Strychnia : its source, chemical relations, physiological action (typical and irregular), mode of detection, and methods of treatment in cases of poisoning / by James St Clair Gray.

STRYCHNIA;

(10)

ITS SOURCE, CHEMICAL RELATIONS,

PHYSIOLOGICAL ACTION (TYPICAL AND IRREGULAR), MODE OF DETECTION,

AND METHODS OF TREATMENT IN CASES OF POISONING.

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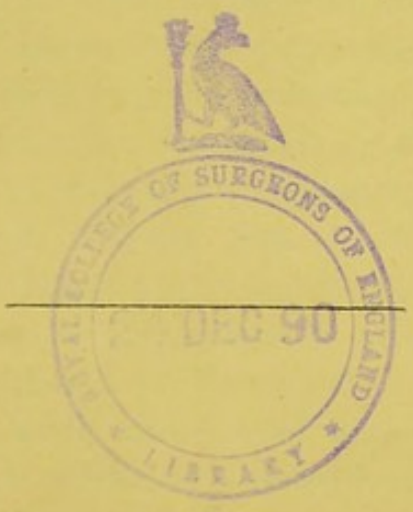

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STRYCHNIA.

FROM the Strychnos Nux Vomica, Strychnos Ignatii, Strychnos Tieute, as well as from several other plants belonging to the same natural order, Loganaceæ, are derived three alkaloids, strychnia, brucia, and igasuria, which there exist in combination, partly with lactic acid, and partly with a vegetable acid peculiar to this group of plants, called strychnic or igasuric acid.

The proportion which these alkaloids bear to one another in plants belonging to different species, and even in different parts of the same plant, varies exceedingly; thus, in the seeds of the Strychnos Nux Vomica there exist from 4 to 6 parts of strychnia in the thousand, or about ½ per cent.; while in the seeds of the Strychnos Ignatii, the quantity of strychnia is trebled, varying from 12 to 18 parts in the thousand, or about 1½ per cent.; again, the proportion which the strychnia bears to the brucia is much greater in the seeds of the Strychnos Nux Vomica than in any other part of the same plant, while the former appears to be entirely wanting in the bark.—Miller's Elements of Chemistry, Vol. III., page 543.—And lastly, in the Strychnos Tieute we find the brucia entirely wanting, while the strychnia is present in considerable quantity.

As to the ratio which igasuria bears to the other alkaloids, and to the general bulk of the plants or parts of plants yielding it, there seems to exist considerable diversity of

opinion, which is probably to be accounted for by the great difficulty experienced in obtaining it in a state of perfect purity; while Schutzenberger (Ann. de Chemie., III., liv., 65) states that the alkaloid, commonly known as igasuria, consists of nine bases closely related to one another by chemical formula and physiological action, but separable by fractional crystallization from boiling water.

In the following pages, however, we shall not have occasion to refer to brucia and igasuria, it being intended to confine attention to strychnia, and the plant from which in the British Pharmacopœia it is directed to be prepared—the Strychnos Nux Vomica, a plant found in some parts of India and Ceylon.

The Strychnos Nux Vomica is a small tree, having a thick, short, and generally crooked trunk. Its branches are irregular, covered with smooth, ash-coloured bark, while the young shoots are highly polished, and of a deep olive-green colour. The wood is white, hard, close-grained, and possessed of a peculiar, persistent, exceedingly bitter taste. The leaves are opposite, short-stalked, oval, shining, smooth on both sides, from three to five-nerved, or rather between that and triple or quintuple, differing in size from one and a half to four inches in length, and from one to three in breadth. The flowers are small, of a greenish-white colour, and collected in small terminal corymbs; the calyx is five-toothed, and permanent; the filaments, if present, are extremely short, and are inserted over the bottom of the divisions of the corolla; and the anthers are oblong, and situate half in and half out of the tube. The ovary is two-celled, with many ovules in each cell, attached to the thickened centre of the partition; the style is of the same length as the tube of the corolla; the stigma is capitate. The berry is round, smooth, of the size of a moderately large apple, and covered with a somewhat hard shell, of a rich, bright orange colour when ripe, and filled with a white, soft, gelatinous pulp, in which the seeds are imbedded.—(Lindley's Flora Medica, page 528.)—The seeds—which, as the officinal parts of the plant, are to us the most important—are very peculiar, and

highly distinctive. They may be described as irregular concavo-convex discs, varying from three-quarters of an inch to an inch in diameter, and from one to two lines in thickness; externally they are of an ash-grey colour, and are covered with short satiny hairs, which give to them a peculiar glistening appearance; internally, the seeds consist of a translucent, tough, horny material, perfectly devoid of odour, but like the bark, intensely bitter to the taste. From these (*i.e.*, the seeds) the following is the process directed in the British Pharmacopœia to be pursued in the preparation of strychnia.

The tough hard seeds are rendered soft and easily cut, by exposure to steam for about two hours. They are then chopped or sliced and thoroughly dried at a temperature not exceeding 212° Fah., immediately after which they are ground in a coffee-mill, and the coarse powder thus obtained is digested for twelve hours with a mixture of two parts of spirit and one of water, after which it is strained through linen, the residue being strongly expressed. The residue is then again digested with another quantity of the spirit and water, strained, and again strongly expressed. In the filtrates, there is by this process obtained the greater proportion of the soluble ingredients, consisting principally of the igasurates and lactates of strychnia, brucia, and igasuria, with colouring and extractive matters. From the filtrate the spirit is then removed by distillation, and the watery residue evaporated to the consistence of a thin syrup, and when cold filtered. To the filtrate acetate of lead is then added, until further precipitate ceases to be thrown down. By this means the acetates of the alkaloids are obtained in solution, while the lead is removed as an insoluble igasurate. The precipitate having been separated by filtration, the filtrate is evaporated to the consistence of a thin syrup, and ammonia in slight excess added, the result of which is that the acetate of ammonia is produced in the solution, while the alkaloids are gradually precipitated. After the lapse of about twelve hours the materials are filtered, and the filter, with its contents, after being thoroughly washed with cold

water, is dried in a vapour bath, and then boiled with successive quantities of rectified spirit. The different portions of the resulting spirituous solutions being added together, the whole is evaporated to the consistence of a syrup and set aside to cool. During the cooling process, the strychnia, which is the least soluble of the three alkaloids, is deposited. The mother liquor, containing the greater proportion of the igasuria and brucia, is then strained off from the crystalline deposit, and this deposit, after being thoroughly washed with a mixture of cold spirit and water, to remove any deposited brucia, is dissolved in boiling rectified spirit and slowly allowed to crystallize.

Strychnia, represented by the chemical formula C_{42}, H_{22}, N_2, O_4, when thus prepared, occurs in right square octahedra, or prisms, or rather four-sided prisms, terminated by four-sided pyramids (Pelletier and Caventou). These crystals are small and white, with a vitreous lustre. The cleavage-faces show a pearly appearance. The hardness of these crystals varies from 2 to 2·5 (Kengott Pogg., XCV., 614): they are permanent in air and unaltered by light. They produce a rotation of polarised light to the left.

Besides this form, the crystalline, strychnia is found in commerce as a white amorphous powder; to this, however, the crystalline form is to be preferred, as there is less risk of its being adulterated, for, while the crystals of strychnia are so distinctive to one acquainted with such matters that any addition to them of other crystals must at once be discovered, yet, in the case of an amorphous powder, for ascertaining the purity of which there is no tangible characteristic, a fraudulent admixture with some other white powder might quite easily escape detection. But in whatever form strychnia exists it is entirely devoid of odour, but is possessed of an extremely penetrating and persistent bitter taste. It is soluble only to a very limited extent in water, cold water taking up but one part in every 6667 parts, while one part of the alkaloid requires for solution 2500 parts of boiling water (Pelletier and Caventou); small, however, as the proportion dissolved is, it imparts to the solution its intense

and persistent bitter taste, and this solution, even if diluted with 100 parts of water, is still distinctly bitter, yet here the proportion of the strychnia to the water is only as one is to about 700,000. In boiling rectified spirit, in alcohol, ether, chloroform, benzole, and the essential oils, it is more soluble, thus—bisulphide of carbon and commercial ether, take up one part in every thousand; benzole, one in every two hundred and fifty parts; absolute alcohol, one in every two hundred parts; amylic alcohol, one in every one hundred and twenty parts; Dutch oil, one in every thirty parts and chloroform, one in every eight parts.

Strychnia is also very soluble in the acids, both organic and inorganic, forming with them definite crystallizable salts. For a detailed account of these, their chemical formulæ and crystalline form, I must, however, refer the reader to such works as treat of these subjects, as "Watt's Dictionary of Chemistry." But as their potency as poisons depends to a considerable extent on their solubility in fluid, it may be asked what is the most soluble salt of strychnia? what the least, and what relation as to solubility does there exist between those salts which occupy an intermediate position? These questions, it seems to me, may be most clearly answered by the following table, in which the phosphovinate, as being the most soluble, is placed first, while the tannate, metantimoniate, and chloride, as being little if at all soluble, occupy the last place, the intermediate positions being held by the other salts in their order of solubility. The data on which this table is constructed are derived from various sources, and have all received confirmation in various experiments which I have made, with a view to establish the relative potency of the various salts of strychnia, which relative potency I find coincides exactly with relative solubility, the most soluble being the most energetic, and those of very slight solubility possessing correspondingly weak toxic power.

SALTS OF STRYCHNIA—ARRANGED ACCORDING TO THEIR DEGREES OF SOLUBILITY AND TOXIC POWER.

