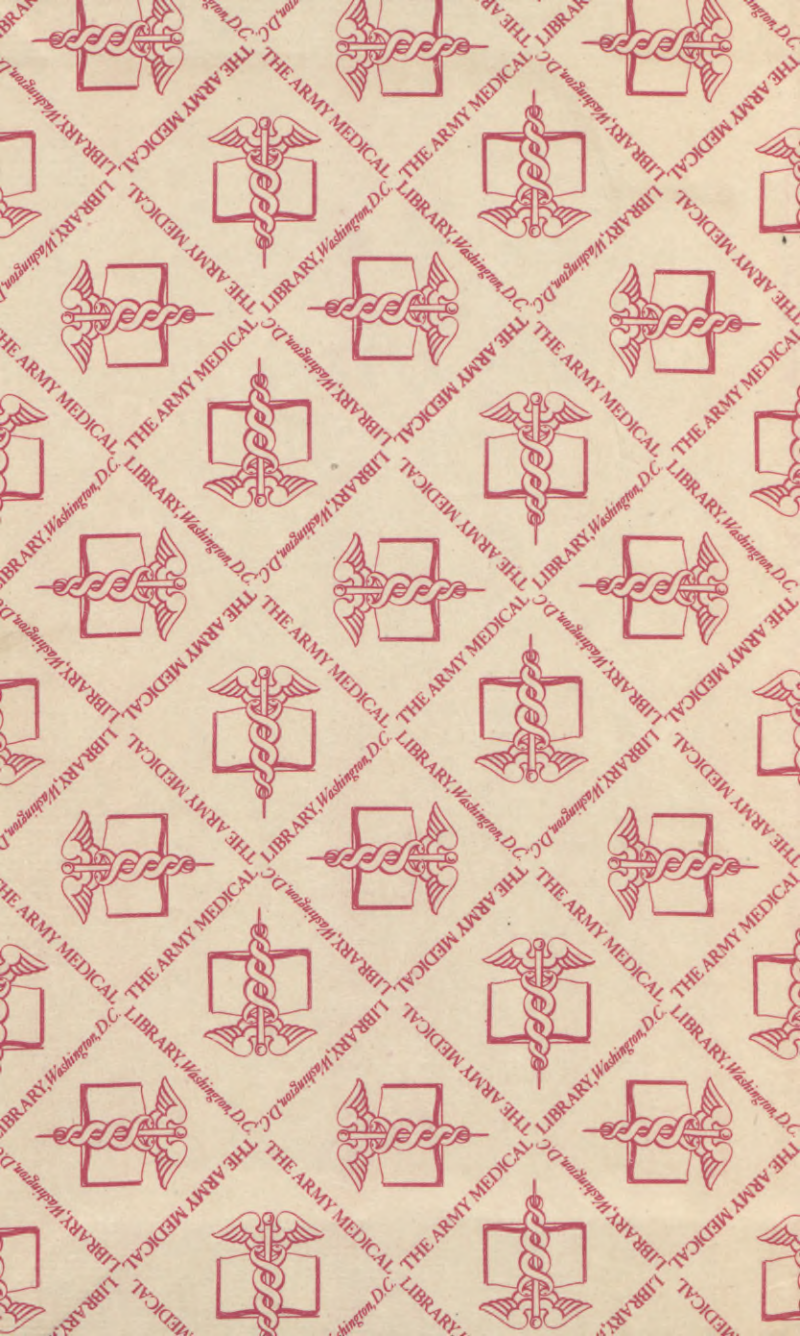
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A CONTRIBUTION TO THE

# PHYSIOLOGICAL STUDY

OF

# VERATRUM VIRIDE AND VERATRIA,

*(With Experiments on Lower Animals, Made at La Grange St. Laboratory, 1869).*

BY

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# PREFACE.

The experiments which will be related in the following paper were performed with the assistance of Messrs. Wood, Boutelle, Bridge, Spooner, Putnam, Pierce, Brigham and Cutler. Many points of interest still remain uninvestigated; but, as it may be several months before experiments with this drug can be resumed, and as we think the results thus far obtained are in one or two respects an advance on what has been hitherto recorded, at least in the English language, we venture to present them in this, comparatively, incomplete state. We wish to call attention to the fact, that the historical investigations on this subject were not commenced, until after our experiments had been performed.

# VERATRUM VIRIDE AND VERATRIA.

Veratrum *viride* was not brought into notice until a little more than two years ago. Several practitioners had used and found this drug to be of great value; but its advantage was not generally known until Drs. Cutter, Rickard and Ingalls, in behalf of the Middlesex District Medical Society, called the attention of physicians to its use, and prepared an account of their experience with it, which was published in the *American Journal of Medical Sciences.*

Dr. Cutter's monograph attracted attention in Europe, and the drug was experimented upon there.

*Veratria.*—Previously the alkaloid *veratria* had been studied, but this was obtained from the seeds of veratrum sabadilla,

and seems in some respects only to imperfectly represent the virtues of veratrum viride.

Magendie experimented with an impure veratria in 1820. In 1829 Bardsley published an article on the Therapeutical Value of Veratria. In 1844 Dr. Gebhard compared the action of veratria and strychnia. These are a few of the authors referred to by Van Praag.* A pricking or tingling, especially of the hands and feet, compared by some to the sensation produced by electricity, is mentioned by many; also, a sense of warmth followed by a feeling of coolness.

Van Praag noticed in several cases that the animals upon which he experimented had a peculiar spasm, which he likens to St. Vitus's dance, a stiffness of the limbs which ended in a dancing movement. He states that the cardiac pulsations were first

* Veratrin Toxikologisch-pharmakodynamische Studien von J. Leonides Van Praag, in Virchow's Archiv. 7, Band, 1854, s. 252.

increased and then diminished, irregular and then weak. The respiration was affected only when large doses were taken, when it was embarrassed or ceased entirely. He noticed, also, the weakness of the muscular power, but in his summary this seems not to have attracted his attention so much as the spasms. In some cases the pupils were dilated; there was evidence, also, of pain in the mouth or throat. Nausea and vomitings occurred constantly. No inflammation was seen in the *primæ viæ*. He performed experiments, also, on birds, frogs and fishes. His conclusions are :—

"The respiration and circulation diminish in intensity. The muscles lose their tension. The irritability of many nerves (especially the peripheric cutaneous nerves) is considerably lowered. After very small doses vomiting follows; often, also, diarrhœa, but this more frequently after large doses. The secretion of urine is not notably excited. Salivation is considerably increased. * * * The stage of stimulation

[*erregungsstadium*] is shown by accelerated respiration, increased frequency of the pulse, cramp-like tension of the muscles, increased irritability of the nerves. Death from veratria poisoning seems to proceed from paralysis of the spinal cord."

He states, also, that veratria acted in a similar manner upon man. In no case did he find any signs of inflammation, and the results of *post-mortem* examination were entirely negative.

*Veratrum viride.*—Much has been written in regard to the use of veratrum viride in different diseases; and, so far as the record of cases gives an insight into the physiological action, this agrees with our experiments. The therapeutical and pharmaceutical character and uses of this drug are not, however, the subject of our investigation, and will be entirely disregarded.

Drs. Cutter and others investigated its action.* They remark that the benefit de-

* American Journal of the Med. Sciences, Oct., 1858.

rived from its use is due to its sedative power over the circulation and the nervous system. The reduction of the pulse is mentioned in almost every case (40 to 60 beats per minute in the course of twelve to eighteen hours), as well as the general depression from prolonged sedation. Generally there was no nausea after its use, though this symptom is mentioned by other writers. Most of the facts mentioned in this paper are, however, therapeutical, and are not included in the plan of our investigation.

Another paper* by the same authors gives one or two cases worth referring to. In the first case detailed below, the effect of the drug upon the respiration is noticed. The case was reported by Dr. Minot, of Boston.

Case.—A young man, 18 years of age, with acute pericarditis, having an irregular pulse (96–116), took of Thayer's fl. ext. of

* American Jour. of Med. Science, Oct., 1861, p. 400.

of veratrum viride gtt. iv. The respirations numbered 30 per min. He became more comfortable during the day. The pulse in the evening was 96. This was October 12th.

| *Date.* | *Pulse.* | *Resp.* | *Remarks.* |
|---|---|---|---|
| Oct. 13 | 87 | 36 | Had taken seven doses; stopped on acount of vomiting. |
| " 14 | 112 | 36 | Resumed the medicine. |
| " 15 | 112 | 30 | Six doses taken; dose increased to gtt. v. |
| " 16 | 114 | 40 | Took three doses. |
| " 17 | 112 | 24 | (Pleurisy.) gtt. v. ev. 4 hrs. |
| " 18 | 96 | 22 | Five doses; vomit. after last. |
| " 19 | 96 | 24 | Four " nausea. |
| " 20 | 100 | 30 | Three " " |
| " 21 | 96 | 28 | Four " " |
| " 22 | 96 | | Five " " |
| 23–25 | 100 | | |

The medicine was omitted for a time, and then renewed, but neither pulse nor respiration were noticed particularly.

