Notes of three lectures on the physiological action of strychnia / delivered by George Harley.

Notes of Three Lectures

ON THE

PHYSIOLOGICAL ACTION

OF

STRYCHNIA.

DELIVERED

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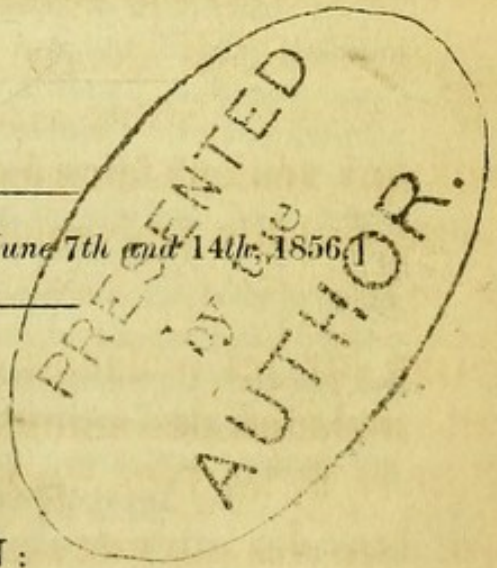

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ON THE

PHYSIOLOGICAL ACTION OF STRYCHNIA.

After one or two preliminary remarks, Dr. Harley proceeded to demonstrate by direct experiment — 1stly, the manner in which strychnia enters the system; 2ndly, its mode of action; and 3rdly, the way in which it destroys animal life.

The following is a brief summary of the remarks made :—

To the first question—How is strychnia or any of its compounds, all of which have a similar physiological action, received into the system?—the answer is, by absorption; the manner of this absorption being very various. The poison is absorbed by the mucous membrane of the stomach and intestines, when administered by the mouth, as in the case of the animal now operated upon (a frog); it enters directly into the circulation when introduced through a wound, as is now done. (Some solution of strychnia was introduced into the cellular tissue of another frog.) It is absorbed by the skin, as will be shown in the case of this third frog, upon whose back a few drops of acetate of strychnine are now poured.

The poison may, in fact, be introduced into the body in every conceivable manner: by the mouth or by the rectum; by the cellular tissue or by the organs; by the epidermis covering the external surface, or by the serous membranes lining the interior cavities of the body. When once the poison has entered the blood, its mode of action is in all cases identical.

The time required for the development of the poisonous qualities of strychnine varies, however, in different species of animals, and even individuals of the same species, being influenced by the age, strength, &c., of the animal. The rapidity

with which this substance kills depends, moreover, on three distinct causes:—*a*, the form, solid or fluid, in which the poison is administered, the latter form being the most favourable for absorption; *b*, upon the part of the body at which it is introduced, its action being the more speedy the quicker it obtains entrance into the circulation: for example, it affects the system more rapidly when injected into a vein than when given by the mouth (see below, second experiment on dog); it is absorbed much more rapidly when introduced into the thoracic or abdominal cavity than when applied to the skin. In proof of this I take two drops of a solution of acetate of strychnine, so weak that each drop contains not more than $\frac{1}{1000}$ of a grain; dilute still further with a small quantity of water, and divide the solution into two equal portions. In one portion I place a frog, in order that the strychnia may be absorbed into his body through the skin; the remaining portion I inject into the abdominal cavity of a second frog, exactly similar to the first in size. The frog into whose abdomen $\frac{1}{1000}$ of a grain of strychnia was injected will become tetanic very much sooner than the one into contact with whose skin an equal quantity of the poison has been brought.

The idea of employing frogs as tests of the presence of strychnia originated with Dr. Marshall Hall, and, so far as my experience goes, I consider this test the most delicate and the least liable to error of any with which we are acquainted. There exists, however, a method of administering the poison by which a far greater effect is produced, in a much shorter time, upon the animal, than when applied, according to Dr. Marshall Hall's recommendation, to the skin: I allude to the injection of the suspected solution into the thoraic or abdominal cavity. We may judge of the relative delicacy of the methods by the rapidity with which the poisonous qualities are developed. The frog into whose abdomen the $\frac{1}{1000}$ of a grain of strychnia was injected is already tetanic (in three minutes); the other has as yet exhibited no symptoms of being poisoned, and will not become tetanic before the expiration of at least an hour and a half.