Phospho-vinate	of	Strychnia.	Acid oxalate	of	Strychnia.
Formiate	,,	,,	Hypophosphite	,,	,,
Mallate	,,	,,	Hyposulphite	,,	,,
Fluosilicate	,,	,,	Borate	,,	,,
Acetate	,,	,,	Neutral tartrate	,,	,,
Pyro-phosphate	,,	,,	,, oxalate	,,	,,
Meta-phosphate	,,	,,	,, sulphate	,,	,,
Ortho-phosphate	,,	,,	Chromate	,,	,,
Acid sulphate	,,	,,	Bromide	,,	,,
Hydrochlorate	,,	,,	Mellitate	,,	,,
Acid tartrate	,,	,,	Iodate	,,	,,
Citrate	,,	,,	Iodide	,,	,,
Arseniate	,,	,,	Sulphocyanate	,,	,,
Arsenite	,,	,,	Carbazoate	,,	,,
Gallate	,,	,,	Tannate	,,	,,
Nitrate	,,	,,	Metantimoniate	,,	,,
Nitrite	,,	,,	Chloride	,,	,,

The above table is not by any means complete as regards all the salts of strychnia, but contains only those which are more common, and to these I have confined my observations. I have also purposely avoided any attempt to classify the numerous double salts of this alkaloid, failing to perceive any useful end which could thereby be attained. These double salts have been carefully observed by various chemists, and especially by Messrs Nicholson and Abel, to whose contributions on this subject I would refer those who may wish further information. Besides these, there is another series of chemical substances containing strychnia, and called substitution compounds, thus, there are methylstrychnia, ethylstrychnia, amylstrychnia, chlorostrychnia, and their various salts, but as these substances have already received considerable attention in their chemical relations from Messrs Stahlschmidt, How, Mènètriès, Schützenberger, Tilden, Herapath, and Laurent, and in their physiological bearings from Messrs Crum Brown, and Fraser, I must refer the reader for information on this subject to the writings of these observers. Pursuing further the properties of strychnia, we find that in the caustic alkalies, fixed and volatile, it is perfectly insoluble. It is not, if pure coloured, on being treated with the strong mineral acids cold or boiling, but when, as is

generally the case, there is present a small proportion of brucia, nitric acid gives with it a yellowish colouration, which varies in intensity according to the quantity of brucia present. When heated to a moderately high temperature it fuses, and to a certain extent sublimes, and on continuance of the application of the heat, acquires a brown colour, evolves abundance of smoke possessed of a rather agreeable odour, and gradually deposits carbon. But although this is the case, it certainly is the least destructible of the alkaloids, resisting, as it does, the action of boiling, concentrated sulphuric acid, neither its chemical constitution nor power of producing tetanic phenomena suffering thereby, and although exposed to the action of decomposing animal and vegetable matters for months, it may be recovered from such substances perfectly intact, and its chemical reactions and physiological effects demonstrated. In proof of this, I may state that I have repeatedly detected strychnia, both by its chemical reactions and its physiological effects on frogs, in the bodies of animals in very advanced stages of putrefaction to which during life the alkaloid had been administered in dose just sufficient to ensure a fatal result; as, for example in five rabbits poisoned each with $\frac{1}{20}$ of a grain of strychnia—this being in my experience the smallest reliably fatal dose administered hypodermically—I was able in two, twelve months, in three, eighteen months after death, to separate the alkaloid in quantity sufficient to yield distinctly the crystals, the colour reactions with sulphuric acid and bichromate of potassium, and to produce the tetanic phenomena in frogs. This fact has also been noticed by Professor Calvert, of the Royal Institution, Manchester, by Messrs Roger and Girdwood, by Dr Cicetta, Professor of Medical Jurisprudence, Zurich, and others, but as we shall have occasion to revert to this point at greater length hereafter, we merely note the fact *en passant.*

While, however, strychnia thus resists the action of strong boiling sulphuric acid, and the action of decomposing animal and vegetable matters, it is curious to note the following as a mere matter of observation, what may be the exact signifi-

cance thereof, or the change induced, I am at present unable to state. Strychnia, when treated with moderately strong hydrochloric acids, and allowed to digest for about six weeks therewith, acquires a peculiar pinkish-brown colouration, which, as time passes, becomes deeper, till a smoky colouration appears, without any apparent precipitation. This solution, on dilution with water, throws down a substance possessing the property of yielding colour reactions, indistinguishable from those yielded by strychnia, yet the substance is less soluble than the freshly prepared hydrochlorate and much less poisonous; in some cases the quantity required to produce death in rabbits by subcutaneous injection reaching, in successive doses, the large amount of four grains. Whether or not there is here produced a substance bearing the same relation to strychnia which has been shown to exist between apomorphia and morphia, I am not at present in a position to state.

Closely related to this part of the subject are the chemical properties and reactions of strychnia, and these we shall now examine, not considering these as tests in the restricted sense of the word, but merely as relations subsisting between strychnia or its salts, and various other chemical substances. Such of these as seem to me useful in the detection of the poison, as such, we shall afterwards take up with the mode of procedure required to demonstrate the presence of the alkaloid in matters subjected to analysis.

Taking, then, for convenience, the pure alkaloid in its dry state either in powder or in crystals, the first reactions to be noticed are what have been termed the colour tests, which are applied in the following manner:—

A small quantity of the alkaloid is placed on a white porcelain slab, on a white crucible cover, or on a watch-glass placed on a piece of white paper, and there treated with sufficient pure concentrated sulphuric acid to dissolve it, and into the solution so obtained there is introduced a small crystal of the bichromate of potassium, when there is developed around the crystal and spreading thence over the fluid a beautiful violet colouration, which passes gradually

into a purple, then a red, and lastly, a yellowish or brownish yellow tinge. These colour reactions are apparently due to the oxidation of the strychnia by the oxygen as ozone, liberated from the bichromate of potassium by the sulphuric acid in presence of the strychnia, part of the bichrome being at the same time reduced to the state of oxide of chromium. This experiment may also be modified by obtaining a fresh solution of the bichromate of potassium in pure concentrated sulphuric acid, the strength of the solution found to be most serviceable for this purpose being one of the former to a hundred of the latter. A small quantity of this solution is then placed on a white porcelain slab, and a small crystal or quantity of the poison dropped into it when the play of colours is obtained. This method of procedure has been much advocated by Messrs Rogers and Girdwood, but I cannot see any great benefit to be derived from this more than from the more simple plan, that first noticed, and which was first published by Otto, in 1847. To Marchand, however, is due the honour of having first drawn attention to the fact that when strychnia is treated with strong sulphuric acid containing one-hundredth part of its weight of nitric acid no colouration is produced, always provided the strychnia be pure, but if to this there be added peroxide of lead, the play of colours already noticed is obtained (Journ de Pharm et de Chemic 3 me sèr IV., p. 200, 1843). In 1846, Mack proposed the substitution of peroxide of manganese for the peroxide of lead; and in 1850, Bruger suggested that chromic acid might be used instead of the bichrome advocated by Otto three years before. Since Bruger's proposal many other substances have been advocated as preferable —thus, iodic acid, iodate of potassium, peroxide of barium, ferricyanide of potassium, permanganate of potassium and nitroprusside of sodium, have each had their supporters. On the whole, it may be stated that all substances in which oxygen exists as ozone, that is the class of substances called by Schonbein ozonides, are capable of yielding, with sulphuric acid in presence of strychnia in a manner more or less distinct, the several plays of colour already adverted

to, but the question of which is to be preferred for delicacy and for distinctness of result is a much contested point. Thus, Dr Taylor prefers the black oxide of manganese, Dr Guy, the permanganate of potassium, Dr Letheby, the peroxide of manganese, Messrs Ogle of Oxford, Dr Reese of Philadelphia, and Messrs Rogers and Girdwood, the bichromate of potassium, Mr Horsley, the nitro-prusside of sodium, Dr Lyman of Rockford, Ill. U.S., the permanganates of potassium and silver and the ferricyanide of potassium; such may be taken as a sample of the discrepancies existing between the opinions of recognised authorities.

Taking, however, all the facts of the case together, and after numerous comparative experiments, it appears to my mind quite clear that the bichromate of potassium is to be preferred as the most delicate, and as affording results more distinct and characteristic when small quantities of strychnia are concerned than any other chemical reagent yet applied to this purpose. After the bichrome I should be disposed to arrange the other substances proposed in the following order—chromic acid, peroxide of manganese, peroxide of lead, permanganate of potassium, nitroprusside of sodium, and peroxide of barium. By the use of the bichromate of potassium and sulphuric acid in obtaining the oxidation colours from strychnia, Dr Reese and Messrs Rogers and Girdwood have been able to detect the one millionth of a grain of the alkaloid, Messrs Ogle the one hundred and forty thousandth of a grain, while, from my own experience, I should be inclined to limit the delicacy of the test to the two hundred and fifty thousandth of a grain, and this I think far exceeds the demand of practical chemical research. It has, however, been urged as an objection to the colour tests collectively that they do not show distinctly in presence of certain extraneous substances, such as tartar-emetic, sugar, gum, nitric acid, nitrates, chloride of sodium, tartrates, bile, morphia, salicine, &c., &c. With many of these and such statements I entirely disagree, but some have a considerable show of reason. All such objections are, however, quite easily refuted by the following statement—

viz., the colour tests ought not, nay, are never intended, to be applied to compound mixtures; previous to their application a separating process ought to be, nay, always is, applied to the substance under investigation, and if this process fail either from deficiency on its part or through carelessness on the part of the operator, it is surely hardly fair that for the misdeeds of others, this, a distinctive reaction, a reaction so characteristic as conclusively proves the presence of the poison, should be condemned as unreliable. In any case, a separating process, to fulfil its proper end, must separate the whole of the poison, or, at least, a known proportion thereof, the separated poison must be free from all impurities, at any rate from all such as are liable to interfere with the processes or reactions required to demonstrate its presence; if in this it fails, it fails in all; and if failure in separation tends to failure in detection in the case of inorganic poisons, such as arsenic or antimony, how much more must it affect the result when the organic alkalies are concerned, of which the only means of determining the total quantity present is the separation from the substance to be analysed of the alkaloid as a pure alkaloid in bulk, and weighing the substance so obtained; as, however, this subject will come up for a short consideration when discussing the separating processes, we shall for the present dismiss it, and now consider a modification of the colour tests proposed by Dr Letheby, and by him called the galvanic test. It consists in treating the spot on which the strychnia is, with pure strong sulphuric acid till dissolved, and then transferring the solution so obtained to a small cup of platinum foil, connected with the negative pole of a one-celled Smee's battery. The positive pole is then dipped into the solution, and at once the violet colour is developed. This is perhaps as delicate a test as that with the bichromate of potassium, but is wanting in the character of simplicity. Should the materials, however, be within reach, the experiment should always be made. In describing the colour tests it has too often been the case that the succession of tints has been expressed in language calculated to impress the mind with the idea of mere instan-

taneous flashes; this is, however, not the case; the primary colouration lasting from thirty to sixty seconds, the secondary from one to five minutes, and the third for nearly an hour, though in some cases it lasts much longer. The period of duration, in fact, varies considerably, according to the quantity of the alkaloid operated on, and the quantity of the reagents employed, but under no circumstances, be the quantity of the poison ever so small, can the play of colours be said to have but a momentary existence.