Another case* is reported by Dr. Forsaith, in which the pulse was reduced from 120 to 40, and the respiration was only 15, an over dose having been accidentally taken.

In another case,† reported by Dr. C. S.

* Am. Jour. of the Med. Sciences, Oct., 1861, p. 403.
† Idem, p. 406.

Bishop, of Philadelphia, a medical student who had been injured by fireworks; the pulse, at first 100, was kept at 60 for thirty-six hours, and "*from the time that the sedative influence of the veratrum viride became manifest he felt no pain.*"*

In the *Edinburgh Medical Journal*†, Dr. J. Watson gives the results of experiments on himself and on several patients, from which we can derive some knowledge of the action of this drug. He took gtt. viij. of a tincture (made according to Dr. Cutter's direction) at 3 o'clock, P.M. Two hours after, his pulse was unaffected. At 5 o'clock he took another dose, and then had tea. At 6 o'clock his pulse was the same as at 3 o'clock. Towards 7 o'clock he was troubled with flatulence. Some minutes before 7 he began to feel nauseated and would have vomited, but restrained himself. The force and frequency of the pulse became diminished There was griping of

* Italics in the original.

† January, 1864.

the bowels, sickness and weakness, with considerable pain in epigastric region; he had a heavy, dull headache, with, occasionally, painful throbbing in the temples. His pulse, 70 at 3 o'clock, was reduced to 64. The pain in the bowels continued, and he felt himself growing weaker; but as he wished to experience the full effects, at 7 o'clock he took another dose of eight drops. From 7¼ he felt about as described above. Soon he became weaker and felt that he must vomit. The pain in his stomach and bowels became much more severe; a clammy cold sweat broke out on his brow, and at 7½ he vomited with much pain. While vomiting he required all his strength to support himself; his back became extremely weak; and, when a fit of retching came on, he felt as if he was going to be asphyxiated; he had one or two cold shivers; his feet and hands became cold and benumbed, though there was a large fire in the grate; the cold, numb feeling crept up the legs and arms, and, at last, his whole

body felt as if enveloped in cold, damp cloths, and he became quite prostrate.

At a little after 8 o'clock his pulse was 40 and very weak. The flatulence continued, till a quarter past eight, when he again vomited slightly. The cold, clammy sweat continued, and the whole surface of the body was numb. At 8¾ his pulse was 56. After vomiting his face was quite pale, but there was no dilatation of the pupil. He felt prostrated during the evening, but the next day was quite well.

This is one of the most valuable experiments recorded, and, so far as it goes, agrees with what has been found in animals.

Dr. Watson administered the tincture in three cases. In one the patient was suffering from phthisis with a pulse of 120. At quarter to 9 o'clock, gtt. viij. of the tincture were given, which dose was repeated in one half an hour, as no effect had been produced upon the pulse. In half an hour more the pulse was still the same, but in a

few minutes she was found retching violently and vomiting. Her pain was intense and her prostration excessive. She continued vomiting at short intervals till within a few minutes of 11 o'clock. A cold, clammy sweat broke out over her whole body, but especially upon the face. At 10½ the vomiting was diminishing in severity (brandy had been given), but the prostration became more marked. Just before the vomiting commenced her pulse was at 120, but at 10½ it had sunk below 60, and was very weak. At a quarter before eleven it was 60, and at 11 o'clock it was 80 after taking wine and morphia. She was very much frightened on account of a *dead* feeling she experienced, especially in her limbs, and to a certain extent over her whole body. The following table shows the rapidity of her pulse:

| | | | | | |
|---|---|---|---|---|---|
| 9.45, | P.M., | 120 | 12, | midnight, | 76 |
| 10.30 | " | below 60 | 12.15, | A.M., | 72 |
| 10.45 | " | 60 | 12.30 | " | 72 |
| 11 | " | 80 | 12.45 | " | 80 |
| 11.15 | " | 72 | 1 | " | 80 |
| 11.30 | " | 72 | 9 | " | 120 |
| 11.45 | " | 80 | | | |

In this case, the symptoms were essentially the same as in the previous experiment.

In the second case the tincture was given to a young man, aged 16 years, who had undergone amputation of the thigh on account of a tumor.

At 7 o'clock, 4 minims were given.
At 7.15, he had nausea.
At 7.30, he vomited.

His pulse was as follows:—

At 7, P.M., 152.
7.15 " 152.
7.30 " 136.
7.45 " 136.
8 to 9 " 132.
9 " 4 minims more were taken.
9.15 " 132; nausea increased.
9.30 " 124.
9.45 " 124; vomiting, with great weakness.
10 " 124; vomiting.
The next day, 11, A.M., 150.
The following day, 10, A.M., 132. Tincture again taken in the dose of 4 minims.
10.15, A.M., 132; feels sick.
10.30 " 124.
11.15 " 124.
11.30, A.M., 120.
11.45 " 126; 4 minims more.
12 " 124; great nausea and occasional vomiting.
12.30, P.M., 124.
1 " 128.
3 " 132.
The next morning, 160.

In the third case, the tincture was given to a man, aged 52, who had a fracture of

the thigh-bone. Six weeks after the accident his pulse was high, but the general health of the patient was good.

At 7.15, P.M., pulse 100; gave 4 minims.
7.30 " 100.
8 " 100; gave 4 minims.
8.15 " 96; flatulence and nausea.
8.30 " 92.
8.45 " 88.
9 " 100; patient retching.
9.15 " 94; vomiting over, though great nausea.
9.30 " 88.
9.45 " 36; great nausea.
10 " 86.
11, A.M., 92.

On the second day the medicine was again tried.

At 10, A.M., pulse 100; gave 4 minims.
10.30 " " 100.
11 " " 96; flatulence.
11.15 " " 96; sickness and flatulence.
11.30 " " 92; " "
11.45 " " 94; another 4 minims.
12, noon, " 94; flatulence.
12.30, P.M., pulse 94; great nausea.
1 " " 90; other 4 min.; great nausea.
1.30 " " 96. "
2.15 " severe fit of vomiting, which lasted from 20 to 30 minutes.

He complained of a sinking at the heart, pain in the stomach and bowels, and, after the vomiting, of great depression, and of a *dead* feeling in the limbs. After vomiting, the pulse fell to 80, but at 3 o'clock, after

taking stimulants, it was 92, and the next morning it was at 96.

In the *Medical Times and Gazette** is recorded by Dr. Edwards a case of accidental poisoning with veratrum viride.

A chemist took an over dose of the tinct. ver. vir. for the purpose of testing its effects. He took ℥j., equal to about 12 grs. of the powder. He was found sitting in the water-closet, vomiting into the pan. His features were sunken, skin cool and covered with a profuse clammy sweat; his pulse was quite imperceptible. He complained of intense pain in the epigastrium. The *vomitus*, at first, appeared to consist of food and contents of stomach, afterwards of a glairy mucus. He received immediately ℥jss. of pure brandy, which checked the vomiting. He was removed into a room, and on to a couch in front of the fire. The surface of the body was still very cold, especially of the extremities. The clammy sweat con-

* Jan. 3d, 1863.

tinued, but the pulse could be indistinctly felt, beating feebly and with irregularity, about 44 a minute. Under the use of brandy warmth gradually returned to the surface, and the pulse became better in volume and power. He fell asleep, and awoke better. The next day he was well. There was no diarrhœa. He stated afterwards, that before and during the vomiting he had a sense of constriction in the throat, and excessive pain. His mind was calm, though consciousness was clouded for a time. Immense circles of green color were seen around a candle flame, which turned to red on closing the eyes. There was a tendency to cramps in his legs when they were touched.

M. Oulmont has published* in a memoir, read before the Académie de Médecine de Paris, the results of his experiments with this drug. He sums up the results of his experiments (which are not related) with veratrum viride, as follows :—

* Bul. Gén. de Thérap., 1868, tome lxxiv. p. 145.

"1st. It quickly causes nausea, vomiting and diarrhœa, which two former may last fifteen to twenty hours.

"2d. The respiration is greatly modified, becoming irregular; sometimes, very rapid, sometimes so retarded, that there may be but one or two respiratory movements during a minute; sometimes in frogs it is completely suspended.

"3d. The circulation is very rapidly diminished in frequency; the pulse, at the end of a quarter or half of an hour, as much as 20, 40, or 60 pulsations a minute. In man not in a febrile state, veratria (in the dose of 1 to 3 centigrammes) causes the pulse to fall thirty to forty beats.

"4th. The temperature follows a descending scale a little less marked; at the end of half an hour to two hours only, it descends 2°, 3° or even 5° (C.), and may remain there twenty-four hours without death resulting.

