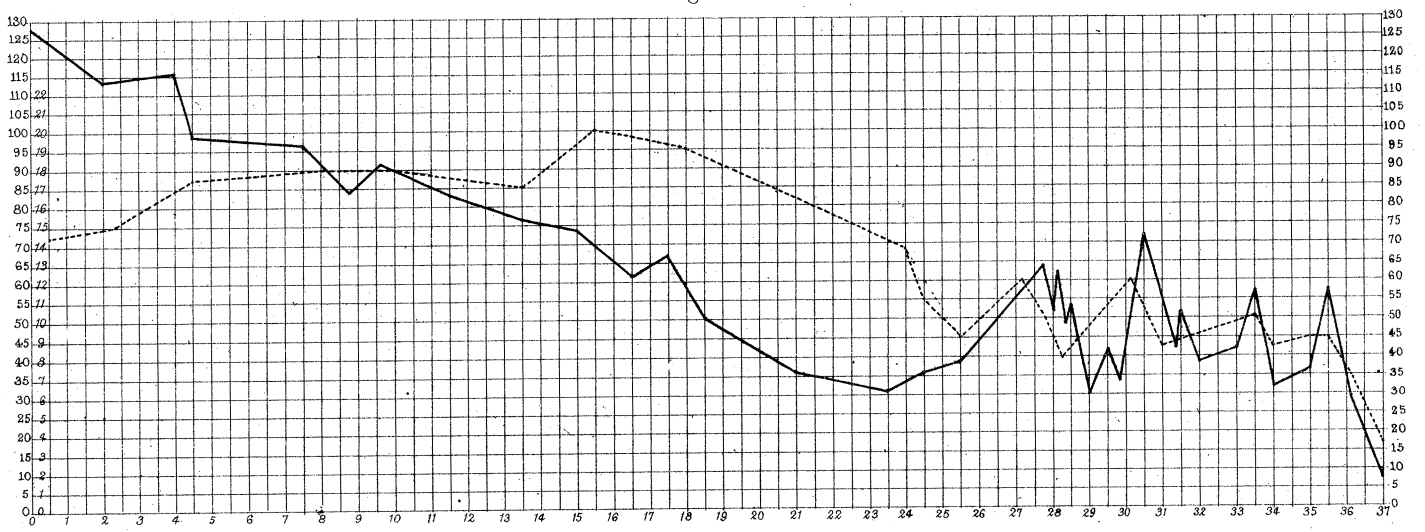
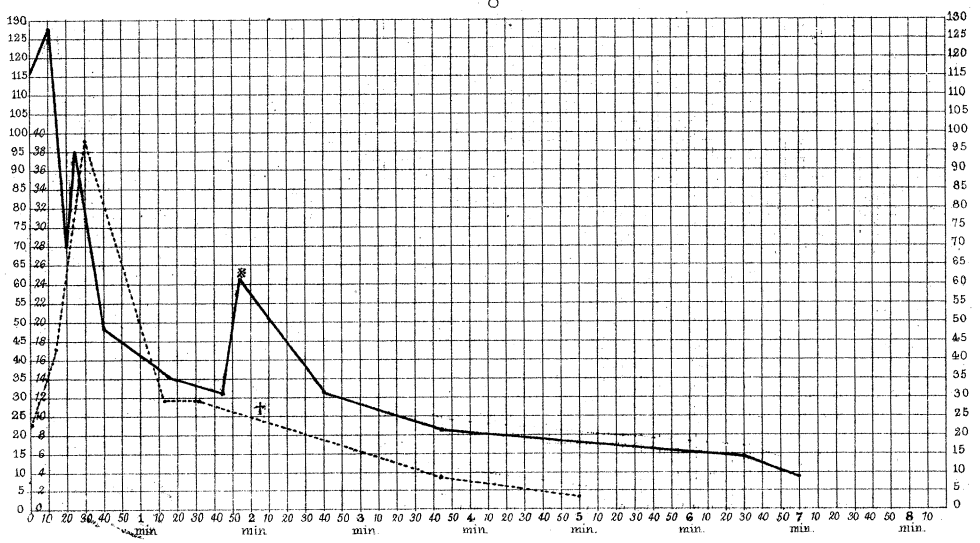


Fig. 6.



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