The fatal effects of strychnia manifest themselves in a longer or shorter period of time, according to the amount absorbed. The result in the first three frogs, operated upon by three different methods, the poison being given by the mouth, through a wound, and by the skin, is seen to be similar in all.

Each is suffering from convulsions, and these convulsions are of the kind usually termed tetanic, from the spastic rigidity of the voluntary muscles. One of the frogs, you observe, is in a state of emprosthotonos; its hind legs are stretched out, its back is curved upwards, its fore-legs are crossed upon its breast, and its hands tightly pressed against each other, while its head is bent inwards; and, during the spasm, the animal, were it not for its fore-legs being crossed upon its breast, would rest entirely upon the point of its nose and the toes of its hind-feet. Emprosthotonos is not the only form which the complaint assumes in the frog. The frog to which the strychnia was administered through a wound is in a state of opisthotonos; his head is thrown back, his hind-legs are slightly raised, and he rests entirely upon his belly and fore-legs. In the human subject labouring under tetanus, opisthotonos is most common; while in the frog, judging from my own observations, emprosthotonos seems more frequent. All three animals before us have lock-jaw.

The spasms, though they follow each other rapidly, are not, you will observe, continuous; and the intervals between them are longer if the animal is allowed to remain quiet. A knock on the table, a stamp on the floor, or even the mere scratching of the tablecloth in the vicinity of the animal, induces a paroxysm. This arises from the superexcited state of the nervous system, and must not be regarded as a symptom peculiar to tetanus; for it is occasionally observed in other diseases. Seven years ago I had under my care a child suffering from tabes mesenterica, ending in perforation of the bowels. In this case the slightest noise in the room, as the falling of a key or spoon, would bring on spasm of the abdominal muscles; and from the noise of the flatulence and the undulations of the abdominal walls during a paroxysm, I even believed that there was a severe peristaltic action of the intestines, their involuntary muscles, which are as we well know exceedingly sensitive to mechanical irritation, having been thrown by the mere noise into violent action.

The next point to be considered is, the action of strychnia upon the body. It was formerly believed that all poisons which killed rapidly acted by a direct influence upon the nervous system. This is, however, a mistake, as no poison can injure or destroy life before it has entered the blood. The application of strychnine to a nerve will never produce poison-

ing, nor can a nerve serve as the channel of introduction of poison into the system. In proof of this, I take a frog, the tissues of one of whose hind-legs have been completely cut through, (experiment first proposed by Magendie,) with the exception of the nerve which still serves to attach the limb to the body. This leg, thus hanging only by the nerve, is introduced into a solution of strychnia, and not the slightest symptom of poisoning will ensue. In another frog the tissues of a hind-leg, including the nerves, are cut completely through, with the single exception of the femoral artery and vein, which still remain to keep up the communication between the body and the amputated limb. Distinct symptoms of poisoning will appear soon after I place this limb in the very same solution of strychnia as in the last case.

The strange fact that a poison acting so powerfully upon the nervous system as strychnine should remain harmless when brought into immediate contact with the nerves themselves can, according to Stilling, be clearly explained by experiment. If a few drops of a solution of strychnine are allowed to fall upon the exposed spinal cord of a frog, the animal will in a few minutes become tetanic; while if, in another case, the spinal marrow be divided into an anterior and a posterior half, and strychnine be carefully applied to one of the portions, tetanus occurs only in that part of the body supplied by nerves arising from the portion of the spinal cord brought into contact with the poison. The remainder of the body is not affected. A portion of the body of a frog may be rendered tetanic in the same way as the whole body. (Upon the upper half of the severed body of the frog a few drops of strychnia were poured, and it became tetanic in the course of a few seconds.)