"5th. The debilitating action of veratrum viride is manifested from the beginning. Feebleness and prostration continually increase,

and when they have attained the highest point the animal dies.

"6th. There never results contraction, muscular rigidity or tetanic convulsions.

"7th. The poisonous dose of veratrum viride for frogs is 20 drops of the tincture, for rabbits 60 to 80, and for dogs 120 to 150."

He concludes from comparative experiments that veratrum album is much more unequal in its effects, and more severe in its action. He thinks that the action of veratrum viride does not depend on the alkaloid veratria,* as the latter causes muscular contractions and spasms.

M. Limon† found that the tincture of veratrum viride causes diminished frequency in the pulse and reduction of temperature. The pulse decreased from 112 to 54, and the temperature from 39 to 37 (C.). He noticed, too, that the sphygmograph showed an in-

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* According to our experiments, this distinction cannot be maintained.

† De l'action du Ver. Vir., Gaz. Méd. de Strasbourg, in Bull. Gén. de Thér., Jan. 30th, 1869.

creased arterial tension, when the pulse is reduced in frequency. Its effects passed off rapidly, and there was no cumulative action. He, also, mentioned the vomiting.

Two cases, well reported and observed by MM. Tuber et H. Hirtz, *internes aux Hopitaux de Strasbourg*, were reported by M. Oulmont to the Society of Therapeutics.

The first was a case of pneumonia in a woman, 30 years of age, mother of three children, pregnant with a fourth. She entered the hospital on the evening of the 9th of March, on account of pneumonia of the left lung. The temperature was 39° (C.), pulse 112.

March 10th.—Temp. 38.8° (C.); pulse 108; respiration 80. Antimony and bleeding had been her treatment. In the evening the temperature was 39.2° (C.); the pulse 108; respiration 48.

March 11th.—Asphyxia seemed imminent. Temperature 39.7° (C.); pulse 112; respiration 76.

Veratrum viride was now ordered in

granules containing 1 centigramme of extract. This was first given at 9½ o'clock.

| *Hour.* | *Dose.* | *Temp.* | *P.* | *R.* | *Remarks.* |
|---|---|---|---|---|---|
| 9.30 | 1st gran. | 39.7° | 116 | 76 | |
| 10.30 | 2d " | 39.4 | 108 | 76 | |
| 12 | 3d " | 38.7 | 98 | 68 | Vomiting. |
| 1.30 | | 38.1 | 68 | 42 | |
| 3 | | 37.8 | 64 | 44 | Temp. of vag. 38.6°. |
| 4.30 | | 36.8 | 64 | 38 | |

The vomiting which arose after the third granule caused considerable distress, which was of short duration. During the evening the symptoms recurred in severity.

March 12th, A.M.—Temperature was 39.2° ; pulse 104 ; respiration 80. Veratrum viride was again given.

| *Hour.* | *Dose.* | *Temp.* | *Pulse.* | *Resp.* | *Remarks.* |
|---|---|---|---|---|---|
| 10 | 1st gran. | 38.8° | 108 | 74 | |
| 11 | 2d " | 38.3 | 100 | 50 | |
| 12 | 3d " | 37.4 | 82 | 50 | Vomiting. |
| 1.30 | | 38.3 | 60 | 30 | |
| 2.30 | | 38.6 | 60 | 40 | |
| 3.30 | | 37.7 | 64 | 40 | |
| 4.30 | | 37.5 | 72 | 40 | |
| 5.30 | | 37 | 68 | 28 | |
| 6.30 | | 37.5 | 80 | 40 | |
| 7.30 | | 37.5 | 80 | 36 | |
| 8.30 | | 37.2 | 80 | 36 | |
| 9.30 | | 37.9 | 80 | 36 | |
| 10.30 | | 38.1 | 80 | 36 | |
| 11.30 | | 36.6 | 96 | 40 | |

March 13th.—Temperature 38.7°; pulse 96; resp. 32. She gradually recovered.

The second case is one of generalized bronchitis in a man 37 years old.

We do not think it worth while to transcribe this case, which agrees in every essential with the one detailed above.

## Summary.

The conclusions in regard to the physiological action of veratrum viride, and the alkaloid, veratria, which can be drawn from these experiments and cases recorded by others, confirm those that we have been induced to draw from our own experiments. We need only mention, here, the influence which is exerted upon the nervous system. In some respects resembling the action of woorara, it differs from that poison in less energetic action, in attacking the sensory fibres as well as the motor, and in diminishing the frequency of the cardiac pulsations. We have not performed any experiments to show whether the periphery

or centre of the nervous system is affected, or whether the whole nervous tract is influenced.

The influence over the cardiac pulsation is, however, such that we are disposed to suspect that the nerves supplying that viscus are influenced at their central origin. The reduction in temperature indicates that the metamorphosis of tissue by which the temperature is sustained is interfered with; but this is most marked in cases of abnormal excess of temperature. The reduction of temperature would, also, indicate an influence over the vaso-motor system; the paleness of face, the dilated pupils, which have been sometimes noticed, and the increase of the arterial tension, observed by Limon, point to the same conclusion. If this be so, the weakness and paralysis may be due to an excessive contraction of the arterioles. Our experiments do not allow us to decide whether it is the spinal cord which is affected by this contraction, or whether it is the nervous trunks, or the

terminal fibres of the nerves, or the nervous plates, which form the connection between the nerve and the muscle ; but inasmuch as the respiratory and cardiac movements, the arterial contractility, the motor and sensory powers, and the secretory functions are all more or less affected, it seems more reasonable to refer the disturbance to the spinal axis, as that part of the nervous system through which the influence is exerted, and from which all the above-mentioned results are produced.

The nausea and vomiting, the sensation of tingling, the prickling in the fingers and toes, and other abnormal sensations in the throat and elsewhere, which seemed to be present even when the drug was administered hypodermically, might be caused by the direct contact of the drug upon these parts as it circulates through them in the blood. A local application produces a numbness and deadens the pain of neuralgia. The deadness and diminished sensibility may, likewise, be due to the local

contact of the drug; or, both these effects, viz., the loss of sensitiveness and the abnormal sensation, may be due to its influence over the central nervous system.

In one case only, that of accidental poisoning, does there seem to be a cloud over the intelligence.

These are the conclusions which follow from what has been recorded by others, and it will be well to bear them in mind in considering our experiments, which will now be given.

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It is proposed to show, by the following experiments, the symptoms produced in various animals by veratria, and at first from a poisonous dose.

Exp. I.—Green-colored frog. Before the administration of the poison, the thorax is opened, and the number and force of the cardiac pulsations noticed:—Respiration 10; pulsations 32. Veratria placed upon the web of the frog's foot.

| *Hour.* | *Respiration.* | *Pulsation.* | *Remarks.* |
|---|---|---|---|
| 0.21 | feeble. | | |
| 0.31 | very feeble. | | |
| 0.36 | | | veratria applied to heart itself. |
| 0.41 | nearly ceased. | very feeble. | heart pale. |
| | | 28 | tetanic spasms; right lung forced out of thoracic opening and ruptured. |
| | | the same. | |
| 0.58 | ceased. | very feeble. | tetanic spasms every few minutes. |
| 2.21 | | still goes on. | |
| 2.31 | | | obliged to leave; muscular fibres contract to stimulation. |

*Post Mortem,* twenty-one hours after. Continued rigor mortis; muscles, heart and liver all very pale. No muscular contractility to stimulation or by electricity. Lung tissue contains air. No transverse striæ visible by the microscope in cardiac muscular fibres, which seem to be replaced with granular spots.

In this experiment it may be noticed that veratria is not very readily absorbed by the skin of a frog; and, also, that after its topical application to the cardiac muscles, it does not cause paralysis of the heart's ac-

tion, though it does produce cessation of the respiratory function. It produces various muscular spasms, to which the frog, of all animals, is the most liable, and which may, after all, be voluntary movements.

Exp. II.—Russet-colored frog. As it is stated by some observers, that phenomena produced in the green-frog and in the russet-frog are dissimilar, the effects are reproduced upon the latter that a comparison may be drawn. The *tincture* of veratrum viride was used in this case.

Tinctura veratri viridis gtt. q. s. Subcutaneous injection to leg.

| *Hour.* | | *Pulse.* | *Resp.* | *Remarks* |
|---|---|---|---|---|
| 0.07 | Thorax opened. | 22 | | |
| 0.07 | | weaker. | | |
| 0.13 | | 22 | | |
| 0.18 | | | very feeble | spasms. |
| 0.35 | | do. | | |
| 0.40 | | 18 | | |
| 0.53 | | 10,irreg. | | |
| 1.00 | | 12 | | |
| 1.12 | | 10 | | |
| 1.22 | | 12 | ceased. | |

*Post-mortem* examination showed diminished response to electrical stimulation in

the leg to which the injection was administered; striated muscular fibres of this leg somewhat disintegrated, though the striæ can be distinguished. This is specially true of the cardiac muscles. Rigor mortis very marked.