The next test to which I would refer is the sublimation test, first proposed by Dr Helwig, of Mayence, in 1865, in a monograph entitled "Das Mikroskop in der Toxikologie," and since then warmly supported by Dr Guy in an excellent paper in several numbers of the *Pharmaceutical Journal*, from June to October, 1867, as also in the *Journal of the Royal Microscopical Society*, January, 1868. To obtain a sublimate of strychnia, any quantity not less than the one ten thousandth of a grain will suffice—the mode of procedure, which must be rigidly observed to ensure success, being as follows, quoted from "Dr Guy's Forensic Medicine," page 541:—

"A fragment of a crystal or a speck of powder is placed on a clean, dry, crucible cover, in the centre of a ring of glass. A glass disc or microscopic slide is dried and heated in the flame of the spirit-lamp, and placed on the ring. The flame is then applied to the porcelain till its temperature is considerably raised, when a mist will appear on the glass disc, and upon this, one by one, several milk-white circular spots, remaining distinct or coalescing, are seen to form. To such a sublimate as this, and indeed to sublimates that are much less characteristic, the colour tests as well as all the liquid tests, which give good results with strychnia, or its solutions, may be applied with confidence.

"The parts of the sublimate which are least characteristic should be chosen, and to those the several reagents should be applied in succession, under the microscope, the more characteristic crystalline appearances being preserved intact."

When this sublimation is conducted, so as at the same time to determine the temperatures at which the various changes occur after the manner described at page 386 of "Dr Guy's Forensic Medicine," strychnia is found to remain unchanged up to a temperature of about 345°, when it will

begin to yield sublimates. At 430°, it melts and continues to yield sublimates till it is exhausted and reduced to a carbonaceous film.

When the sublimates are examined under the microscope, they are found to assume many different forms. They may consist of drops or wavy patterns, colourless or discoloured as if smoked, but the greater number are more or less crystalline, and may present many forms. "For representations of the crystalline forms so obtained, see the paper contributed by Dr Guy to the Royal Microscopical Society, October 1867, and published in its Journal. As also Dr Helwig's Photographic Plates, in the work already referred to—Taf. IX. and X., in which also the crystalline forms obtained by treating the sublimate with various chemical reagents are figured." Besides the crystalline forms, an amorphous centre, with penniform or lattice-shaped borders, is not uncommon, and it may be stated generally, that while the sublimates of morphia ("Dr Guy's Forensic Medicine," fig. 104, p. 499,) are made up of curved lines, those of strychnia consist (*Ibid.*, fig. 134, p. 543,) of lines either straight or slightly curved, with parallel feathery lines at right angles. The sublimates of strychnia then assume so many forms that they are not in themselves conclusive of its presence; but it fortunately happens that there is no form that does not give with certain liquid reagents, results which prove the existence of strychnia beyond the reach of doubt.

As already stated, the colour tests act on the sublimate with extreme delicacy, so that to a small spot consisting of the one ten thousandth of a grain, all these tests may be applied with ease and certainty, minimum drops of sulphuric acid being used, and the smallest visible speck of the colour producing substance.

This test, when carefully performed, affords pretty uniformly a good result, but as the process of necessity involves a certain loss of substance, it seems to me better calculated to take the place of a corroborative than of a reliable and conclusive test, especially as failure in obtaining a sublimate

does not necessarily imply the absence of the poison. It has, however, the advantage that whatever exists as a sublimate is sure to contain, if it be present, the strychnia in a pure form, and hence might be employed with advantage, when there is any suspicion that the alkaloid obtained from a chloroform solution in the separating process, to be afterwards described, contains, besides the strychnia, a small trace of organic matter which would interfere with the clear development of the colour reactions. The deposit to which I here refer, does sometimes occur, and in most, if not all, the cases arises from a certain quantity of organic matter dissolved in the chloroform, and probably obtained in the process of its manufacture. But this may be prevented by redistilling at a low temperature all the chloroform used in the various steps of the process. I would, however, caution those who intend trying this—the sublimation test—to make many experiments, first with small quantities of what is known to be pure strychnia, then on strychnia separated from organic mixtures which are known to contain it, and when the requisite degree of skill has been acquired, then and there only will this test become reliable. This, like many other tests which the medico-legalist has to perform, can only be relied upon at the hands of one who has carefully and practically not alone theoretically studied it, of one who first under circumstances the most favourable, and then under conditions progressively less favourable to easy attainment of the end in view, has learned the points on which attendance, nay, rigid attendance, is absolutely essential to success.

Another very beautiful and characteristic reaction consists in adding to a small quantity of the material a few drops of a solution of carbazotic acid of such strength that every two hundred and fifty parts of the solution contains one of the pure acid. In a very short time small round greenish brown spots show themselves, and these spread, sometimes coalesce, and ultimately form delicate arborescent, crystalline groups, of which a very good representation may be seen in the work of Dr Guy, to whom we are indebted for the first account of

this peculiar reaction. The representations to which I advert will be found in Dr Guy's Forensic Medicine, pages 543 and 544, figs. 136, 137, and 138. Reducing these groups to their elements, they are seen to consist of a series of hooks or claws closely aggregated together, dense towards the centre, and more loosely bound together at their edges. Crystals or crystalline groups bearing even the most distant resemblance to this form are very rare, so that the reaction is eminently characteristic and well worthy the confidence reposed in it by its proposer.

Besides this, Dr Guy recommends the addition to a portion of the substance of a few drops of an aqueous solution of the bichromate of potassium, of strength one to a hundred, which often instantaneously, but always speedily, develops isolated yellow plates, which may be square, oblong, or grouped. For a drawing of these crystals, see Dr Guy's Forensic Medicine, p. 544, fig. 159, which may be compared with the representation of the residue obtained, by allowing to evaporate spontaneously a solution of bichrome alone of the same strength, to be seen, *Ibid.*, p. 494, fig. 99, while those desirous of further information will find it in the paper communicated by Dr Guy to the *Pharmaceutical Journal* from June to October, 1867.

Such are the chemical reactions by which strychnia in the dry state may be recognised. There are, however, a few further processes to which, if the quantity admitted, the substance, might be subjected, thus the solubility of the material in various media might be tried as what proportion dissolves in ether, alcohol, chloroform, bisulphide of carbon, benzole. Then, further, solutions so obtained might be evaporated spontaneously, and the crystalline residue microscopically examined and compared with the crystalline forms assumed by pure strychnia similarly treated. This might also aid in the determination of how much strychnia was present, or approximately at least might guide to an estimation of the relative purity of the sample.

Again, a solution in a dilute acid might be evaporated on a microscopic slide, and the crystalline character and form

of the residue compared with a sample of the salt formed by the action of the same acid under similar conditions, on pure strychnia. This mode of microscopically comparing crystals I look upon as a most valuable adjuvant to medico-legal investigation, not only in the case of strychnia, but also in many other cases. In adopting this method of procedure, I should advise the use of sulphuric, acetic, mallic, oxalic, or tartaric acid, the resulting salt in each of these cases being possessed of characters as to crystalline form, which are highly distinctive. On no account should hydrochloric acid be used, as the salt so obtained is liable to considerable variation in crystalline form.

We have, then, now to consider the ways and means by which, from its chemical character, strychnia or any of its salts is to be recognised when in solution. And first, a part of the solution should be evaporated to dryness, and the crystalline form of the residue determined. The residue should then be compared microscopically with all the salts of strychnia yielding crystalline forms resembling it. By this means it may not only be made out that strychnia or a salt thereof is present, but also a fair presumption may be formed of which salt it is. Having done this, the colour tests may be applied to the residue, as previously described, and a portion subjected to the sublimation test of Drs Helwig and Guy. Should there then still exist a small portion of the residue, it may be treated in part with carbazotic acid, and in part with the solution of bichromate of potassium, as pointed out by Dr Guy, and noticed in a former paragraph.

To another portion of the solution, liquor ammoniæ, in slight excess, should be added, when, if there be present a salt of strychnia, there is obtained a crystalline precipitate, the time required for precipitation varying according to the degree of concentration of the fluid, a strong solution yielding a copious precipitate at once, while a very dilute solution requires a considerable time to elapse before the precipitate becomes distinctly visible, and about 24 hours before total precipitation occurs. This experiment may also be

performed with the fixed alkalies, as they afford results as regards delicacy quite equal to those obtained with liquor ammoniæ. It has been said, and by some the opinion is strongly advocated, that the mono-carbonates, or even the bicarbonates of the alkalies, fixed and volatile, answer equally well with the caustic or hydrated alkalies; but this is by no means the case. When first I began to experiment on this subject, I used quite indiscriminately a free alkali or its mono-carbonate, believing that their precipitating power was equal, and that by both alike the total quantity of the alkaloid present in the solution was thereby thrown down. But it shortly appeared that the results obtained by the addition to the solution of a free alkali were much more satisfactory than those obtained when the mono-carbonate of the same or any other alkali, fixed or volatile, was used, and, in order to determine exactly their relative power of precipitation, as well as the cause of the difference, if such difference really existed, I adopted the following mode of procedure:—

A solution of the acetate of strychnia was prepared of such strength that 9000 water grains contained one grain of the acetate. To one portion of this solution liquor ammonia was added in slight excess, to another a solution of caustic potash in slight excess, to another a solution of caustic soda in slight excess, and to three other equal portions the mono-carbonates of these alkalies were added. After the lapse of 24 hours, there were found well-marked crystalline precipitates, deposited in the solutions to which the caustic alkalies had been added, but no appearance of any such in those to which the mono-corbonates had been added. The solutions were, however, allowed to stand undisturbed for 48 hours longer, but no apparent change could be observed. This experiment was repeated several times, but the results were found perfectly uniform, the solutions to which the alkalies were added in the caustic or hydrated state yielded distinct crystalline precipitates, whereas no such precipitation occurred in similar solutions to which mono-carbonated alkalies were added. It therefore appeared evident that the caustic

alkalies might be thoroughly relied upon to produce a precipitate of a crystalline character in a solution of this strength, while the mono-carbonates were not to be so trusted. In order then to determine the degree of concentration required to obtain a precipitate of the dissolved strychnia on the addition of a mono-carbonated alkali a number of experiments were made, the results of which conclusively established the fact that no precipitates could be obtained under such circumstances when the proportion of the strychnia to the solution exceeded 1 to 2000. Hence then it would appear that in delicacy of result a free alkali possesses powers of precipitation of strychnia from solutions of its salts, greater by 4½ times that of its mono-carbonate. It then occurred to me that the probable cause of the difference might be found in the formation on the addition of the alkaline mono-carbonate —of a carbonate of the alkaloid the solubility of which in water was greater than that of the alkaloid in its free state. To determine this point, I made a solution of the acetate of strychnia, in which the proportion of the strychnia to the water was as 1 to 1000. To a portion of this solution there was added solution of mono-carbonate of potash in excess. After the lapse of 24 hours, a considerable precipitate had formed, but to ensure total precipitation, 48 hours were allowed to elapse, after which the precipitate was removed by filtration, and the filtrate treated with caustic potash in excess. In 24 hours a perfectly distinct crystalline precipitate had formed, and this precipitate, when separated, dried, and treated with pure strong sulphuric acid, and a small crystal of the bichromate of potassium, yielded the colour reactions already alluded to, as being characteristic of the presence of strychnia. It, therefore, appeared that by the addition of mono-carbonate of potash the total quantity of strychnia present was not precipitated; and also that a certain proportion, if not all the alkaloid retained in the solution after this partial precipitation, could be precipitated by the addition of a solution of the free alkali.