If the aorta be tied, and strychnia afterwards administered by the mouth, no symptoms of poisoning will ensue. When the vessels of one of a frog's hind legs are tied, and strychnine is given, tetanus occurs in the whole body, including the limb whose vessels are ligatured. If, however, the nerves of the limb are cut, and the vessels left free, tetanus occurs throughout the body, with the single exception of the limb with the divided nerves. This proves that strychnia stimulates the spinal cord similarly to galvanism. When administered by the mouth, it reaches the spinal cord only through the blood; no effect is therefore produced if the circulation be interrupted.

The artificial disease, tetanus, has no seat in the limbs, and

the tetanic spasm of a limb is produced by no superexcited state either of its nerves or muscles, but by a stimulus derived from the spinal cord, and acting through the nerves. During the tetanic paroxysm, I divide the nerve supplying one of the hind legs of a frog, and the spasm in that limb, you observe, instantly ceases. Tetanus, therefore, does not exist in the limb itself.

To show still further the total absence of superexcitement in the limb, I will compare the amount of muscular irritability produced by applying a direct stimulus, in the form of galvanism, (by means of the galvanic forceps,) both to the nerves and muscles in the limb of the poisoned animal, with the amount of irritability yielded by a healthy frog, prepared according to Galvani's method. Thus you see demonstrated, by direct experiment, not only the total absence of super-irritability in the limb of the poisoned frog, but the existence of even a lower degree of irritability than is found in the healthy animal.

Having seen that strychnia is absorbed by the vessels, and not by the nerves, the next point is, to determine the class of vessels, lymphatics, or veins to which this property is to be assigned. If the jugular vein of an animal be dissected from the surrounding tissues, and a piece of card passed under it, a few minutes after a solution of strychnia has been dropped upon the vein, symptoms of tetanus will supervene, and these can be interrupted by ligaturing the vessel, (Magendie.) When, after the thoracic duct has been tied, strychnine is introduced into the intestines, poisoning still takes place, (Brodie.) Magendie observed that when an animal had been fed, and the lymphatics divided after they had become distinctly visible, the animal was easily poisoned by introducing strychnine into the intestines; and Segalas has pointed out, that if the bloodvessels are ligatured, and the lymphatics left entire, poisoning does not occur in an hour. This experiment will now be demonstrated on two large frogs.

I begin by ligaturing this large vein, which you see on the inner surface of the anterior abdominal wall, a vein which does not exist in quadrupeds, but only in certain reptiles. I next ligature the portal vein, and into the loop of intestines contained between two ligatures introduce a few drops of a strong solution of strychnine. In this second frog, all the vessels, the veins as well as the lymphatics, are left free, and a similar quantity of strychnine introduced as in the former case into the loop of intestines included between two ligatures. In the

first example, where the bloodvessels are ligatured, and the lymphatics alone left free, no symptoms of poisoning will occur up to the termination of the hour. In the latter case, where none of the vessels are tied, tetanus will supervene within five minutes. (This took place, entirely confirming the assertion of Segalas.)

To sum up the manner in which strychnia acts upon the body, the foregoing experiments have shown, that to produce symptoms of poisoning, strychnia must be absorbed by the bloodvessels, in order to reach the spinal cord; that it cannot be conveyed thither by the nerves; that the spinal cord alone is the seat of the artificial disease; that it is the nerves which, though not superexcited themselves, convey the effects of the disease to the circumference of the body. In a word, the vessels convey the poison to the spinal column, the spinal column becomes supercharged like a Leyden jar, and the nerves are the wires which distribute the shocks.

The third and last point to be determined is—the manner in which strychnia destroys life. This is still an open question. According to some authors, animals poisoned by this substance die in three ways: Firstly, from exhaustion; secondly, from asphyxia induced by spasmodic closure of the glottis; and thirdly, from suffocation, arising from the spasms which affect the respiratory muscles and put a stop to the breathing process.

Not one of these views appearing to me satisfactory, I shall not offer any remarks on the subject, but at once proceed to experiment, leaving you to form, from the results obtained, your own estimate as to the correctness or incorrectness of one or all of these theories.