This last experiment agrees in general with the previous one, but the symptoms and other effects are more intense, probably, because the dose of *veratria* was larger.

Exp. III.—Frog (green). Tinctura veratri viridis gtt. xii. placed under skin of a frog's leg. When it touched the flesh the frog jumped and kicked.

1′. Respiration spasmodic.

5′. " irregular and jerking; violent struggling.

11′. Respiration slower and jerking; violent struggling.

16′. Respiration feeble.

17′. Convulsive movements; bulging of sides, reminding us of the efforts at vomiting by a cat under similar circumstances.

24′30″. Same effects; resp. ceased for a short time, and was then resumed.

1.8′. Muscular quiverings in posterior extremities.

1.45′. All phenomena of life had ceased, including those of reflex action.

*Post mortem.*—The muscles near to the place where the veratria had been applied were, in some places, covered with granular degenerations (as it appeared under the microscope), and, in others, extremely fine transverse striæ were arranged very near each other; the corresponding muscles of the opposite leg had nothing of this peculiarity. The cardiac muscles were easily separated into fibrillæ, some showing a coarse striation, others the same granular appearance above referred to. The hearts of each of the two frogs (Exp. II. and III.) were pale and muscles somewhat contracted, each animal having an abundance of fluid blood in its body.

These peculiarities were afterwards explained by a more careful examination,

made with the use of alcohol and ether, which cleared up the field of observation, leaving the striæ more distinctly marked, though the fibrillæ were a good deal disintegrated and broken up. We were led to suppose that these dubious effects were due to mechanical deposition of the drug, as both the solution of veratria and the tincture of veratrum viride under the microscope had these same spots, and muscles soaked in either of the above were covered with these same globules.

This last experiment shows, in a general way, how the respiratory movements in a frog are modified, and that death can be induced by a dose of 12 drops; also that the *post-mortem* changes reveal little to show by what cause the vital functions are interrupted. It will be interesting to compare these first three experiments, taken from a number made upon frogs, with

Exp. IV.—Upon a cat.

A small amount of veratria (by estimation

3 to 5 centigrammes) on the point of a scalpel was inserted beneath the skin of the back, just over the upper lumbar vertebra. The cat immediately licked the wound.

5′. Champing of jaws and salivation; eyes closed; sneezing and retching; no loss of power over limbs; continued twitching of tail, occasionally crying; head held up with her nose in the air.

35′. Another dose (of equal amount) is administered in the same manner. Seems to cause much pain, from the crying induced. Apparent loss of muscular power in posterior extremities; great uneasiness and distress.

40′. Has a dejection; after which, seems disinclined to move.

1.9′. Eyes shut; when opened, pupils appear round and bright.

1.45′. Another defecation.

2.0′. Retching with cries, followed immediately by others, which were continued with much violence.

2.5′. Another more violent attack of retching, the cat dragging her face along the floor for six inches.

2.15′. Vomits a small portion of liquid food. Some loss of muscular power in posterior extremities.

2.20′. More veratria administered, followed by continuous moaning; violent spasms, pawing at mouth, loss of muscular control; respiration very rapid; violent efforts at vomiting, drawing her up and off her feet.

2.35′. Convulsions and vomiting; respiration diaphragmatic. No loss of sensation.

2.55′. Ejection of urine followed by tetanic spasms and muscular twitchings.

2.55′. No respiration, no cardiac pulsation —death.

*Post-mortem* examination. Heart normal —lungs congested, ecchymosed and emphysematous, the lower lobes covered with white spots. Stomach rather pale; liver and intestines show no peculiarities; bladder empty; muscles of heart showed broken-up fibrillæ with the striæ somewhat irregular. In a muscle from the thigh the striæ were distinct.

The first peculiar effect produced by this drug, it may be noticed, is salivation; and this is followed by retching, movement of the bowels, vomiting, &c.; after this, the respiratory efforts are hurried, muscular ac-

tions are imperfectly performed, spasm of the bladder causes ejection of urine. Finally, death occurs, preceded by tetanic spasms.

Exp. V.—We will now compare with these another experiment, upon a small rabbit weighing only 15 ounces Troy.

| *h.m.s.* | *Resp.* | *Condition of Pupil.* | *Circulation.* | *General Symptoms, Remarks, &c.* |
|---|---|---|---|---|
| 0.00 | 92 | carefully examined. | 240 | 1 centigr. inserted under skin of back, which made the animal cry out in a few seconds. |
| 0.02 | | | | Animal now quiet. |
| 0.05 | slow & jerk'g. | contract'd. | 144 | Champing of jaws. |
| 0.07 | | | 108 | |
| 0.09 | | dilated. | | Large quantity of saliva oozes from the mouth. |
| 0.11 | | | no pulse. | Ears very cold and pale. Chest opened; heart pulsates feebly; r. ventricle and auricle distended with blood. The contraction of auricle more rapid than that of ventricle (96 : 48) (120 : 30). Pulsation of each becomes more and more feeble and irregular, although the heart is kept moist. In 33 min., there is no pulsation visible. |

Examination of the body, made immediately, showed the veins turgid, fauces and œsophagus pale, no peristalsis of bowels to stimulation or to galvanic current, very

slight contraction of leg muscles on electrical stimulation, heart empty, the lungs ecchymosed (one small hæmorrhagic spot in right side), brain normal.

An examination of this last experiment, showing that salivation is caused even when the drug is administered hypodermically, would induce us to consider, that it is not local irritation of the buccal mucous membrane which causes the salivary gland to throw out its saliva, but that this effect is probably caused by an irritation of the lingual nerve, or submaxillary ganglion, which Bernard* has shown will cause salivation; but, before we investigate this phenomenon, let us compare with these first experiments that of the action of veratria on a dog.

Exp. VI.—To a vigorous bitch, of about forty-five pounds weight, was given ℥ss. of chloroform until she became quiet. Then ether was used, and the animal bound upon the operating board.

* Vide Compt. Ren. de l'Acad. des Sci., 25 Aug. 1862.

| *h.m.s.* | *Pulse.* | *Resp.* | *Remarks.* |
|---|---|---|---|
| | 148 | 34 | Before the inhalation of chloroform. |
| | 174 | 56 | Imperfect anæsthesia. |
| | 142 | 40 | Perfect anæsthesia. |
| | 134 | 40 | |
| | | | Veratria gr. $3\frac{3}{4}$, dil. acetic acid, q. s., injected in right leg subcutaneously. |
| 0.02.00 | 112 | 40 | |
| 0.05.15 | 120 | 36 | Animal is calm. |
| 0.06.15 | 112 | 40 | |
| 0.08.30 | 120 | 36 | |
| 0.09.30 | 116 | 32 | |
| 0.10.00 | 116 | 16 | |
| 0.12.30 | 114 | 15 | Muscular quivering in trunk. |
| 0.14.00 | 108 | 12 | *Ether is now removed.* |
| 0.16.00 | 108 | 10 | Abdominal respiration. |
| 0.18.00 | 102 | $8\frac{1}{2}$ | |
| 0.20.30 | 104 | $8\frac{1}{4}$ | Respiration feeble. |
| 0.25.00 | 102 | $12\frac{2}{5}$ | Animal gasps. |
| 0.27.00 | 88 | 11 | Animal struggles. |
| 0.30.00 | 36 | 32 | Another gasp. |
| 0.31.30 | 80 | 28 | Skin is cold. |
| 0.35.00 | 72 | 22 | |
| 0.37.30 | 84 | 17 | Pulsation stronger. |
| 0.40.00 | 98 | 10 | Difficult and noisy inspiration. Struggles. |
| 0.45.00 | 98 | 14 | Expiration slow and noiseless; muscular contraction by electric stimulation feeble, especially in posterior train. |
| 0.49.00 | 108 | | |
| 0.52.00 | 120 | 15 | Struggles violently. Irreg. resp. |
| 0.54.00 | 120 | 13 | Musc. relaxation; loss of sensat'n. |
| 0.56.30 | 126 | 20 | Difficult respiration, with violent movements of neck muscles. |
| 1.00.00 | 108 | 12 | Respiration very feeble, with mucous râles in throat. |
| 1.05.00 | 128 | ceas'd | |
| 1.09.00 | 92 | | |
| 1.09.30 | gone. | | No response to electrical stimulation of nerves, though the muscular fibres contract when the poles are applied to these directly |
| 1.12.00 | | | |
| 1.15.00 | | | Nerves of neck and forearm exposed; electrical stim. does not cause muscular contraction. |

*Post-mortem* examination (immediately). —Heart normal in appearance ; clots in left ventricle ; fluid blood in right ventricle ; right auricle contains blood which is slightly diffluent ; left auricle empty. Lungs apparently healthy ; crepitate between the fingers. Liver, kidneys, spleen and pancreas all normal. Stomach and intestines show slight arborescent redness. Stomach reddened on the inside, and nearly full of a viscid fluid like saliva. Bladder nearly empty.