The other alkalies and their mono-carbonates were then used in the same way, and the results so obtained were found

quite to substantiate those obtained with potash. But still further to prove this point, a fresh precipitate was produced in a solution of the acetate of strychnia similar to that previously used, the precipitant employed being mono-carbonate of ammonia. The liberated strychnia so obtained was then extracted by agitation with pure chloroform, the chloroform solution separated, and a fresh quantity of chloroform added. After agitation in a test tube for several minutes, the second quantity of chloroform was separated, and this process repeated, until the separated chloroform on evaporation was found to yield no residue. Liquor ammoniæ was then added to the solution, and chloroform immediately agitated therewith. After agitation for several minutes, separation and subsequent evaporation spontaneously of the chloroform, there was obtained a residue of a crystalline character which yielded, with pure concentrated sulphuric acid and bichromate of potassium, the colour reactions already noted. That similar results were invariably obtained when the mono-carbonate of any alkali was used in the first instance, and subsequently the corresponding alkali in its free state, was proved by the results of numerous experiments, in which, in rotation, potash, soda and ammonia, with their mono-carbonates, were used. From these results it must then be inferred that the free alkali is to be preferred to its mono-carbonate in setting free the alkaloid from its state of combination with the acid; but it may be asked wherein lies the difference in their powers of resolving salts of strychnia into their two proximate principles, the acid and the base? Is the strychnia in both instances liberated as free strychnia; or, in the one case, is there a compound formed, insoluble in chloroform, but decomposed by the addition of a free alkali, and, if this be the case, what is the compound? These questions, it seems to me, may be met by the following statement, which affords, I think, a very rational solution of the difficulty. On the addition of a mono-carbonate of an alkali to a solution of a salt of strychnia, a union of the liberated acid with the alkali takes place, this being accompanied with the evolution of carbonic anhydride

in the gaseous form, but this is not all that occurs; a portion of the carbonic anhydride uniting with the strychnia forms a carbonate of the alkaloid, while it appears that another portion of the strychnia unites with a portion of the mono-carbonate to form a double sub-carbonate of the alkali and the alkaloid.

Now both these compounds are perfectly insoluble in chloroform, but are soluble to a much greater extent in cold water than is pure strychnia. In this way the difference is easily, and, I believe, perfectly rationally and consistently explained.

That a carbonate of the alkaloid does exist can easily be shown by passing a current of carbonic anhydride through a saturated solution of the pure alkaloid in pure distilled water, fresh quantities of the pure alkaloid being added from time to time as solution takes place. After the continuance of the current for some time the added strychnia is observed slowly to dissolve, and after about two hours sufficient carbonate is formed, clearly to demonstrate the development of a compound which is much more soluble in water than the pure alkaloid, and almost, if not quite insoluble in chloroform, ether, and benzole. To obtain the carbonate in its pure state, the solution prepared as above noted should be allowed spontaneously to evaporate when there is obtained a residue which, when examined by the aid of a microscope, is found to consist of prismatic crystals, which may be distinguished from those of pure strychnia by the characters as regards solubility already adverted to, and by the fact that when treated with sulphuric or hydrochloric acid they evolve carbonic anhydride, this evolution being accompanied by effervescence.

To sum up, then, the results of these experiments, and the deductions derivable therefrom, it appears

That, a free alkali has the power of liberating from its state of combination with an acid strychnia as such, and causing its precipitation, and that this power is exercised only when the degree of dilution does not exceed 1 in 10,000.

That, mono-carbonated alkalies also possess, though to a less degree, this power of precipitating the alkaloid from solutions of its salts, the degree of saturation required being 1 in 2000, so that the power of precipitation possessed by the free alkali is five times greater than that possessed by its mono-carbonate.

That, this difference lies in the fact of the development in the solution of a carbonate of strychnia, and a double sub-carbonate of strychnia, and the alkali employed, both of which are more soluble in water than pure strychnia, but less so in ether, chloroform, and benzole.

That, founded on these results the main rule for practice is to avoid, if possible, the use of the carbonated alkalies in the precipitation of strychnia, especially when the quantity of the alkaloid relative to the total bulk of the solution is small, or when it is required to precipitate as much as possible of the poison with a view to the estimation either of the proportion or of the total quantity present in the sample.

Another reaction, which is very delicate, consists in the formation of the sulphocyanide of strychnia, which exists in long prismatic needles, generally of a pinkish tinge, and very slightly, if at all, soluble in water. This salt is produced whenever a solution of sulphocyanide of potassium is added to a solution containing strychnia or any of its salts. No precipitate of the sulphocyanide will, as a rule, be obtained if the proportion of strychnia to the solution is less than 1 to 7000.

A solution of strychnia or of any of its salts also yields a very copious precipitate on being treated with a solution of the double iodide of mercury and potassium in excess, and this precipitate, on being heated, becomes dissolved, but, on cooling, the precipitate again appears. If the strychnia be present in considerable quantity the precipitate, after being allowed to stand for some time, generally separates into strata, the upper stratum being whitish and milky, and the lower curdy and yellowish. A distinct precipitate may with this reagent be obtained, although the proportion of strychnia to the solution does not exceed 1 to 12,000, but when the experi-

ment is performed with a solution so dilute as this, a little time is required to obtain the precipitate perfectly distinctly, whereas if there be present a considerable proportion of the strychnia, the result is obtained at once. Care should also always be taken to add the reagent in excess.

Solutions of salts of strychnia also yield with a solution in water of carbazotic acid, 1 to 250, a precipitate which at first is of a yellowish gelatinous appearance, but which, after a time, becomes aggregated into feathery tufts of a light yellow colour. This reaction, which was first, I believe, pointed out by Dr Guy, is highly characteristic, and is very delicate. An enlarged sketch of the appearance of these tufts may be seen in Dr Guy's work on "Forensic Medicine," page 546, fig. 142.

Then again, a solution of corrosive sublimate on being added to a solution of a salt of strychnia causes the development at first of a dense white cloud, which resolves itself gradually into white crystalline tufts, which are highly peculiar. For a representation of the appearance which they present on being viewed through a powerful magnifying glass or microscope, see Dr Guy's "Forensic Medicine," page 546, fig. 143.

Besides these, which may be taken as the reliable and distinctive reactions by which strychnia may be differentiated from the other alkaloids, there are many others which are not so clearly distinctive, some yielding similar precipitates with other alkaloids besides strychnia, while some of the others can only be looked upon as being precipitants of the alkaloids generally. To these I shall at present devote no lengthened consideration. As, however, they are by no means unimportant, I shall enumerate some of the numerous chemical reagents which yield precipitates with solutions of strychnia or of its salts. Thus, there are phospho-molybdic acid, palladio-chloride of potassium, chloride of palladium, metantimoniate of potassium, bichloride of platinum, terchloride of gold, perchloride of iron, chloride of copper, iodic and tannic acids, bromine, chlorine, iodine, iodide of potassium, iodated-iodide of potassium, chlorinated lime,

nitro-prusside of sodium, chromate of potassium, protochloride of tin, bichromate of potassium, ferrocyanide of potassium, and ferricyanide of potassium.

Such are the chemical reactions by which strychnia may be distinguished from all the other alkaloids, reactions all of them of great delicacy and highly characteristic; indeed, there is no other alkaloid which yields so many peculiar, one might almost say pathognomonic reactions as strychnia.

But, although this exhausts the chemical tests for strychnia, it does not embrace the physiological test of Dr Marshall Hall, a test which for delicacy and distinctiveness of result, is excelled by none. This test, however, I propose to reserve for consideration hereafter, as the experiments which I have on this subject made connect it more closely with the detection of the alkaloid in the contents of the stomach, in the blood, and in the tissues of animals poisoned therewith, than with the simple recognition of the alkaloid in its dry state, or in ordinary solution.

We are now then, I think, so far advanced with the consideration of the subject as to take up the physiological action of strychnia; but this, like that of most other medicinal and poisonous substances, is subject to considerable modification, resulting from the operation or influence of certain conditions and circumstances, and these, I think, it may be better first to examine before passing to a full consideration of the physiological action of the drug.

The modifying circumstances and conditions to which I shall refer are—dose, state of aggregation of the particles of the poison, the surface to which the poison is applied, if given by the stomach the condition of that organ, whether full or empty, and the chemical combinations or decompositions which may there occur, age, general condition of body, sex, presence of disease, habit, idiosyncrasy, co-existence of the physiological action of some other medicinal substance, and lastly, the influence of the accession of sleep shortly after the exhibition of the alkaloid. These are, I think, the principal modifying circumstances, and each of them we shall now shortly consider.

And, first, dose.