Into the thoracic cavity of a dog I inject half a grain of the acetate of strychnine; you observe, he at once begins (in thirty-six seconds) to become tetanic. The eyes are starting from their sockets, and the pupils are widely dilated; the spasms cease (in one minute and a-half); the limbs become relaxed; there is no perceptible pulse; no respiration can be detected; (the thorax of the dog was speedily opened); the heart is seen to quiver feebly but twice; it has now ceased to beat, and the animal is dead. What has been the cause of death? Certainly not exhaustion: the number of spasms and their duration—two minutes at most—preclude this idea. Let us proceed to test on another animal the value of the two remaining theories regarding the mode of death by strychnia.

In order, in the first place, to determine if animals poisoned by strychnine die from suffocation, in consequence of closure of the glottis, I shall perform tracheotomy, and introduce a wide tube into the windpipe of a dog before poisoning him. If he dies, it is clear that death cannot possibly result from air not entering the trachea, as the opening in the tube will admit an abundant supply. (Experiment suggested by Professor Sharpey.) If the animal exhibits signs of approaching death in spite of the complete freedom of the passage for the admission of air into the lungs, I shall immediately supply to those organs, by means of an artificial respirator invented by Dr. Marcet, the amount of air necessary for the maintenance of life. This will determine if the symptoms of suffocation are caused by spasm of the respiratory muscles. If the animal dies, in spite of the artificial respiration, we shall have obtained proof that strychnine does not suffocate by spasm of the respiratory muscles, and shall be forced to seek another explanation of the cause of death. [The trachea of a full-grown small dog was laid bare, and a glass tracheotomy-tube of large calibre inserted into it, without appearing to cause the slightest inconvenience to the animal. The jugular vein on the right side was next dissected from the surrounding tissues, and a solution containing $\frac{1}{12}$ of a grain of acetate of strychnine carefully injected into the vessel. In four seconds, before the nozzle of the syringe could be removed from the vein, the animal became tetanic, the spasms rapidly following each other, and during the first thirty seconds gradually increasing in intensity. The convulsions of the voluntary muscles of the limbs and of the semi-voluntary muscles of respiration were not continuous. On placing the hand in front of the tracheotomy-tube, the air was felt to be expired by sudden jerks, and, from the frequency of the respirations and the force with which the air was expelled, the animal seemed to breathe more than in his normal state. In fifteen minutes, when the animal began to gasp as if for air, notwithstanding that an abundance seemed to be supplied, artificial respiration was resorted to, and not interrupted until the gasping ceased and the animal appeared more easy. The pulse was 104, and the artery felt at times to the finger as if affected by spasm. There was no lockjaw. As the gasping returned, artificial respiration was again kept up for a few minutes. The animal again appeared relieved, but in a very few minutes symptoms of im-

pending suffocation recurred. The artificial respiration was this time found to be unsuccessful.* Twenty-eight minutes after the administration of the poison the pulse ceased; and though artificial respiration was kept up during nearly a quarter of an hour, it failed to restore the animal to life.] The experiments made prove that death from strychnine may occur independently, 1st, of exhaustion; 2nd, of asphyxia from closure of the glottis; and 3rd, of suffocation from spasms affecting the respiratory muscles.

It was a remarkable circumstance in the case of the last animal operated upon, that while a large interchange of gases was constantly occurring in its lungs, it presented all the appearance of an animal dying for want of a sufficient supply of air. This must have arisen from the fact that the oxygen in the lungs was either not absorbed into the blood, or not assimilated after absorption. The absorption of oxygen by the blood being a purely physical process, we must, in the absence of any reason for its non-absorption, set the first hypothesis aside. The second seems less open to objection, particularly if we consider the results of some experiments which I made on the action of strychnine upon the blood.† I found that strychnia, as well as brucia, possessed the property of diminishing the power of the constituents of the blood to take up oxygen and yield carbonic acid. For example:—

Experiment 1.—A certain quantity of fresh calf's blood was first shaken with renewed portions of air until it had become thoroughly saturated with oxygen, then introduced into a graduated glass vessel with 100 per cent. of ordinary air, corked carefully up, and kept during twenty-four hours in a room of moderate temperature. In order to favour the mutual action of the air and blood, the vessel was frequently agitated. At the expiration of the twenty-four hours, the gas was analyzed by Bunsen's method, and the following was found to be its composition. In 100 parts—

Oxygen	11·33
Carbonic acid	5·96
Nitrogen	82·71
	100·00

* This experiment has been five times repeated, and the results have been found uniform.