It may be noticed that chloroform and ether were administered to produce anæsthesia. This was preliminary to an operation to measure the arterial tension which will be described and commented upon elsewhere (Exp. VI. *b*). This experiment is related in this place, as it was conducted with great care, and many assistants aided in the taking of observations, which it may be noticed are very accurately described. Attention is called to the fact that the general effect of the drug upon the vital

functions agrees with other experiments upon animals not under the effects of an anæsthetic. The effect upon the respiration, if carefully observed, shows at first the depressing action of both veratria and ether; but from thirty minutes after the commencement of the experiment, and sixteen minutes after the removal of the ether, probably the peculiarities of respiration were due only to the veratria, viz., great irregularity of force and frequency, but less than one-half the number of respiratory efforts as in the normal condition, and this gradually reduced to zero. The effect upon the circulation can best be understood in connection with observations taken by means of the cardiometer. Suffice it merely to note that the sedative effect is progressive from the first, and that the heart stops pulsating after the respiration ceases, and this, too, very suddenly; though its force may have been very feeble for some time previous.

The stoppage of the respiratory effort

resembles that of a person dying from paralysis, in consequence of lesion of the spinal axis, and we are strengthened in this supposition, by noting no part of the nervous system that will conduct electrical stimulation to the muscular fibres, though these last by direct stimulation will themselves contract. A careful examination of the *post-mortem* appearance points to no organic lesion, as all the viscera are apparently healthy, and death by asphyxia does not seem very manifest, there being no venous engorgement or sufficient ecchymosis of the lung tissue. We shall probably find as we continue our study that the cause of death is due to some physiological rather than anatomical lesion, perhaps to some vital derangement of the nervous system; but before we discuss this point, we will notice what important vital functions are interrupted or modified.

Absence of vomiting may be noticed in this experiment; and, consequently, the exhaustion induced by this terrible symp-

tom cannot be the cause of death in the experiments previously reported. The fact that there was no vomiting in this case would tend to show that the chloroform or ether may have, by its peculiar action, prevented the appearance of this symptom.

### Circulation.

We will now consider the effects produced by this drug upon the circulation, illustrative of which will be the following carefully recorded experiment.

Exp. VII.—Green frog. Thorax opened and cardiac pulsations viewed.

| *h. m. s.* | *Pulse.* | *Resp.* | *Remarks.* |
|---|---|---|---|
| | 25 | 48 | Before administration. |
| | | | Tinct. veratri viridis officin. gtt. xij. now injected in groin. |
| 0.02.00 | 26 | 46 | |
| 0.06.00 | | 34–38 | |
| 0.09.00 | 28 | | Struggles occasionally. |
| 0.11.00 | 24 | | Respiratory movement feeble. |
| 0.16.00 | 24 | ceases | |
| 19–23 | 24 | | |
| 0.25.00 | 24 | | |
| 0.28.00 | 24 | | Spasmodic movements. |
| 0.35.00 | 26 | | Heart's contractions regular in force and frequency. |
| 0.36.00 | 26 | | Position of animal changed. |
| 0.39.00 | 26 | | |
| 0.59.00 | 24 | | |
| 1.05.00 | 27 | begins | Spasmodic movements. |
| 1.10.00 | 30 | | Recovers & lives for a few days. |

This may be considered the *therapeutical* action of this drug, as the animal recovered from the effects.* The depressing effect upon the respiratory function is remarkable, and seems to be the sole symptom worthy of record, except that of the heart, which, instead of being slower, becomes more rapid than before the drug was given.

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* In this case respiration was, probably, carried on through the skin, until the drug was eliminated sufficiently to allow the respiratory movements of the thorax to be reëstablished. In my notes, I find an experiment in which a frog lived one hour and twenty minutes under an atmospheric pressure varying from ·100 to ·010 m. Respiration having ceased, he was placed on a table. The next morning he was found alive upon the floor.

R. A.

Exp. VIII. Green frog. Tinct. ver. vir. gtt. xxiii.

| *h. m. s.* | *Circ.* | *Resp.* | *Remarks.* |
|---|---|---|---|
| | 40 | 50 | Before administration. Thorax opened. Hypodermic injection of the above in groin. |
| 0.01 | | 48 | |
| 0.02 | 32 | 33 | Respiration feeble. |
| 0.05 | 40 | | Muscular quiverings. |
| 0.12 | 32.8 | | Respiratory movements too feeble to count. |
| 0.15 | 35 | | Respiration ceased. |
| 0.17 | 33.3 | | |
| 0.20 | 30 | | Moistened the animal with water. |
| 0.21 | 35 | | Causes an improvement of circulation. |
| 0.24 | 35 | | |
| 0.26 | 31 | | Muscular quiverings. |
| 0.30 | 31 | | Pulsation feeble. |
| 0.33 | | | Animal again moistened with water. |
| 0.34 | 33.3 | | Causes temporary improvement. |
| 0.36 | 32 | | Slight spasm. movements; mus. quiverings in posterior limbs. |
| 0.38 | | | Circ. very feeble. Gasps once or twice; resp. spasmodic. |
| 0.41 | 30 | 14 | |
| 0.44 | 31 | 12 | |
| 0.47 | 31 | 5½ | Reflex movements in lower limbs. Ventricular contraction very feeble. Auricle not visible. |
| 0.50 | 31 | | |
| 0.53 | | 4½ | Animal appears sensitive to irritation. |
| 0.54 | 33 | | Reflex response less active. |
| 0.57 | | 15 | Respiration jerky. |
| 0.59 | 32 | | |
| 1.00 | | 15 | Respiration feebler. |
| 1.02 | 34 | | Respiration ceased. Sensation apparently preserved. |
| 1.06 | 35 | | |
| 1.21 | 30 | | Musc. quiverings still continue. Spasms. |
| 1.25 | 30 | | Spasms. Reflex response continues. |
| 1.36 | 30 | | Spasm. movements at intervals. |
| 1.39 | 28½ | | Reflex response diminished. |
| 1.42 | 28½ | | |
| 1.44 | 27 | | Slight spasm. Reflex response gone. |
| 1.48 | 25 | | |

The animal was found dead the next day, and looked as if this happened very soon after the experimenter left. Here the action upon the respiration is very marked, and long after the cessation of this function, and for a short time after the loss of reflex action the cardiac pulsation is not materially modified. It may be objected to by some that the injury to the thorax caused more of the trouble than the drug. In reply to this it may be stated that the effects upon the circulation and respiration of frogs agrees with that of other and warm-blooded animals. But to settle any doubts the following experiment was tried and will now be related.

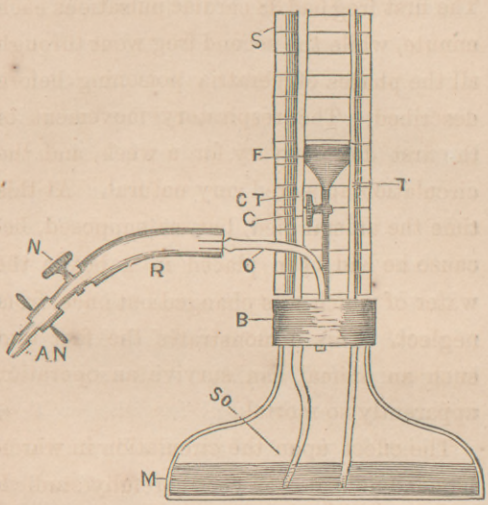
Exp. IX.—A frog was operated upon in the same manner as before described, by opening the thorax and exposing the ventricle and auricle (by the way, a very common experiment among physiologists), and the pulsations compared with those of another frog treated in the same manner, but

to whom a poisonous dose of a solution of veratria had been injected hypodermically. The first frog had 38 cardiac pulsations each minute, while the second frog went through all the phases of veratria poisoning before described. The respiratory movement of the first did not vary for a week, and the circulation appeared very natural. At this time the animal died, but, as supposed, because he had been placed in a bottle the water of which was changed but once, from neglect. This demonstrates the fact that such an animal can survive an operation apparently so mortal.

The effect upon the circulation in warm-blooded animals has been carefully studied, and especially so by an instrument to measure the pressure of blood in the vessels.

*Description of the Instrument.*—The instrument used corresponds, with a few modifications, with one described by Dr. Brunton in his monograph on Digitalis. The results arrived at have been observed

with four different instruments, always agreeing in every essential.




S. Scale, divided into centimetres and millimetres.
F. Copper funnel and tube, passing through the brass cap.
C. Stop-cock to shut off escape or entrance to air.
C T. Capillary tube, with constriction at lower end.
T. Capillary tube, uniform diameter.
O. Tube through which the blood-pressure is exerted.
B. Brass cap, fitting on to the glass stand by a screw and washers.
S O. Cavity of glass stand.
M. Mercury.
R. Rubber tube connecting with nozzle.
N. Brass nozzle, with stop-cock.
A N. Nozzle upon which the artery is fixed.