Should the quantity administered be such as to fall within the limits of what may be called an ordinary medicinal dose, strychnia acts as a tonic and stimulant of the medulla oblongata and spinal cord, to which it appears to cause an increased flow of blood, and, acting through the spinal cord, it stimulates to greater activity the various organs receiving their nervous supply therefrom. As, however, this degree of physiological effect will come up for consideration in relation to the therapeutic use of strychnia, it may be better to postpone its consideration till then. From this degree of physiological effect then, let us pass on to the effect produced by a dose of the alkaloid such that, being beyond the limits of a medicinal dose, falls short of being sufficient to cause death. In this case there is felt a peculiar sensation of alarm, with a certain degree of stiffness of some, at least, of the voluntary muscles, followed by tremors sometimes accompanied by spasms of these structures. Along with these there are sometimes associated cramps in the abdomen, slight trismus and difficulty of articulation—these two latter phenomena being, however, very rare. The circulation and respiration are in such cases generally, but slightly, affected; but, if affected, the action of the heart is generally accelerated, and the respiration rendered somewhat intermittent. If, however, the dose be sufficient to account for, or rather to cause, death, the physiological effects may vary; thus there may, after the administration of the poison, occur a considerable interval of apparent quiescence, followed by a general tremor of the whole voluntary muscular system, at first slight, but gradually increasing in intensity, till it passes into a powerful spasm, which in a few minutes, it may be moments, proves fatal; or, again, the first spasm may pass off, and after an interval of longer or shorter duration, be succeeded by another, which may be of greater intensity, and which may be followed successively by interval and spasm, the interval becoming gradually shorter, the spasm gradually of longer duration and greater intensity, till death occurs; or,

again, there may be little, if any, variation in the intensity of the spasms, which may, however, last for such a length of time as thoroughly to exhaust the nervous system, and thus occasion a fatal result; or, the premonitory tremors may be entirely awanting, and suddenly a severe spasm come on, from which recovery never takes place; or, lastly, there may be an absence of all symptoms whatever, till there occurs what may be termed merely a bound into the air, and death occurring instantaneously leaves the whole muscular system in a state of perfect relaxation. These are the modifications which are produced by dose, aided perhaps to a slight extent by other modifying circumstances; but, generally speaking, the smaller the dose producing the fatal results the more prolonged are the symptoms, while, if the dose be large, the symptoms are usually correspondingly severe, and tend to produce a fatal result more rapidly.

We have now, then, to consider the state of division of the particles of the alkaloid as a source of modification of the physiological effect, and here, broadly stating the results of experience, it may be said that the more finely divided are the particles the more rapidly is the effect produced, and in an equal time the more powerful is the effect. Thus, if two animals under exactly similar conditions have administered to them equal doses of strychnia, the one dose being, however, given in solution in water, the other in hard pill, in the former the effect will be produced more rapidly, and at a given time the effect will be more powerful than in the latter. The most rapid, powerful, and uniform results are produced by the administration of strychnia in solution, while, if the poison be administered in powder, coarse crystals, or hard pill, the effect is less rapidly produced, the symptoms less rapidly become severe, and have less of uniformity, this being due, in the former case, to rapid absorption of the poison, while, in the latter case, it is due to the slow, it may be irregular, absorption which occurs. This slow absorption is easily accounted for, when it is remembered that the absorption of solids must be preceded by their solution, and that physiological action bears a

constant ratio to absorption; the more rapidly absorption progresses, the more rapidly is the physiological effect produced, and *vice versa*, consequently, anything which tends to increase or diminish the rate of absorption to a corresponding degree accelerates or retards the development of the physiological phenomena. Hence it is that strychnia administered in hard pill is so slow in producing the physiological effects, and that these effects are less uniform than those resulting from the exhibition of the alkaloid in solution.

Closely allied to this, in so far as it relates to the facilitating or retarding of absorption, is the surface to which the poison is applied. To arrive at a definite understanding of the exact ratio as to absorptive power possessed by the various structures is very difficult, nay well nigh impossible, on account of the great difficulty of applying the poison at once to a large surface, or at least to surfaces of uniform extent in two different parts of the body; thus, it is very difficult to apply the poison simultaneously to a surface of muscle equivalent in extent to that of the stomach; but without attempting rigidly to define the exact ratio, we have, I think, sufficient data to determine at least the order in which the various structures should be arranged so as to indicate their relative absorptive power. Thus, injection of a solution of strychnia into the veins, which is the manner of administration most favourable to a rapid accession of symptoms, and a rapidly fatal result, causes generally, almost instantly, the development of tetanic phenomena, without the appearance of the preliminary tremors usually found in cases of poisoning by this alkaloid. Thus I have frequently injected a solution of the acetate of strychnia into the jugular vein in dogs, cats and rabbits, and I find it almost uniformly the case that the spasms come on almost simultaneously with the administration of the poison, and the spasms are rarely preceded by the tremors already adverted to. In these cases death was preceded by more uniform symptoms and occurred in a much shorter time than when any other method of

application was resorted to. Next to injection into the blood-vessels comes injection into one or other of the great serous cavities, the pleura, pericardium, or peritoneum. This may be easily accounted for by the very rapid absorption which takes place from these surfaces. By this means Dr Christison has killed a wild boar in ten minutes, and, on several occasions, I have seen dogs die in seven, five, and even four minutes, when strychnia in solution was administered to them by these channels. After this, in order of rapidity of absorption come injection into the tissues, and application to wounds and excoriations, in which cases, the absorption is only but slightly slower than in the case of the serous cavities. After these, application to the mucous membranes is the most rapid means of obtaining the physiological effect. The mucous surfaces which are usually chosen for this method of exhibition are those of the alimentary canal, but in a few cases application to the mucous membrane of the lachrymal canal and urinary bladder has been followed by serious, and, in the latter, by fatal consequences. But in the case of application to mucous surfaces the period elapsing between administration of the poison and the accession of symptoms is universally found to vary exceedingly; the first symptoms are very irregular in character, and generally the cases present less of uniformity than the other methods of administration of which mention has already been made. Next comes appliction to the skin deprived of its cuticle by such vescicants as cantharides, while lastly, application to the brain substance seems to be followed by no phenomena whatever of a tetanoid character. Of course, in exhibiting strychnia in this way, one must carefully avoid so applying the poison that it may come in contact with the small blood-vessels, else the conditions become altered, the poison is then directly applied to the circulatory system, by it absorbed, and at once the tetanoid phenomena are developed, leading rapidly to a fatal result.

The next two modifying circumstances which we shall consider are so closely related that they may be very fitly taken up together. They are both founded on the pre-sup-

posed idea of administration by the stomach, the first referring to the state of the stomach itself, whether full or empty, the second relating to any chemical combinations which may there occur between the strychnia and any material, alimentary, or otherwise, with which it comes in contact. If the stomach be distended with food, as it often is when poison is administered, there is a greater probability of the occurrence of vomiting, but, even should this not occur, the absorption of the poison is very much interfered with, and if the matters present in the stomach are very indigestible, there is just the possibility that the materials, poisonous and otherwise, might be excreted before the poison had produced its physiological effect, or, at least, before it had produced an effect of such intensity as the dose would lead one to expect. Thus, if strychnia be given along with, or immediately after, the inhibation of a full meal of such indigestible matters as dough or large quantities of fat, these and other such substances might form a dense envelope for the poison, thereby preventing absorption, and, therefore, the development of the physiological effect. On the other hand, if the stomach is empty, spontaneous vomiting is not so apt to occur, and should it occur, cannot be efficacious in removing all the poison, while the absorption of the alkaloid into the system is greatly facilitated, so that the effect is produced more rapidly, and generally more powerfully than when the stomach is distended with food.

Again, the presence of certain kinds of food or other substance in the stomach may lead to the formation of a compound of the poison with that substance, the effect of this combination being one of three things, either to increase or diminish, or not at all to affect the toxic power of the drug. Thus, suppose the strychnia to have been administered as an iodide which is comparatively insoluble and only very slightly active; this, however, let us suppose, comes in contact with a free acid, whose affinity for strychnia is greater than that of the iodine; a decomposition occurs, there is produced free iodine or iodic acid, and a new salt of strychnia more soluble, more highly poisonous, and hence

the physiological effect, in its full intensity, is very shortly produced. But while this is a case which cannot be often expected to occur, the next case which I shall suppose is one perfectly consonant with experience. If a person, previous to the exhibition of the poison, have partaken of a full meal of food containing a large proportion of tannic acid, the alkaloid may be precipitated in a form almost insoluble, and, so far as physiological action is concerned, nearly totally inert. Under circumstances such as these, may it not be argued, with some show of reason, that we may be able to explain many of the anomalous cases of poisoning which have been recorded. I think we have quite sufficient ground here on which to account for such occurrences as the exhibition of a large dose of the poison, followed by the production of physiological phenomena in no way so powerful as one would expect from the quantity administered; or, again, how the symptoms may, in some cases, be so long delayed as to give rise to great doubt as to the exact time at which the alkaloid was administered; as also how the symptoms may be delayed for a considerable time, be of short duration, and, after a considerable period of apparent quiescence, be followed by a severe attack of tetanoid spasms and death—the sudden development of these latter phenomena being due to the chemical decomposition of the tannate of strychnia by some other substance, whose affinity for either of the constituents of this salt exceeds in power that of the strychnia for the tannic acid; and, still further following out this line of reasoning, may we not find in it a very feasable explanation of what has been called the cumulative action of strychnia, as in a case similar to one which I shall now suppose.

A person much addicted to the use of tea is ordered by the medical attendant to take of some preparation of strychnia, a dose equivalent to $\frac{1}{4}$th of a grain per diem, this being continued for several days. Now, as each dose is taken it is quite conceivable that the tannin contained in the tea forms with the strychnia the insoluble tannate. Thus, day by day the quantity of strychnia in the system increases till

by some means the tannate becomes decomposed, and symptoms of poisoning at once manifest themselves. That cases of cumulative poisoning, in some degree at least, similar to this, have been reported, all who have inquired into this subject know, and, as far as I can see, this affords a very rational explanation of the phenomena observed.

Now we come to consider age as a modifying condition, and as we would naturally expect, we find it the case that children and those advanced in years are much more easily affected, and that with smaller doses than persons of middle age. The general rule regarding this point apparently is, that the more perfect the development of the nervous system is, the less amenable is it to the action of the poison; while, on the other hand, the more rudimentary, inactive, or deficient the nervous system is, to such a degree is it more susceptible to the physiological action of the alkaloid. Thus, a case is recorded as occurring in the practice of Mr Blacklock, of Dumfries, in which $\frac{1}{16}$th of a grain proved fatal in four hours, to a child aged between two and three years (for a report of this case, see Dr Taylor's monograph "On Strychnia," page 138); and in several cases I have in the aged seen very alarming effects produced by very small doses of this substance, both as the pure alkaloid and as the extract of nux vomica in pill.

