Researches on strychnine / by I. L. Crawcour.

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RESEARCHES ON STRYCHNINE.

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The recent trial in England, of poisoning by strychnine, has invested this alkaloid with a peculiar interest, and will probably cause its properties to be at length fully investigated. It is astonishing what misconceptions and mis-statements are to be found, even in the works of the best authors, respecting it. According to Brande, and the statement is corroborated by Gregory in his Organic Chemistry, it is "neither fusible nor volatile and insoluble in alcohol and ether"—our own experience is diametrically opposed to this assertion. Like all the organic radicals, it is decomposable at an elevated temperature, but by a proper management of heat it may be divided into two distinct substances, each possessed of peculiar properties, and is very soluble in ether.

Strychnine, as we ordinarily find it in commerce, is crystalline, very slightly soluble in water, exceedingly bitter, soluble to but a slight extent in cold alcohol, and composed of the following elements, viz.: carbon 44, hydrogen 24, oxygen 4, nitrogen 2. On exposing it to a moderate heat, it fuses into a brownish liquid, and on increasing it to about 600° F., a portion sublimes, and may be condensed in a cool receiver, while a peculiar resinous and viscid solid remains behind; on still further increasing the heat, the resin is burnt off and a bulky coal is left. As it is solely in the sublimate that the peculiar properties of strychnine are found, I propose distinguishing them as follows: the sublimate we will call strychnine proper, the resinous residue, strychnine extractive. The sublimed strychnine or strychnine proper, condenses in fine arborescent crystals, is like ordinary strychnine exceedingly bitter, is insoluble in cold alcohol, and re-

acts like ordinary strychnine, with the usual tests. The strychnine extractive, is viscid, freely soluble in cold alcohol, exhales when burnt an odor resembling the Tonka bean, is of a fine green color, and as far as I have hitherto examined it, is tasteless. Dissolved by sulphuric acid, it changes to a dirty brown solution, failing to give the usual re-action with bichromate of potass, or any of the strychnine tests. It is highly probable that in the sublimate alone, the medical properties of strychnine are to be found, and as the proportion in which it exists in the alkaloid of commerce is not very large, we may by subliming it, become possessed of a product, whose powers may be enormously increased, while the dose may be infinitely small. Time has not yet allowed me to investigate the properties of the extractive, it is probable it may exert a tonic action devoid of the poisonous principle of its congener. I propose at a future day to enter more fully into its history. I may mention, that the sublimate entirely volatilizes at about 300° F.

The tests for strychnine are well marked, and as far as I have seen, are free from fallacy. Dissolved in acetic acid, it gives a yellow precipitate with chloride of gold, and on boiling, the liquid assumes a pink color. If a crystal be dissolved in concentrated sulphuric acid, and a few grains of powdered bichromate of potash be added, an intense violent hue will be developed at each point of contact, spreading through the whole liquid, gradually shading off to a blue and ultimately into pink ; if instead of bichromate of potash, we use peroxide of manganese, or lead, a similar effect is produced.

The tests are of extreme delicacy, especially the bichromate test. I took a grain of strychnia free from brucia, and dissolved it in a thousand minims of water—each minim consequently contained the one thousandth of a grain—by this means I could ensure the most perfect exactness in determining the limits of each test. I found, that while with the peroxides of manganese and lead, the defining limit was fixed at about the three thousandth of a grain ; with the bichromate of potash, I could with the most perfect ease detect the forty thousandth, and by varying the manipulation the sixty thousandth of a grain. With these minute quantities, it is requisite that the strychnia should be in crystals, and perfectly dry. The following was the mode of manipulation : one minim containing the thousandth of a grain of strychnia, was diluted with sixty minims of water, and of this one minim was taken and dropped upon a piece of clean white porcelain—the cover of a Berlin porcelain crucible forms an admirable in-

strument—this was evaporated to dryness on a water bath; when cold, a minute drop of strong sulphuric acid was placed in the centre of the plate, and a small portion of powdered bichromate of potash taken up on a finely pointed glass rod; by moving this about in the acid and running the rod over the plate, lines of an intense blue, rapidly changing into red, were produced whenever the rod came in contact with the strychnia. In experimenting upon these minute quantities, two things are necessary, first that the strychnia shall be perfectly dry, (the minutest quantity of moisture defeats the experiment), and secondly, that the heat shall be most carefully applied, as otherwise decomposition of the alkaloid ensues, and the test is of no avail. I have little doubt that by a moderate amount of patience and care in manipulation, the hundred thousandth of a grain of strychnia might be discovered by this test. I must be understood, however, to refer to strychnine wholly unmixed with any other salt, or organic matter. We are simply now examining the limits of defining power. So easily is strychnine detected, that if a drop of water containing the thousandth part of a grain be allowed to dry on a glass slide, a large space will be found covered with crystals, forming a most beautiful microscopic object, and the forty thousandth of a grain is distinctly visible to the naked eye. Much has been said, and I think without any show of reason as to the fallacy of colored tests, but the fact is that both in inorganic and in organic analysis, we depend entirely upon the color of precipitates for the detection of substances. No one has yet questioned the fact, that, if on adding the ferrocyanide of potassium to a colorless solution we get a blue precipitate, iron must undoubtedly be present, or if a red color be produced by addition of perchloride of iron, which color is not destroyed by solution of corrosive sublimate, a salt of opium is present. The tests for copper, arsenic, bismuth, hydro-cyanic acid, iodine, and a host of others, all depend upon the peculiar colors, produced by the action of re-agents, and no one has yet questioned their accuracy, and I consider the peculiar blue, produced by bichromate of potassa and sulphuric acid, on a salt of strychnia, to be as fully distinctive as any of the above. The fact is, that in medico-legal investigations, we must not be satisfied by any *one* test—but each must be rendered corroborative of the other. No one would positively swear to the presence of arsenic, from the yellow precipitate produced by the ammonio-nitrate of silver, but if the same solution should in addition give a green color, with ammonio-nitrate of copper, I question whether we should have any doubt of the presence of the poison. In like manner, if we have a