† The experiments in question are extracted from a series made at Heidelberg, in 1855.

A second portion of the same blood, to which 0·005 grams of strychnine were added, was confined with the same quantity of air, for the same time, and treated in every respect in a similar manner. The gas yielded in this case—

Oxygen	17·82
Carbonic acid	2·73
Nitrogen	79·45
	100·00

On comparing the result of the first analysis with the composition of the common air (oxygen 20·96, carbonic acid 00·002, nitrogen 79·038) which had been introduced into the vessel, it is seen that 9·63 oxygen had disappeared, and 5·96 carbonic acid now exists where only a trace of its presence could be detected. In the second experiment, where the strychnine was present in the blood, no more than 3·14 oxygen had disappeared, and only 2·73 of carbonic acid had formed. Thus it is seen that strychnine possesses the strange property of preventing the constituents of the blood from absorbing oxygen and exhaling carbonic acid, and of thus becoming fitted for the purpose of nutrition. Strychnine is not the only alkaloid obtained from the nux vomica possessing this power; for brucia I found to act in a similar manner, though its effects were less marked. For example: a certain quantity of blood from another calf was confined with the same quantity of air, and treated in exactly the same manner as in the foregoing cases. At the expiration of twenty-four hours the analysis of the gas confined with the pure blood yielded—

Oxygen	6·64
Carbonic acid	3·47
Nitrogen	89·89
	100·00

While that confined with blood to which had been added 0·005 grams of brucia gave—

Oxygen	11·63
Carbonic acid	2·34
Nitrogen	86·03
	100·00

Thus proving that brucine, like strychnine, possesses the property of diminishing the power of the organic consti-

tuents of the blood to unite with oxygen and give out carbonic acid.

If the same action takes place in the blood circulating in the living animal as we here find to have occurred out of the body, a direct explanation is at once afforded us why the dog upon which we experimented should feel a want of oxygen, notwithstanding that a quantity sufficient to support life in the healthy condition of the animal was supplied. The animal, probably, was dying, not for want of the presence of a sufficient quantity of oxygen in its blood, but because the constituents of its blood could not assimilate the oxygen. The convulsions would not, in this case, be caused by the stimulating effect upon the spinal cord of an excess of carbonic acid in the blood; for strychnine and brucine, we have seen, acting upon blood removed from the body, cause its constituents to absorb less oxygen and exhale less carbonic acid than in a normal state. There would be therefore no excess of carbonic acid. The convulsions were probably due to disordered nutrition; the spinal cord receiving nutritive materials which, not having undergone the oxidizing process, were unfit for assimilation. A derangement of the functions of the nervous system would be the result.

Post-mortem Examination of the Dog killed by $\frac{1}{12}$ of a grain of strychnine, made twenty-four hours after death.—Rigor mortis had disappeared (it was very marked eighteen hours after death); the apex of the heart felt excessively hard, as if the muscle were in a state of rigor mortis; the right side of the heart was full of blood, the left side contained but little. Contrary to the general idea, the blood was found partly coagulated. No other appearance worth noticing was presented.

May not death have occurred by failure of the heart's power? It is generally supposed that venous blood excites the heart's action. I think, on the contrary, that the beatings of the heart are excited by the act of nutrition—i. e., by the stimulus given when oxygen is absorbed and carbonic acid exhaled. For if we put a frog's heart into an atmosphere of oxygen, it continues to beat for a very long time, whereas if it is placed in carbonic acid, the pulsations cease in a few minutes. With the cessation of the chemical changes, for the want of oxygen, the beatings of the heart are arrested.