Closely allied to this is the general condition of the body, as a condition likely materially to influence the action of strychnia. That the weaker a person is, the more easily are they affected by strychina can easily be seen, if a glance be but cast over the various cases reported of poisonous effects resulting from medicinal doses of the alkaloid; and although in many such cases other modifying circumstances partake largely in increasing the susceptibility of the patient to the action of the alkaloid, it will be found that especially in persons of weak nervous temperaments, as it is by some termed, the drug acts more rapidly and severely than in persons of robust habit, and what may in opposition to the other term be expressed as possessed of strong nerve. If, however, the experiments detailed in Vierordt's Archiv. für

Phys. Hulk. Helf I., p. 145, 1855, by Dr Kraupp, should receive confirmation, the inference will clearly be that blood-letting tends, at least, considerably to retard the accession of the tetanic phenomena, and to mitigate their severity when produced.

As to the influence of sex as a modifying circumstance, there cannot much be said at present, as, from the number of cases already reported, though that number is very considerable, I have been unable to fix any definite value on the modifications thereby produced. However, females with a marked tendency to hysteria seem to show a number of rather anomalous symptoms when treated with even moderate doses of strychnia, as is well illustrated in a case which occurred in the practice of M. Vigla of the Hotel Dieu, Paris, and by him published in the *Gazette des Hopitaux* of October 7, 1848. In this case the dose did not exceed the $\frac{1}{6}$th of a grain, and yet its administration was followed by a very peculiar train of hysterical phenomena, accompanied by hallucinations. It may also be noticed that in overdose strychnia in the male is apt to produce priapism, and in the female, in whom pregnancy co-exists, there is a considerable liability of the occurrence of abortion or miscarriage.

We have next to consider the influence exercised by the presence of various diseases in modifying the physiological effects of this drug. Now, there are two different ways in which disease may operate—the one tending to diminish susceptibility to the production even by large doses of the physiological action of the poison, the other tending to increase in a remarkable manner its influence over the nervous system, and the production by very small doses of very powerful toxic effects. Thus, in cases of hemiplegia depending upon inflammation of the spinal cord or its membranes, in the acute stage strychnia invariably causes an aggravation of the symptoms; but, after the acute inflammatory symptoms have subsided, large doses of this alkaloid are borne exceedingly well—indeed, in such cases it has been given to an extent such that, had the diseased condition not been present, no one would have ventured to prescribe. In

cases of tetanus too, as well as in many acute febrile diseases, strychnia, though administered in very small doses, almost invariably gives rise to very alarming, if not injurious, results.

As to the influence of habit as a modifying circumstance, much has been written for and against, and much of theorizing might still be advanced, though, I think, with very little benefit. It is, however, just conceivable that in certain cases a long continued use of a small dose might necessitate an increase of the daily allowance in order to produce the same amount of physiological effect as that at first produced; but, as far as one can judge from cases at present reported, there is no evidence in favour of this idea—in fact, the ascertained facts rather tend to prove the reverse.

Passing now to the influence of idiosyncrasy, the evidence here is unmistakable. Cases have been frequently reported in which an ordinary medicinal dose has produced an effect so powerful as to raise serious doubts as to recovery in the minds of the medical attendants. In private practice, I can call to mind several such cases; but perhaps as remarkable a case as any is that related by Dr Anstie in his valuable treatise on "Stimulants and Narcotics," at page 151. The case here referred to was originally one of hemiplegic paralysis, but this having passed off, left behind it an intense feeling of cold, with visible sluggishness of the capillary circulation, and very considerable distension of the abdomen from tympanitis, due to partial paralysis of the muscular coat of the intestine. For the relief of these symptoms strychnia in doses of $\frac{1}{10}$th of a grain thrice daily was ordered. "On the occasion of the man's next visit," I quote Dr Anstie's own words, "I thought at first that he was drunk, as he had the uncertain gait, meaningless smile, and flushed perspiring cheeks characteristic of intoxication. To my surprise, however, I found that this effect had been produced by a dose of the strychnia taken half an hour previously, and he had come to me to complain of the medicine, because it 'made him drunk.' This, I ascertained subsequently, by personal observation, was really the

fact." The dose was reduced to the $\frac{1}{32}$nd of a grain, and no longer were these effects manifested. Such cases as these, though rare, are, I think, quite sufficient to prove that in certain constitutions there is a predisposition on the part of the individual to become affected by extremely small doses of strychnia. That some cases have occurred in which large doses have been taken without serious injury there is abundant proof, but not, I think, of such a character as would lead to the founding thereon of any positive statement as to the effect in these cases of idiosyncrasy.

There then falls to be considered the influence of the accession of sleep, immediately, or at least very shortly after the exhibition of the alkaloid, in modifying at least the duration of the interval, which elapses between the minute of administration and the time at which there is noticed the first accession of the symptoms, as well as in modifying their mode of accession. It does not seem to be of any material consequence whether the sleep be natural or the result of the operation of narcotics; if sleep, real or artificial, occur to the extent that external impressions are not distinctly conveyed to the sensorium, this seems all that is required. This is to my mind one of the most important modifying circumstances connected with poisoning by strychina, and one which should always be remembered in the consideration of cases in which the time of administration comes to be a matter of importance. From various cases already reported, as well as from numerous observations on animals, it seems that sleep tends to delay to a very material extent the accession of the symptoms. Thus, in the case of Assistant-Surgeon Bond, strychina was taken to the extent of 2 grains in hard pill. Patient shortly afterwards fell asleep, and for two hours continued in this condition, awaking then and finding himself affected with convulsive twitchings of the lower limbs. Again, in the *Lancet* of November 16, 1861, there is a case reported by Dr W. B. Tarleton, published by Dr Harley, in which a boy, aged 12 years, took accidentally 3 grains of strychina in hard pill. He afterwards fell asleep, and so remained for two hours and

a half, at which time he awoke screaming in a tetanic spasm. From these two selected cases it will be seen, I think, that sleep very materially modifies the length of time elapsing between the time of administration and the time of accession of the spasms, and in such cases it generally happens that the awaking occurs in the first spasm, as was well illustrated in the case reported by Drs Cowan and Laurie in the *Glasgow Medical Journal* for 1857, p. 162, in which a medical man swallowed 3 grains of strychnia, afterwards fell asleep, and remained so for an hour and a half, awaking with loud cries in a tetanic spasm. But it may be asked, How does sleep tend to retard the accession of the symptoms? This may be a point on which difference of opinion may exist; but from experiments on animals, especially frogs, it is my opinion that for the development of the tetanoid phenomena it is necessary that either some external impression should act on the peripheral sensory nerves, and being conveyed along them, so act on the sensorium as to demand a reflex action, or that some demand for reflex action should arise spontaneously in the sensorium. This theory I found on the observation that, if to a frog a dose of strychnia be given, it generally remains quite quiet for a comparatively long time, and if not allowed to move about the spasms do not come on, but if touched or moved in any way, or if the material with which its body is in contact is caused to vibrate, the spasms are at once developed. Thus I have frequently given comparatively large doses of the acetate of strychnia to these animals, and if allowed to remain absolutely at rest, have invariably noticed that a long interval, even three-quarters of an hour, may elapse without any spasm appearing, which I have never noticed to occur if the frog be caused to hop about, or say, at the end of ten minutes, it is touched with a glass rod, or in some other way stimulated. It is also a recognised fact, from the experiments of Kölliker and others, that if a frog be anointed with hydrocyanic acid, which destroys sensibility to external impressions, strychnia fails to produce tetanoid spasms; if, on the other hand, all, save one leg of the animal be so anointed, and

then strychnia be given, no spasms ensue till the limb not anointed is irritated, irritation of the anointed parts failing to induce the tetanoid phenomena. These experiments I have frequently performed, and with uniform success. To the absence, then, of the conveyance of these impressions to the cord, and thence to the sensorium, or it may be to the absence of these impressions, is, I think, the modifying influence of sleep to be ascribed, and had these cases been closely observed from the first, I think it is not at all impossible that some involuntary movement, causing perhaps the sudden contact with the bed clothes of some part of the body not formerly pressed on by these, or the knocking together of two parts of the body, would have been found to be the prime moving cause in inducing the first accession of the spasms.

We have next, and lastly, to consider, as a modifying circumstance or condition, the presence in the stomach, or in the system at large, of some medicine or medicines whose physiological action is antagonistic to the action of strychnia, or more properly the pre-existence, co-existence or subsequent development by some other drug of physiological effects opposed to those of strychnia or such, that the two effects cannot together become developed in the same organism. To find proof that such modification does occur is very easy, it requiring but a glance to be cast over the many proposed antidotes, each of which is backed up by several cases of recovery in man or animals from poisonous doses of this alkaloid. As, however, we shall have to consider this matter more fully when we come to treat of antidotes, nothing more need at present be said on this subject.

But before passing on to the consideration of the physiological action proper of strychnia, I think a short *resumé* of a case which occurred in the practice of Dr Tschepke, on the 26th November, 1861, and by him published in the *Deutche Klinik*, may not be uninstructive, as it exemplifies much of what we have treated in this division of the subject. The patient, a druggist's assistant, after a meal

consisting of a soup composed of flour and cranberries, swallowed, at half-past eight o'clock, a dose of the nitrate of strychnia equal to from 8 to 10 grains, dissolved in an ounce and a half of bitter almond water, but finding, after a short time, no effect to be produced, he took an additional dose of 12 grains of pure strychnia, likewise dissolved or suspended in bitter almond water. No symptoms yet appearing, he swallowed 10 grains of acetate of morphia, diffused in an ounce of bitter almond water, and about ten minutes later, recollecting that he had some chloroform at hand, he poured some on his pillow, and placed his head over it with a view to hasten death. For a short time he seems to have remained insensible, but soon awoke with a feeling of intolerable itching of the nose and limbs (due to the morphia), but no symptom of the action of the strychnia having yet appeared, he tried to look his watch, but found himself unable to move, this being probably due to the combined action of the morphia and the hydrocyanic acid of the bitter almond water. In this state of partial insensibility and utter helplessness he remained till a quarter past eleven, when a fellow-assistant entered his apartment. The patient heard him enter, but, on his leaving to obtain assistance, was seized with violent cramp and cessation of respiration, but these were unaccompanied with pain. Consciousness, then, for a short time forsook him, but in a few minutes he was again seized with a spasm, and at 11 o'clock Dr Tschepke called. He found the patient in bed, pale, eyes closed, body rigid as a corpse. One of the persons present produced the bottle containing nitrate of strychnia, of which the patient had swallowed some. Dr Tschepke took the hand to feel the pulse, which act immediately induced a spasm, which seized the whole body like an electric shock, the pulse became barely perceptible, and the respiration was suspended. In a few minutes the patient opened his eyes, and, in answer to a question, stated that he had taken strychnia. Spontaneous vomiting immediately occurred, the vomited matters consisting of a reddish-brown matter, having the smell of hydrocyanic acid. An emetic of ipecacuan and

antimony was then administered, and also three grains of tannic acid in solution. The emetic produced two copious discharges, after which the patient scratched violently his face and body, and tore his hair; then supervened startings, clonic spasms, tetanic rigidity, opisthotonos, and apparent suspension of circulation and respiration. Touching the arm produced, as at first, a fresh attack. The tannic acid and emetic were given alternately every fifteen minutes—vomiting and cramps succeeded one another—the same train of symptoms continued till midnight, when the patient stated the different substances which he had taken. Half an hour after midnight a quarter a grain of codeine was given, with three grains of tannic acid, and this repeated every half hour. Occasional vomiting and cramp recurred till four o'clock next morning. There was great anxiety, accompanied with prostration and dryness of the throat; the respiration was short and hurried. There was great thirst, and to allay this milk of almonds, milk, tea, and seltzer water were administered freely. Micturition was for a time painful. In two days no trace of the poisoning remained.