salt, which in addition to the above color produced by bichromate of potash and sulphuric acid, should give the same hue, with peroxide of lead, and have an intensely bitter taste, I do not think we could doubt the presence of strychnia, and any two of the above would be sufficient.

The detection of the poisonous alkaloids, when taken into the system, is frequently extremely difficult, and this may depend upon two causes. First, the extreme tenuity of the quantity necessary to destroy life, by which its separation in a crystalline form is rendered nearly impossible; and, secondly, the probability of the conversion of the poison into some other substance, by the action of the vital force of the organism. At present I am strongly inclined to believe in this doctrine, especially when the poison is exhibited in very minute quantity. It is exceedingly likely that the portion detected may be the unabsorbable surplus, and that the portion which has performed its deadly work, is changed by the process of absorption and digestion to which it has been subjected. All organized bodies are unstable, and none more so than those into whose composition nitrogen enters, and we have already seen that by a slight increase of temperature, strychnia is changed into two substances. Metals and metalloids being elements are unchangeable, and must be absorbed as such. Arsenic circulates as arsenic throughout every particle of the system, and iodine may be detected in all the emunctories as iodine; but with compound bodies the case is different, and it is probable that the organism is capable of taking up and converting to its own use a portion even of the most deadly poison, and that it is only the surplus, whose presence has paralyzed the organs of assimilation, which can be detected. No chemist would venture to assert that caffein and thein exist as foreign bodies in the system. We know that they subserve to its wants, but there is no question that if a large quantity were taken, a portion would escape absorption, or might pass unchanged into the excretions. So with quinine, between whose composition and strychnine there is a strong chemical analogy, a dose of one or two grains is absorbed and assimilated, a large quantity undoubtedly would remain as quinine, and might be distinguished by the ordinary tests. We must not forget that the word poison is but a term of comparison, and that all the articles of the materia medica, and even some of daily food, are poisons, if administered in sufficient quantity. To assert, therefore, that the minutest quantity of any poison can be detected in the human body, because an infinitesimal quantity can be detected out of it, is to assert a dogma, that yet remains to be proved. It is possible that improved methods

of analysis may yet lead to the proof that change does not take place within the organism, but all I can say, at present, is, that analogy is strongly in favor of the contrary view. Both views require to be diligently investigated, and we can only arrive at the truth by administering to animals the minutest doses of any organic poisons, that will cause death, or even such as are insufficient to destroy, and then searching in all the tissues for the poison. It was stated on the trial of Palmer, by those opposed to the view I have been advocating, that although strychnine could be detected when administered in the smallest quantity, nux vomica, could not. Now this statement is simply an absurdity. Strychnia being the active principle of the nux, undoubtedly ought to have been discovered, if the analyst were as capable as he represented himself to be. Dr. Taylor mentioned, that he had given to a rabbit two grains of strychnia, and had detected the poison, with ease; to another he had given one grain, and could only perceive a bitter taste; in a third killed by half a grain, no trace of the poison existed. It would seem, therefore, that half a grain is the quantity capable of assimilation in a rabbit. In order to examine for myself, I gave to a rabbit half a grain of strychnia, and to render it more easy of absorbtion, and more difficult of detection, I administered it in a solution. The next day I made a rigid and searching analysis, but could find no trace of strychnia. I intend, however, to carry on still further the investigation, and shall report my progress in the Journal. The rabbit died in half an hour, and as its mode of death was somewhat at variance with what has been supposed to be the mode of death by strychnine, I append a description of the phenomena. Five minutes after the administration of the poison, the animal was seized with an universal trembling; in eleven minutes it walked with difficulty, and a tetanic spasm was produced on touching it. Soon after it was seized with an universal tetanic spasm, and its breathing was very rapid—the spasms were attended with perfect relaxations—the hind legs became paralyzed, the fore legs being unaffected. In about twenty minutes it began to utter faint moans, the spasms still continuing though alternating, with long intervals of perfect relaxation: tetanus could at any time be induced by a light touch, but firm pressure seemed to give relief. In about twenty-five minutes, it was seized with a violent convulsion, which lasted some time, and then passed off, leaving the animal perfectly relaxed, in which state it died seemingly of exhaustion. After death, the body was perfectly flaccid, and presented no appearance of having died from the administration of a poison, which is said always to produce the most intense rigidity. The symptoms were those of death from exhaustion.