The accompanying plate will perhaps give a more definite idea of the hæmadynamometre. A glass stand is fitted with a brass cap (B) into which are inserted two glass tubes (T and C T) of the same calibre, though C T has a capillary constriction near its lower extremity where it dips into the mercury (M); also, a copper funnel-shaped tube (F), furnished with a stopcock (C) and another glass tube of larger capacity (O), with which the artery is connected by means of a rubber tube (R), in which is inserted a brass nozzle (N), furnished with a stop cock, and another nozzle (A N) furnished with a shoulder, by means of which a ligature will prevent the artery from slipping off, and to prevent escape of blood, this latter (A N) fitting snugly on to the former (N).

This instrument was exhibited, and its action illustrated, to the Boston Medical Improvement Society, and to the Norfolk District Society.

By means of this instrument several experiments were undertaken, with a view to

determine any especial condition of the arterial pulsation which might be induced by the exhibition of this drug upon the lower animals. From these a few experiments are selected as having the most direct and positive bearing upon this question.

Exp. VI. *b*.—With hæmadynamometre in carotid artery. Dog, weighing 45 pounds.

| *h. m. s.* | *Max.* | *Min.* | *Pulse.* | *Resp.* | *Symptoms and Remarks.* |
|---|---|---|---|---|---|
| 0.00.00 | 5.00 in. | 4.65 in. | 134 | 40 | Chloroform ½ oz., followed by ether inhalation. |
| | | | 148 | 34 | Anæsthesia; bound on the table. |
| | | | 174 | 56 | Veratria grs. 3¾ in acid. acet. dil. hypoderm.; struggling. |
| 0.02.00 | 4.30 | 4.00 | 112 | 40 | |
| 0.05.15 | 4.00 | 3.60 | 120 | 36 | Animal calm. |
| 0.06 .15 | 3.50 | 3.10 | 112 | 40 | |
| 0.08.30 | 3.10 | 2.80 | 120 | 36 | |
| 0.09.30 | 3.40 | 3.00 | 116 | 32 | |
| 0.10.00 | 3.30 | 2.90 | 116 | 16 | |
| 0.12.30 | 3.50 | 3.10 | 114 | 15 | Muscular quiverings, especially in trunk. |
| 0.14.00 | 3.45 | 3.00 | 108 | 12 | *Ether removed.* |
| 0.15.00 | 3.40 | 3.30 | | | Oscillation of mercurial column slight. |
| | 2.90 | 2.50 | | | |
| 0.16.00 | 3.10 | 2.80 | 108 | 10 | Abdominal or diaphragmatic respiration. |
| 0.18.00 | 2.50 | 2.00 | 102 | 8½ | |
| 0.19.00 | 3.00 | 2.50 | | | |
| 0.20.30 | 3.40 | 3.10 | 104 | 8½ | Resp. feeble. Arterial tension increased on inspiration. |
| 0.25.00 | 3.60 | 3.00 | 102 | 12⅔ | Animal gasps. Mercurial column ascends. |
| | | | | | Instrument cleaned, as oscillation of merc. col. ceased. |
| 0.27.00 | 4.70 | 4.40 | 88 | 11 | |
| | | | | | Instrument again cleaned, as oscillation has ceased. |
| 0.28.00 | 3.90 | 3.70 | 80 | | |
| 0.30.00 | 3.50 | 2.50 | 36 | 32 | Respiratory gasp. |
| 0.31.30 | 3.85 | 3.75 | 80 | 28 | Skin of body cold to the touch. |
| 0.33.30 | | | | | Instrument again cleaned. |

| | | | | | |
|---|---|---|---|---|---|
| 0.35.00 | 3.85 | 3.85 | 72 | 22 | |
| 0.37.30 | 4.50 | 4.30 | 84 | 17 | Oscillation occurs when struggling. |
| 0.40.00 | | | 98 | 10 | |
| 0.45.00 | | | 98 | 14 | |
| 0.49.00 | | | 108 | | |
| | | | | | Instrument again cleaned. |
| 0.52.00 | 3.82 | 3.77 | 120 | 15 | Respiration irregular. |
| 0.54.00 | 3.77 | 3.70 | 120 | 13 | Musc. relaxation. Loss of sensation in the integument. |
| 1.00.00 | 3.95 | 3.92 | 126 | 20 | Difficult resp., with violent movements of muscles of the neck and larynx. |
| 1.05.00 | 3.90 | 3.87 | 108 | 12 | Respiration very feeble and imperfect. |
| 1.09.00 | | | 128 | Ceased. | Coarse mucous râles in throat for the last 30 minutes. |
| 1.10.00 | | | 92 | | |
| 1.12.00 | | | Ceased. | | No response to electrical stimulation of nerves, though the muscular fibres contract when the electric poles are applied to the muscles directly. |
| 1.15.00 | | | | | Nerves of neck and forearm exposed and isolated on glass rods; electricity applied to these, produces no muscular contractions. |
| 1.35.00 | | | | | The spinal axis in cervical and lumbar regions exposed (without bruising or cutting the membranes) and the poles of the induction coil applied to each spot, producing no muscular contractions anywhere; though applied directly to any muscular substances, the contraction of the muscular fibres is very marked. |
| | | | 148 | 34 | Before the operation or administration of chloroform. |
| N. B. | | | 174 | 56 | Imperfect anæsthesia. |
| | | | 142 | 40 | Perfect anæsthesia. |

Exp. X.—With tinct. ver. vir. ℥ij. Dog. Hæmadynamometre.

| *h. m. s* | *Mean height in inches.* | *Pulse.* | *Resp.* | *Symptoms and Remarks.* |
|---|---|---|---|---|
| | | 145 to 200 | 48 | Anæsthesia by chloroform and ether. |
| 0.00.00 | | 145 to 220 | 48 to 48 | |
| | | 168 to 220 | 36 to 48 | Ether removed. |
| | 5.20 | 180 | 40 | Oscillation 2-10ths inch. Hypoder injec. into abdom. reg. |
| 0.03.30 | 5.15 | | | |
| 0.04.15 | 5.25 | 100 | 28 | Animal calm. |
| 0.07.00 | 5.21 | 64 | 26 | |
| 0.09.00 | 5.20 | | 26 | Cries on expiration. |
| 0.09.45 | 5.18 | 64 | | Occasional resp'y gasps. P. feeble. Attempts to vomit. |
| 0.12.45 | 5.20 | 76 | | Spasmodic movement of diaphragm. |
| 0.16.15 | 5.20 | 92 | | Blood dark colored from artery. |
| 0.19.00 | 6.40 | | | Merc. column ascends on inspir. and descends on expir. |
| 0.21.30 | 5.75 | 128 | 16 | |
| 0.23.30 | 5.65 | | 6 | Respiration very irregular. |
| 0.25.15 | 5·61 | | 48 | Respiratory movements suddenly recommenced. |
| 0.26.00 | | 120 | 16 | |
| 0.27.30 | 5.55 | 140 | | Pressure less on inspiration. Respiration irregular. |
| 0.29.30 | 5.53 | | | Three deep inspirations, followed by several gasps. |
| 0.31.30 | | | | Intermission of slow pulsations. |

| | | | | |
|---|---|---|---|---|
| 0.33.45 | 6.00 | | | Surface of skin cold. Several attempts at vomiting. |
| 0 35.30 | | 72 | 40 | Respiration, irregular before, now recommences. |
| 0 39.30 | 3.40 | 60 | | Pulse very intermittent. |
| 0.43.00 | | | | Instrument clogged. |
| 0.44.15 | | | *14 | Dark blood oozes from artery drop by drop. |
| 0.46.00 | | | | No response to pinching or pricking of skin. |
| 0.46.30 | | | | Instrument removed. Respiration jerky. |
| 0.48.00 | | | | Blood still oozing from artery, of a dark color. |
| 0.51.45 | | | 11 | Blood is drawn from artery by a syringe. |
| 0.57.00 | | | | Ineffectual attempts at vomiting. |
| 0.58.00 | | Ceased. | Ceased. | Vomits up yellow mucus. |
| 0.58.00 | | | | Heart ceases its pulsations a few seconds after cessation of respiration. |
| 1.01.00 | | | | Several movements of diaphragm, like those of vomiting Thorax opened. Electricity applied causes muscular contractions of voluntary muscles. Heart will not contract from electrical stimulation. |

*Autopsy.*—Dark fluid blood in right ventricle and auricle. Black clot in left ventricle. No fluid in pericardium. Lungs collapsed—nothing peculiar in appearance. Bladder distended with urine.