Here we have, then, a case in which the physiological action was modified by the distended state of the stomach, this aiding elimination by emesis, and preventing absorption, then the large quantity of tannin in the cranberries was such as to tend to precipitate the alkaloid as the insoluble tannate, there was also the presence of sleep or a period of unconsciousness, and the co-existence of the physiological action of chloroform, morphia, hydrocyanic acid, and codeine, each of which has a well marked antispasmodic action. A point, too, in this case which is very curious, and which has never been explained, is the fact that though the strychnia was first taken, the morphia was the first to demonstrate its presence by physiological action—viz., the itching of the skin.

Such, then, are the circumstances and conditions which modify the physiological action of strychnia; and we have now to consider the physiological action itself, restricting this consideration in the meantime to doses of the alkaloid,

which are capable of producing poisonous effects. From an analysis of 169 recorded cases of poisoning by strychnia or its salts, and apart from poisoning by nux vomica, I shall first construct what I believe to be a typical case. But as in different individual cases the phenomena occurring in the course of the same disease may differ very materially from each other and the type, so, in cases of strychnia poisoning, there are certain modifications of, and variations from, the type. Indeed, there is, as I hope to show, no one group of symptoms, nay, not even a single symptom, which one can single out and say that symptom, if present, conclusively demonstrates the case as one of strychnia poisoning, while its absence as conclusively determines that, to whatsoever else the symptoms may be due, they are not due to the action of strychnia.

Physiological action.

After the exhibition of a poisonous dose of strychnia, an interval, averaging 15 to 20 minutes, precedes the accession of the symptoms. These are ushered in by a peculiar uneasiness, a disinclination to remain absolutely at rest, the muscles feel slightly stiff, and a sense of suffocation gives warning of the near approach of the more distressing symptoms. The breathing becomes short and hurried, the pulsations of the heart are accelerated, while, after a short time, there are noticed slight tremors, affecting first the organs of locomotion, giving rise to an exceedingly curious and characteristic gait. These tremors then rapidly extend to the other voluntary muscles, and, increasing in intensity, they pass gradually into peculiar startings, in many respects resembling the effects produced on the muscular system by a powerful electric shock applied intermittently. During this period the heart's action, as indicated by the pulse, is not only increased in rapidity, but varies in character, beating at one time smoothly, sharply, and clearly, and immediately afterwards irregularly and feebly, while the sensibility of the skin to slight impressions is highly increased, light pressure on the body, especially if applied suddenly, causing the

appearance of the remarkable startings just described. Now, the symptoms completely change, and this change is heralded by a peculiar stiffening of all the muscles of the body, cessation of respiration, diminution of the strength, and frequency of the pulse, pursing of the mouth, and the accession of an anxious, yet startled expression of countenance. The balance of muscular power does not long remain so nicely adjusted, the extensor muscles generally prove the stronger, and coincidently the patient is, so to speak, thrown to the ground—sometimes emitting an inarticulate cry—in a spasm of a tetanoid character. During this spasm there is opisthotonos; the respiration is entirely suspended; the heart's action is rapid and fluttering; the face congested and livid; the expression anxious; the eyes protruded, suffused, and apparently starting from their sockets, pupils dilated; and, as congestion of the head increases unconsciousness for the first time comes on. After a duration, varying from 2 to 5 minutes, the spasm passing off is succeeded by a period of calm, during which the intellect is clear, the respiration and circulation comparatively free, the face more natural in colour and expression, though still anxious, the pupils natural, but the susceptibility of the skin to slight impressions still continues. It may be remarked, concerning this abnormal excitability, that firm pressure rather tends to relieve the spasm than otherwise, and, if carefully applied in the interval, does not tend to reinduce the accession of a spasm. The calm of which we have just spoken does not, however, last long, a fresh spasm comes on, generally induced by some slight nervous impression which may originate in an impression externally arising, or in one arising in the nerve centre. This spasm differs from the first only in intensity, though there is a greater probability of the occurrence of trismus arching of the soles of the feet and clenching of the hands. This alternation of spasm and repose may occur for some time, and may end in recovery or death, and, should the latter occur, the hypersensitiveness above noticed becomes less marked, and, just before death occurs, reaction is totally

abolished, the order of passing off of this reflex excitability being generally from the lower extremities upwards.

Such are the symptoms which, in the majority of cases, are found to succeed the exhibition of a poisonous dose of strychnia, symptoms which, of themselves, are so characteristic as to be, apart from everything else, perfectly sufficient to stamp the real character of the case.

But there are cases which present considerable variations from this type. Thus, the premonitory symptoms may be entirely awanting, as in a case published by Dr Harley in the *Lancet* for 1861, October 26th, of a girl aged 11 years, who died from the effects of strychnia, dose unknown, taken with a view to suicide, and in whom tetanoid spasms came on suddenly, and without the occurrence of the phenomena generally noticed in the first stage. Also, in a case communicated by Dr Chippendale to the Abernethian Society, and quoted by Dr Part in the *Lancet* for 1861, Vol. I., page 336, in which an adult male swallowed, for suicidal purposes, a dose of 4 grains of strychnia, with 4 grains of morphia. In half an hour violent tetanoid spasms appeared, without any antecedent symptoms referable to the action of the poison. This patient ultimately recovered. Again, in a case published by Dr Paley, of Peterborough, in the *British Medical Journal*, August 4, 1860, a female between 17 and 18 years of age, after accidentally swallowing a quantity of a vermin killer, containing strychnia, was suddenly seized with a tetanic spasm, which, after a short time passed off, leaving the patient comparatively free for such a length of time as permitted her walking, with the aid of two persons, a distance of 250 yards. This patient, however, shortly afterwards died. Again, in a case quoted in the trial of Palmer, and published by Dr Watson, of Glasgow, in the *Edinburgh Monthly Journal*, December, 1845, a girl aged 12 years, after swallowing three-fourths of a grain of strychnia, was suddenly, at the end of 20 minutes, seized with tetanoid spasms, which proved fatal in about three-quarters of an hour. Again, in a case published by Dr Watson, of London, in his work on "Practice of Physic," Vol. I., page 553, and

which occurred in the Middlesex Hospital, a man under treatment for paraplegia, received by mistake a dose of strychnia amounting to one grain made into pill with bread crumbs. He became suddenly tetanic, and although he recovered, the paraplegia was not much relieved. Also, in the case of assistant-surgeon Bond, reported by Dr Harley in the *Lancet* of November 16th, 1861; and in a very interesting case reported by Drs Cowan and Lawrie, in the *Glasgow Medical Journal* for 1857, page 162, the tetanic phenomena appear to have come on without any marked preliminary symptoms. In a case, too, recorded by Dr Geoghegan, of Dublin, the patient awoke suddenly in a severe tetanic spasm.

Another and very marked variation consists in the presence along with the typical phenomena of the first stage of cerebral symptoms, as in a case quoted by Dr Christison, in his work on "Poisons," 4th edition, page 895, which was communicated to Dr Bardsley by Dr Booth, of Birmingham, of a man suffering from hemiplegia, for the relief of which strychnia was prescribed in gradually increasing doses till 1½ grains was reached. This last dose proved, however, too large, its administration being followed by great anxiety, excitability, stupor, and loss of speech, and ultimately, tetanic spasms, which led to a fatal result in three hours and three quarters. Also, in a case reported by M. Duriau in the *Annalles d'Hygiene*, Vol. XVII., p. 28, the patient, a female aged 38 years, suffering from diphtheritic paralysis, had one-sixth of a grain of strychnia by mistake; in ten minutes, giddiness and insensibility came on, followed by convulsions. Recovery in this case was not perfect weeks afterwards. In a case by Schüler, published in the *Gazette Medicale de Paris* 1861, No. 6, a patient, suffering from amaurosis, had several times an injection of one-tenth of a grain thrown into the eye, but this being ineffectual in relieving the disease, one-twentieth of a grain was thrown into the lachrymal canal, and in three or four minutes there came on vertigo, inclination to fall forwards, and slight twitchings, with complete aphonia. This patient in a short time recovered. In a case

reported by Mr Sewell, in the *Lancet* of May 17, 1856, giddiness was the first symptom observed. In a case reported by Dr Lüdicke in the *Medecinische Zeitung*, for March 16th, 1842, the patient was suddenly seized with vertigo, and fell to the ground in a state of perfect insensibility.