In frogs suffering from the effects of strychnia, the heart remains almost to the last free from tetanic spasm. In this frog you will observe, although the voluntary muscles are

affected with severe tetanic spasm, the involuntary muscles of the heart continue to act rhythmically. This small quantity of solution of strychnine, however, which I drop upon the organ, will soon produce tetanic spasm of its muscles. (I saw Professor Arnold perform this experiment. I am not aware of its being published.) The circulation, in the web of a frog's foot, seen through the microscope during the tetanic spasm, is observed to be momentarily arrested during the spasm, and then to bound onwards with a sudden jerk.

Here is a frog which was poisoned with strychnine two days ago. While the tetanic paroxysm was very severe, $\frac{1}{500}$ of a grain of Wourali poison was introduced into the cellular tissue. In ten minutes, the limbs had become perfectly flaccid, and no irritation induced a spasm. Two hours afterwards, conceiving the animal to be perfectly dead, I opened it, and was astonished to find the heart beating rhythmically. The next day, the heart was found still beating, and the circulation in the web of the foot slow, yet regular. Galvanism applied to the limb accelerated the circulation. Up to the present moment (fifty hours) the animal has not presented the slightest sign of life; and yet you see circulation continues.*

I have already mentioned, that I consider the physiological test the most reliable one for strychnine; and the method of applying it appears to be by injection into the thoracic or abdominal cavity. When the poison reaches the lungs, it seems to act most speedily. This is easily explained by the rapidity with which the poison will be absorbed into the blood through the pulmonary capillaries. Into this small frog I inject $\frac{1}{2000}$ of a grain of acetate of strychnine; into this other, $\frac{1}{4000}$. You may judge by the rapidity with which the symptoms of poison-

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* Wourali and strychnine have, I find, the effect of reciprocally neutralizing each other, according as the one or the other poison is in excess. Being occupied with experiments on the subject, I shall only cite three:—

1st. A frog was poisoned with $\frac{1}{500}$ of a grain of Wourali. Three minutes after it had become perfectly insensible, $\frac{1}{120}$ of a grain of strychnia was injected. In five minutes it became tetanic.

2nd. A frog was poisoned with $\frac{1}{120}$ of a grain of strychnia. Three minutes after tetanus was strongly marked, it was punctured with $\frac{1}{500}$ of a grain of Wourali. In seven minutes tetanus disappeared.

3rd. $\frac{1}{500}$ of a grain of Wourali, and $\frac{1}{40}$ of a grain of strychnia, were injected into the abdomen of a frog at five minutes past one; at ten minutes past, it became very tetanic; at half-past one (twenty minutes afterwards) it became perfectly flaccid; and the next day it appeared perfectly well. This is the more astonishing, as the dose of strychnia in this case was certainly more than sufficient to kill it. Thus, it would appear, that strychnine might be used as an antidote for Wourali, and Wourali for strychnine.

ing will ensue, how delicate the tests are, (both frogs became tetanic in less than ten minutes). A third frog became tetanic with only $\frac{1}{8000}$ of a grain.

In order to apply either the physiological or the colour-test to strychnia, we must first have the substance in a pure state. If, therefore, we wish to test for its presence in the digestive canal, tissues, or blood, we must first seek to separate the strychnine by a chemical process. The method I adopt, and which appears to me desirable from the ease and rapidity with which it can be applied, I shall now demonstrate to you in analyzing the blood of the dog killed with $\frac{1}{12}$ of a grain. We take the blood from the heart and large vessels, mix it with twice its bulk of distilled water, coagulate by boiling, and acidify it with a few drops of acetic acid. The acid is added for two reasons:—first, to ensure the complete coagulation of the albuminous compounds; secondly, to retain the strychnine which had been introduced into the blood as an acetate, in that state, or, if changed into another salt, to retransform it into an acetate. Our next point is to decolorize the blood; and that can be most rapidly and most effectually done by filtering it, as is now done, through crystals of sulphate of soda,—(this idea, as well as that of decolorizing the blood by boiling it with sulphate of soda, belongs to Professor Bernard,)—or through animal charcoal. The clear filtrate is now to be concentrated, and the strychnine precipitated by the addition of potash, (which, by combining with the acetic acid, sets the strychnia free.) The strychnine is next to be collected on a filter, washed, and redissolved by acetic acid. When thus purified, the physiological test is to be applied in the manner already pointed out. In the blood of the dog poisoned by $\frac{1}{12}$ of a grain of acetate of strychnine, none of the poison was detected in the blood.