Exp. XI.—Hæmadynamometre. Dog, 60 pounds weight. Tinct. ver. vir. ℥iv. and veratriæ q s. Animal bound upon the operating board.

| *h. m. s.* | *Max. in centim.* | *Min. in centim.* | *Pulse.* | *Resp.* | *Symptoms and Remarks.* |
|---|---|---|---|---|---|
| | | | 136 | 21 | Before administration of drug, but after inhala. of ether. |
| | 186* | | | | Instrument connected with right femoral artery. |
| 0.03.00 | 166 | 160 | | | Ether removed. Ver. vir. tinct. 2 dr. in left thigh. |
| 0.06.00 | | | 180 | 24 | Animal crying. |
| 0.20.00 | | | 120 | 20 | |
| 0.28.00 | 170 | | | | Great salivation. |
| 0.31.00 | 160 | 140 | | | Oscillation accords with respiratory motion. |
| 0.33.00 | 200 | | | | Struggling. |
| 0.35.00 | 153 | 150 | | | Instrument,† being clogged, is removed. |
| 0.37.00 | | | 180 | 18 | |
| 0.40.00 | | | 160 | 16½ | Animal cries with expiration. |
| 0.49.00 | | | 150 | 24 | Continues the same till |
| 0.58.00 | | | 120 | | |
| 1.00.00 | | | 150 | 22½ | Animal struggling. |

* 1 centimetre = 0·393 of an inch.
186 centimetres = 7·3098 inches.

† This was of imperfect construction, and only the comparative result is to be considered.

| | | | | | |
|---|---|---|---|---|---|
| 1.04.00 | | | 200 | 20 | |
| 1.08.00 | | | 220 | 20 | Intermission of one pulsation after each ten. |
| 1.09.00 | | | 180 | 18 | |
| 1.12.00 | | | 200 | 18 | Slight muscular quiverings. Expiration shorter. |
| 1.15.00 | | | 180 | 16 | No intermissions. |
| 1.23.30 | | | 180 | 20 | |
| 1.27.00 | | | 220 | 18 | Struggling. |
| 1.34.00 | | | 150 | 17½ | Surface of skin cold. |
| 1.37.00 | | | 140 | 18 | |
| 1.39.00 | | | 180 | 17 | |
| 1.45.00 | | | | 16 | |
| 1.48.00 | | | | | Another dose of 2 dr. hypodermically, in axilla, causing apparent pain. |
| 2.00.00 | 175 | 140 | 160 | 16 | Instrument reapplied. Variation accords with respiratory movement. |
| 2.09.00 | | | 160 | 19 | |
| 2.17.00 | | | 160 | 16 | Animal is quiet. |
| 2.28.00 | | | 144 | 15 | Sensation apparently preserved. |
| 2.35.00 | | | | | Animal is now set at liberty and placed on the floor. Walks with a staggering gait, the muscles stiff and contracted, then falls over on to his side, and lies quietly, occasionally moaning. |
| 2.42.00 | | | | 14 | Tries ineffectually to rise, constantly moaning, and seems uneasy. |

| *h. m. s.* | *Max. in Centim.* | *Min. in Centim.* | *Pulse.* | *Resp.* | *Symptoms and Remarks.* |
|---|---|---|---|---|---|
| 2.50.00 | | | | 16 | Rises with great difficulty, staggering as before, but walking *backwards* more easily; suddenly falls down on to his side and lies with his limbs extended. Moans and constantly shifts position of his limbs; gets up on his belly, and then lies down again, curled up, with his head on his paws, in position of sleep. |
| 3.00.00 | | | | | |
| 3.05.00 | | | | 14 | Great trembling of muscles of head and body. |
| 3.22.00 | | | 120 | 16 | Lying down on side, and then rises to position on his belly. Subsultus tendinum. On being raised to his feet, totters, whines and falls. |
| 4.20.00 | | | | 16 | Has lain quietly, with occasional moaning. |
| 4.30.00 | | | | | Veratriæ, dissolved in acetic acid, is given. |
| 5.10.00 | | | | 24 | Hypodermic in left shoulder and in the lumbar region. |
| 5.20.00 | | | | 40 | Has a dejection of soft fæces. |
| 5.25.00 | | | 68 | 48 | Respiration irregular and sighing. |
| 5.26.00 | | | | 38 | Expiration very short. |
| 5.28.00 | | | 64 | 36 | |
| 5.32.00 | | | 60 | 36 | Pulse very regular. Expulsion of flatus. |
| 5.36.00 | | | | 56 | Got up on his feet, and fell over suddenly; then arose and staggered across the room, falling over in a tonic spasm. |
| 5.37.00 | | | 58 | 56 | |
| 5.48.00 | | | 58 | 48 | Noisy mucous respiration. Spasm. Stepping on the tail |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | causes him to raise the head and to withdraw the tail. Violent vomiting of a viscid fluid, with blood (from his bitten tongue). |
| 5.58.00 | | | | | Another convulsion. Noisy respiration. Mucous râles in throat. Skin cold. |
| 6.03.00 | | | | | |
| 6.18.00 | | | | | Respiration ceased for one whole minute. |
| 6.20.00 | | | 60 | | Occasional respiratory gasps. Ejection of urine. |
| 6.22.00 | | | Ceased. | Ceased. | Reflex action of eyelids gone. Spinal cord exposed at dorsal and lumbar regions without being injured. |
| 6.42.00 | | | | | Electrical stimulation from induction coil produces no muscular contractions, one pole applied to each exposed portion. No muscular contractions when these are applied to an isolated nerve, or when one is placed on the spinal cord and the other on the crural nerve. The same is true of the sciatic nerve, except for the muscles in the immediate vicinity of the pole or poles; but, if the poles are applied to the muscular substance *anywhere*, there ensues violent muscular contraction of its fibres. (The contraction of the above muscles when the poles were applied to the nerves was due to the electric current exciting this muscular irritability, as the nervous filaments supplied by the sciatic nerve had been cut.) All of these experiments were completed within 25 minutes of the cessation of cardiac pulsation. Rigor mortis came on during these last experiments and continued over 30 hours after. |

*Autopsy* (sixteen hours after death).—Dark red coagula in both ventricles and in right auricle. Left auricle empty. Right auricle full and flaccid, as also the right ventricle. All the valves intact and healthy.

Lungs collapsed and filled with dark-colored blood, somewhat like red hepatization, with slight crepitation under the scalpel or between the fingers. Liver healthy. Stomach contracted firmly and empty, with the rugæ well defined. No redness or injection of mucous surface; veins of external portion slightly injected. Blood coagulated as usual in the veins.

From a careful examination of the records of these experiments it will be noticed that the respiration becomes irregular before the depressing action upon the circulation is produced, thus pointing to phenomena which will be hereafter spoken of in connection with the nervous system.

It will be noticed that the operation of connecting the instrument with the circulation was accomplished while the animal

was in a state of anæsthesia from an inhalation of chloroform and ether; but also it must be remarked, that in Exp. VI.*b* the anæsthetic was removed in fourteen minutes, that in Exp. X. the anæsthetic was removed before the drug was exhibited, and that in Exp. XI. it was removed in three minutes after injection of the drug; but that in all of these experiments the effects produced are coincident.

If the effects upon the respiration be carefully noticed, it will be seen that the respiratory movements grow more and more feeble, the muscles which assist in expanding and contracting the thorax perform their office in an imperfect way, and finally they become paralyzed. Our attention was directed early, during our course of experimentation, to this peculiarity, but it was only after an insight into the poisonous action of this drug upon the nervous system was obtained, that the cause of this difficult respiration was remarked.

It will be still further demonstrated by

the *post-mortem* peculiarities. The muscular fibres retain their power of contraction. But, yet, when the nerve going to these muscular fibres is stimulated, there is no contraction. The same is true in the motor-nervous centre, which seems to have lost all vitality, though this is not the case when death is caused through some other agency. The early presence of rigor mortis shows how the equilibrium between the muscular and nervous vitality is destroyed.

The turgescence of the right side of the heart would also point to the probable cause of death ; viz, asphyxia, which would also explain the ecchymosis or marbriform appearance of the lung tissue, and perhaps, partially explain the convulsive movements. The catharsis, also, would show that the nervous influence from the spinal centre which maintains the tonic contractions of the sphincters and checks the peristalsis of the intestines, is lost or enfeebled, thus allowing the involuntary muscular fibres to contract and to evacuate the contents of

the alimentary canal. Another apparent proof of this nervous paralysis is, that by relaxing the voluntary muscular fibres some of the symptoms peculiar to this drug, viz., vomiting, diarrhœa, and tetanic convulsions, are prevented. It is remarked, however, by Bernard in his lectures, delivered during this past winter, that, while in a state of anæsthesia, either the absorption of drugs is delayed or the manifestation of their symptoms is prevented. It is thought by us that the latter supposition is the most correct.

We do not pretend to explain all its peculiar action as being due to the paralysis of the motory centres. There is certainly some action upon the peripheral sensation (we do not use this as a scientific term), by which numbness is experienced; though every symptom proves that this numbness is not due to diminution of function in the nerves conveying the sense of pain, for the prick of a pin causes exaggerated pain. This peculiarity is very marked in cases of ac-

cidental poisoning from veratria, as well as by the local contact of the leaf or tincture of this plant upon the skin or mucous membrane.