We are indebted to Dr. Marshall Hall for a very interesting physiological test for strychnia, viz: its influence upon the frog, even in very minute quantity. Subjoined are a series of experiments performed by my colleague, Dr. Brickell, and myself, with this test, and it will be seen that by modifying Dr. Hall's mode of experimenting, we have succeeded in producing the characteristic phenomena, even with the four-thousandth of a grain:

EXPERIMENTS WITH STRYCHNIA, CONDUCTED BY DRS. I. L. CRAWCOUR AND D. W. BRICKELL.

Experiment No. 1—*Class* 1.—Aug. 7th, 25 minutes past 12, placed a large and very active frog in two ounces of water containing 1-1000th of a grain of strychnia—water just deep enough to cover about one-third of the animal in a sitting posture; 8 minutes to 2 P. M., no effect perceptible. Animal allowed to remain in the solution.

Aug. 8th, 15 minutes to 12, returned, and found the animal sitting in the solution, and to all appearance as well as when first placed there.

Experiment No. 1—*Class* 2.—Aug. 7th, 12½ o'clock, placed a medium sized frog in an ounce of water containing 1-1000th of a grain of strychnia; water deep enough to cover the whole body, but allowing the head to be out. The skin of this frog is of lighter color than No. 1, and the animal has a much more delicate appearance, though it is very active.

Eleven minutes to 1 P. M., convulsive twitches—straightens out the hind legs and throws himself against the side of the glass; 24 minutes after 1, same tetanic movements; 2 P. M., spasms have continued with intervals of repose, to this time. Now very sick, head drops under the water. Now taken out of the water and laid on the table—lies on his back, with rigid limbs, and no respiratory action. Apparently dead, yet slight tetanic spasms induced by touching with a straw.

Experiment No. 1—*Class* 3.—Aug. 7th, 23 minutes to 1 P. M., injected a large and strong frog, through a puncture over the lower portion of the spine, with an indefinitely strong solution of strychnia. Did this to elicit the phenomena of strychnism in the animal. Twenty minutes to 1, violent spasms—legs extended and rigid, arms drawn closely over the chest—animal apparently dead, though twitches of the extremities are readily excited by touching him with a straw.

Experiment No. 1—*Class* 4.—Aug. 7th, 14 minutes to 1 P. M., injected a strong and large frog, through a puncture over the spine, with 1-2000th of a grain of strychnia. One quarter past 1, tetanic spasms

commenced—decided, and easily excited by the slightest touch; 25 minutes after 1, intervals of repose, but tetanic spasms easily excited. Lies on his back without effort to turn over. Respiration very slow and labored; 2 P. M., nearly dead.

Experiment No. 2—*Class* 4.—Aug. 7th, quarter after 1 P. M., injected small and delicate, though very active frog, through puncture over spine, with 1-2000th of a grain of strychnia; 17 minutes after 1, violent tetanic spasms—animal straightened out and perfectly rigid; 18 minutes after 1, quiet, but respiration labored; 20 minutes after 1, apparently dead, though strong convulsive twitches of extremities are elicited by touching; 25 minutes after 1, same movements readily excited, though the animal seems otherwise entirely dead; 23 minutes to 2 P. M., animal perfectly rigid—no further muscular action.

Experiment No. 1—*Class* 5.—Twenty-five minutes after 1 P. M., injected a small and delicate, though very active frog, through puncture over spine, with 1-4000th of a grain of strychnia; 24 minutes to 2 P. M., animal sitting quietly, though respiration very labored. Touched him with a straw, and threw him into violent spasms; 14 minutes to 2, tetanic spasms violent; 12 minutes to 2, violent spasms at intervals; lies with limbs extended and rigid; was nearly dead when we left him.

Experiment No. 2—*Class* 5.—Aug. 8th, 15 minutes to 1 P. M., injected a feeble medium sized frog, through puncture over spine, with 1-4000th of a grain of strychnia; 13 minutes to 1, violent spasms; 12 minutes to 1, animal apparently dead; 9 minutes to 1, slight twitches of extremities when touched; no other signs of life.

Experiment No. 3—*Class* 5.—Aug. 8th, 11 minutes to 1 P. M., took frog of "experiment No. 1, Class 1," (to all appearance as healthy and active as ever) and injected 1-4000th of a grain of strychnia over the spine; 4 minutes to 1, violent spasms, and lying on his back with rigidly extended limbs. Sunk rapidly, and was nearly dead at 2¼ P. M.

STERILITY AMONG NEGROES. A CASE.

From a Country Practitioner.

Barrenness is more common among negro women than whites, in my range of observation. Many reasons are assigned by physicians, planters


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