POSTSCRIPT.

Since the foregoing notes were in the hands of the printer, I have made several experiments, and found the following important results:—

1. *Value of the physiological test.*—Into the lungs of a *very small* frog was injected a solution, containing only $\frac{1}{16000}$ of a grain of the acetate of strychnine, (equal to about $\frac{1}{18000}$ of the

pure alkaloid;) in nine minutes and a half the animal became violently tetanic, and died in two hours.

2. Strychnine *does not* prevent the blood of animals coagulating after death; in some cases it even appears to hasten that result.

3. Death is ushered in by flaccidity of the voluntary muscles.

4. The pupils dilate during the spasms, and contract in the intervals, especially if the latter are well marked.

5. The flesh of animals killed by minimum doses of strychnine does not poison other animals—at least, I have fed a hedgehog on poisoned flesh during fourteen days without being able to detect the slightest symptom of poisoning. The poison must, therefore, have been either decomposed, or not present in sufficient quantity.

6. In animals poisoned by strychnine, the pulsations of the heart cease, notwithstanding artificial respiration being regularly kept up; but after a longer period than when no artificial respiration is employed.

7. In cases of poisoning by strychnine the muscles of the heart rapidly lose their irritability.

8. When animals are killed by large doses, the heart almost instantly loses its power of contraction, and mechanical or galvanic stimulus soon fails to re-induce it.

This can be explained by the following experiments:—

9. If the hearts of two frogs be removed from the body, and one placed in pure distilled water, the other in a solution of acetate of strychnine, the former will pulsate regularly for more than an hour, the latter will cease to beat in from one to five minutes, according to the strength of the solution of the poison. Rigor mortis speedily supervenes.

10. When the hind-legs of a frog prepared after Galvani's method are placed in separate vessels, one containing simply distilled water, the other a strong solution of the acetate of strychnia, the muscles of the former limb will continue to contract when galvanism is applied, either directly to the muscles themselves or through the medium of the nerves, long after those of the limb suspended in the poison have lost their contractile property, and perhaps even passed into a state of rigor mortis.

It would thus appear that strychnine has the power of directly destroying muscular irritability.

Valentin and others have shown that the lower extremities

of a frog, when freed from the skin, absorb oxygen and exhale carbonic acid in definite proportion so long as muscular irritability continues, and have also pointed out that when irritability ceases, an important change takes place in the amount of oxygen absorbed and carbonic acid exhaled. In my experiments on the blood, strychnine was found to destroy the property possessed by the organic constituents of the liquid to absorb oxygen and exhale carbonic acid. May strychnia not act in a similar manner upon the muscles and other tissues of the body? Upon this supposition we can easily explain why the heart ceased to pulsate, and the voluntary muscles to respond to the stimulus of galvanism, when placed in a solution of strychnine, as well as to account for the fact that in animals poisoned by strychnine the irritability of the voluntary and involuntary muscles, as well as the excitability of the nerves, disappears more quickly than when life is destroyed by other means.

Dr. Brown-Séguard thinks that the action of strychnine "consists in an increase of nutrition of the nervous centres, by which excess of nutrition the reflex faculty becomes much increased." The deeper I go into the subject the farther I differ from this view, and the more am I inclined to believe that strychnine acts by destroying the power of the tissues and fluids of the body to absorb oxygen and exhale carbonic acid; in a word, from thus arresting nutrition by preventing the interchange of the gases in the animal economy.