So far as we can learn from our observations, the capillary circulation is not primarily modified by this drug.

*Brain.*—In none of our experiments were there any signs of cerebral lesion. The intelligence seemed to be perfectly retained almost to the moment of death. Indeed, in cases of poisoning in man this fact is corroborated. The animals could see, hear, feel and understand, so far as they ordinarily can. The only times that we examined the brain, there was apparently no cerebral apoplexy, congestion or anæmia, the only lesions which we should expect to find in a drug which causes death so soon after its administration.

*Stomach.*—The excessive vomiting met with in poisoning from this drug has caused us to investigate the condition of that vis-

cus, which only once did we find congested (Exp. VI.), and this we should suppose is accounted for by the fact, that digestion may have been going on at the time the drug was administered. The redness was not like that caused by an irritant, and in this case there was vomiting. Besides all these reasons the drug was administered hypodermically. Therefore, we conclude that the vomiting was not caused by the irritant action of the drug upon the mucous membrane of the stomach, but by irritation of the nervous periphery transmitted to the nervous centre, or of the nervous centre itself. Its effect upon the intestinal excretion being probably due to the same cause, we shall at present merely state that generally, though not always, an evacuation of the bowels occurs.

The secretion in the kidneys seems not peculiarly increased or diminished by this drug. Salivation, noticed in these experiments, is also, most probably, due to irritation, so called, of the nervous system, and

not on account of any increased vascular determination to the secreting glands. Our attention has not been especially directed to the other viscera by the symptoms noticed in our experiments.

*Spinal Cord.*—Veratria causes by its absorption, in a way that we cannot now define, a paralysis, or suspension, of the function of the spinal axis, or of the peripheries and termini of the nerves, and if carried to a certain extent, prevents the vital functions from being carried on, from which death results.

Prevost* attempts by a series of experiments to disprove this supposition, but the fallacy of his reasoning may be determined.

He noticed that, when the vessels of a limb were severed and the nerves intact, muscular rigidity did not exist; that, when the vessels were intact and nerves were cut, there was rigidity of the muscles. This experiment serves but to strengthen our supposition. By cutting the nerves,

* Commentaires Thérapeutique, &c., p. 610.

the nervous equilibrium is destroyed, and the muscular fibres contract in consequence, but if the nerves are whole and the vessels supplying these nerves with the vital fluid are severed, both nerves and muscular fibres lose their vital properties, as shown by Brown-Séquard in *Journal de Physiologie*, and there is no tetanic contraction. What renders Prevost's explanation of his experiment, viz., the direct irritation of the muscular fibres by the poisonous blood, more unsatisfactory is, that it is only by irritation of the peripheral nervous fibres that he produced this tetanic rigidity. The same effect is shown by the rigor mortis ensuing so soon after death.

As we do not presume to admit that there can be different and opposite physiological effects produced by different doses of the same drug, small doses of this drug enfeeble the spinal cord and modify the respiratory and circulatory functions; the former being first affected, as, on account of the embarrassment of the thoracic muscles, this

function would be suspended before that of the heart.

To prove more conclusively the effect of this drug upon the spinal cord, the following experiment was performed.

Exp. XII.—*A black and tan dog killed by asphyxiation; electrical conductibility of nerves.*

A wet towel was firmly held over and around the mouth of the dog, and the trachea compressed by the hand. For

0.10′. Imperfect respiration maintained; heart pulsates 66 per minute. After

13′. The head of the animal, now quiet, was immersed in a basin of water and maintained there till

20′. The cardiac pulsations could no longer be determined. The spinal cord was immediately exposed at the upper dorsal and lumbar vertebræ, at the latter place being slightly injured.

36′. The poles of the induction coil were applied to the cord at the places exposed, and there ensued slight contractions in the muscles of the back and trunk. The sciatic

40′. nerve was then exposed, and isolated on glass rods ; one pole of the coil being placed upon the dorsal portion of the spinal axis, and the other upon the nerve, caused the same muscular contractions. The same was true when the crural nerve, isolated in the same way, was touched by the two poles. The muscular contractility was as strong as usual. All of

45′. these experiments were concluded within twenty-five minutes after the death of the animal.

It may be here remarked, that the increased amount of carbonic acid in the blood (in consequence of death from asphyxia) may have prevented the muscular contractions from being as strong as we have seen in animals whose death has been caused in a different way or by another drug than veratria.

1 hr. 0′. *Autopsy.*—There was no rigor mortis ; muscular relaxation perfect. An examination of lungs showed some congestion of left lower lobe, and a marbriform appearance of the other lobes, which on being cut showed the same peculiarity.

A comparison of this experiment with those by veratria shows that though asphyxia was one, and, perhaps, the principal cause of death ; yet, the action of

this drug is not confined to producing asphyxia, for in the last experiment the electrical stimulation produced a different effect from what was caused in Expts. VI.*b*, and XI.

We can then accept van Praag's conclusion that death is caused by a spinal paralysis, until further experiments may show some other explanation of the phenomena.

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A CONTRIBUTION TO THE

# PHYSIOLOGICAL STUDY

OF

# VERATRUM VIRIDE AND VERATRIA,

*(With Experiments on Lower Animals, Made at La Grange St. Laboratory, 1869).*

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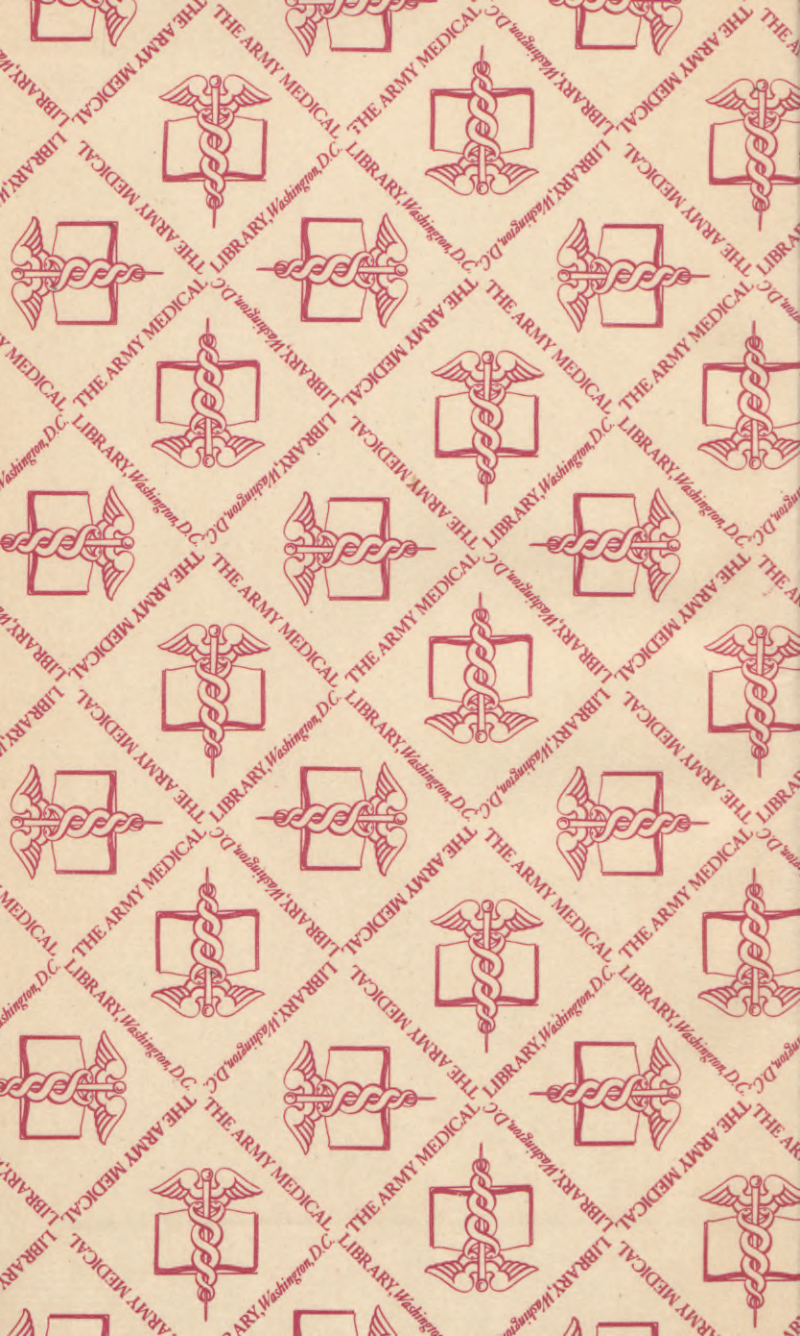
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