As, however, an examination of each individual case, in its various relations, would occupy too large a space, I shall content myself with a simple enumeration of the aberrant symptoms recorded, at the same time stating the number of cases in which particular groups of symptoms were observed. The first symptoms noted as occurring in four cases were the uttering of loud cries or shrieks, accompanied by tossing of the arms and a sense of suffocation. In one of these cases these symptoms were preceded by a train of very pleasant dreams. In one case, that of Dr Warner, the first symptoms experienced were a feeling of contraction of the throat, tightness of the chest, and general stiffness of the muscles, the latter being felt more particularly when any attempt was made to perform any voluntary act. In two cases vomiting was the first recorded symptom, the spasms occurring immediately afterwards. In three cases cramp was the first symptom recorded. In four cases the nape of the neck was the first part of the body affected with spasms, these spasms being preceded by a feeling of stiffness. In one case the bitter taste was not complained of, and the first symptoms consisted in profuse salivation, convulsions rapidly supervening. In one case pain was felt in the back, radiating from the fifth dorsal spinous process, and passing down to the lower extremities, which were affected with short but powerful startings; and in one other case the pain was first referred to the lumbar region, and extended thence to the lower limbs. In one case the expression of the face was the only alteration observed for some time previous to the accession of the spasms, the eyes being wild and staring, and apparently starting from their sockets. In three cases the sensation was the first function interfered with; in one case a sense of burning being experienced; in one a feeling of numbness, and in the third twitches, accompanied by pecu-

liar sensations in the hands and arms, were noted. In two cases twitchings in various parts of the body were present for a considerable time before the accession of the spasms proper. In one case the respiration was suddenly accelerated, and this symptom was immediately succeeded by the appearance of convulsions affecting the whole voluntary muscular system. In one case stiffness of the limbs was recorded as the first symptom observed. In one case a feeling of agitation and alarm, accompanied by a slight spasm of the muscles of the trunk, replaced the symptoms more commonly met with. In one case a sudden twitch or start, causing the patient to fall from the chair, was the first intimation of the action on the system of the drug. These, then, are all the cases which presented abnormal forms as to accession of symptoms, in an analysis of 136 recorded and authentic cases of poisoning by strychnia, independent of nux vomica, and the preparations directly derived therefrom.

Passing now to a consideration of the symptoms occurring in the second or tetanic stage, it may be well, I think, to take up the various functions and organs separately, as, were they all considered together, confusion might arise. I propose then, first to consider the face, and in thirty-eight cases in which attention seems to have been bestowed in the describing of its appearances, of which the following sentences contain a condensed account. In all the thirty-eight cases lividity was recorded, and in four of these, during the height of the paroxysm, a deep purple colour was observable, due to non-oxygenation of the blood. In seven cases there was an anxious expression recorded, while, in one case the expression was described as wild, glaring, and anxious, and in another, as wild and maniacal. In six cases there was present frothing or foaming at the mouth. In one case the palpebrae were described as being constantly in motion. In six cases the eyeballs were described as apparently starting from their sockets; in four as prominent; in four as fixed and staring; in one as distorted; and in one as rolling about under the eyelids, the irides being completely hidden beneath the upper eyelid. In six cases the eyelids were described as

closed. In one case the lips were described as retracted, and in another as swollen. In all the cases the lips were uniformly livid. In three cases there was present contortion of the features. In one case the features were described as distorted and drawn to one side. In four cases risus sardonicus was reported present, in three cases as absent, in the others no mention of this symptom was made. In one case there was present an absolute want of power to swallow even liquids. In one case there was present great itching of the face; and in two cases the face was described as bathed in perspiration.

In twenty-seven cases the state of the pupils was carefully observed; in twelve of these there was present dilatation both in the spasm and in the repose; in four cases they were dilated during the spasm, but their condition in the state of repose was not described; in one case as dilated in the spasm, but natural in the interval; in one as contracted in spasm, but the condition during the period of repose was not stated. In one the pupils were dilated during the spasm, but in the interval were contracted; in two cases they were natural throughout; in one case they were described as widely dilated in both spasm and repose; in one case as widely dilated in the spasm, and dilated, though not to the same degree, during the repose; in one case widely dilated during spasm, and natural during interval; and lastly, in one case they were dilated and non-contractile during spasm and repose alike. Then, as to the presence or absence of trismus, there were reported, out of 136 cases, twenty-one in which it was present, three in which it was absent, and one in which it was present only during the severity of the spasm. In the other cases no reference whatever was made to this symptom.

As to the condition of the respiratory organs. Dyspnœa seems to be a symptom universally present, its presence being recorded in every case in which special reference was made to the state of respiration. In 51 cases, in which the reports were especially full as regards the respiratory system, in seven cases the patients were found to suffer from dyspnœa alone; in one case the dyspnœa persisted throughout the period of repose; in eight cases dyspnœa was present throughout the repose, but, during the spasms, the breathing was entirely suspended; in three cases

there was present a peculiar gasping, suggesting the idea of imminent suffocation, and in two cases the breathing was hard and very rapid. In two cases the breathing was short, laborious, and stertorous, passing during the spasms into a kind of gasp; in one case respiration was short and hurried, the inspirations numbering 40 per minute, while the vesicular murmur was inaudible; in one case there was a hissing sound produced during inspiration and expiration as long as the spasms lasted; difficulty of articulation was present in four cases; and in seven cases loud screams were uttered during, or just anterior to the accession of the spasms. In two cases the inspirations were deep and irregular; in one case the number of inspirations per minute was 25, the character of the respiratory efforts not being described. In one case the walls of the chest were fixed, and the respiration was irregular; in two cases there was loss of speech; in one case the respiration was laboured; and in one case there was present a sense of suffocation. In one case the respiration was irregular, and at times ceased to all appearance, becoming noisy during the spasm, as if drawn through a reed; in another dyspnœa was present during the interval, during the fit ceased altogether, and then became gentle but laboured for a few seconds, the simple dyspnœa then returning; in another the dyspnœa was also present during the spasm, with cessation during the spasm, but the breathing was laboured throughout. In two cases there was super-imposed a sensation of constriction of the throat.

There seems to be no regular rule as to the condition of the circulatory system, the modifications reported being at once diverse and numerous; thus, in thirty-one cases, in which the reports of the state of the pulse was carefully recorded, one was reported as beating 150 per minute, one as 130 full and hard, one as 186, one as 140 small and irregular, one as 88 and regular, and one as 74 and weak. In three cases the pulse was described as very rapid; in one as very rapid, fleeting, and indistinct; in one as rapid, but diminishing towards the close of the case; in three as feeble and frequent; in two as barely perceptible, in spasms sometimes suspended; in two as small and feeble; in one rapid and barely perceptible, in spasm, heart palpitating violently; in one as small and rapid, becoming

almost imperceptible; in one as hurried, small, and regular; in one as small, and in one as imperceptible. In one case the pulse was described as full and incompressible during the spasm, but becoming, in the period of calm, rapid, small, and barely perceptible; in one as faint and rapid, ceasing to touch, but again returning, becoming quick, but fluctuant; in one as faint and rapid, then quick and fluttering; and in but one as unaffected. In one case the impulse of the heart was noted as much increased in force and rate. Out of the 136 cases there were recorded eighty-nine cases in which opisthotonos was present, two cases in which emprosthotonos was recorded, while, in the residual 45, no direct mention was made of this symptom. In twenty cases the hands were reported clenched, in one the hands were described as fixed and stiff, while, in the others, no mention was made of the presence or absence of this symptom. In seventeen cases the feet were reported as arched, and in one case the toes were inverted.

In one case vomiting could not be induced at all, while in ten cases the vomiting was perfectly spontaneous.

In two cases there was present exalted sensation, and in two cases the sensation was perverted. In two cases sensation was described as perfect, while, in the others, no mention was made of the condition of the sensation. Of course this reference to sensation has nothing whatever to do with the hypersensitiveness of the skin referred to as being always found present in such cases.

In twelve cases the intellect was noted as perfectly clear; in one, the mind was stated to be clear to the last; and in ten cases the mental faculties were described as perfectly clear. In three cases it was reported that the patients were conscious throughout; in one case perfect consciousness existed till just before death; in three cases consciousness was lost during the spasm, but during the interval perfect sensibility existed. In one case stupor, late in advent, was reported; in two cases the patient was described as insensible, and in another case as perfectly insensible. In three cases unconsciousness was recorded, and in one the patient was described as sensible to a very slight extent. In one case, reported by M. Vigla, of the Hotel Dieu, in the *Gazette des*

Hospitaux, of October 7th, 1848, a dose of strychnia, equivalent to $\frac{1}{6}$th of a grain produced a peculiar train of hysterical symptoms, accompanied with hallucinations.

In another group of cases distinct from those above, in 33 of which the symptoms are recorded---spasms were present in the muscles of the neck first in two cases. The inferior extremities were attacked first in 14 cases. The feet were arched in 10. The hands clenched in 15. Arms bent spasmodically, generally across trunk, in 22. Complete opisthotonos in 31. Trismus in 11 cases, but always occurring late, and never very severe. Risus sardonicus present to a slight extent in four. Dyspnœa present in 23. In 27 sensibility was perfect throughout. In two it was exalted, and in two the sensibility of the trunk and limbs seemed entirely lost during the intensity of the spasm. Respiration and circulation apparently ceased during spasm in 11 cases. Relief sought by change of position in five cases, and by rubbing in three.

Another point, and one of some interest, is the occurrence of an interval of considerable duration between the spasms. This was noticed in a case reported by Mr Nunnely, of Leeds, in the *British Medical Journal*, January 26th, 1856, in which there was an interval of about an hour, during which the patient was free from spasms. Also, in a case reported by Mr G. M. Jones, of Jersey, in the *Lancet* of September, 1856, in which also about one hour was observed to elapse between the spasms.

With these remarks on the aberrant physiological effects, we conclude our consideration of the physiological effects produced by, or the symptoms of, poisoning by strychnia in man. But it may be well, before leaving this part of the subject, to consider first a few cases of poisoning by nux vomica. Those of my readers who would like, more in detail, to study reported cases of poisoning by this substance, nux vomica, should consult Dr Husemann's contributions on this subject, as published in Reil's Journal fur Toxicologie, 1857, 2 H. p. 469. In this paper there is an able analysis of many cases of poisoning by this substance, with many useful remarks thereon. The cases on which the following remarks are founded are, with one exception, of more recent date, and may form a fitting adjuvant to

the paper already alluded to, while the greater frequency of certain symptoms in poisoning with nux vomica, as compared with those found in poisoning by pure strychnia, is well worthy of notice. The symptoms of poisoning were in five cases out of thirty-three ushered in by spontaneons vomiting; in one case vomiting and diarrhœa. In two cases by tinnitus aurium. In one case convulsions setting in suddenly, and without warning, were the first symptoms; tinnitus aurium, with stupor was first noticed in one case; paralysis of lower extremities in two; general stiffness of the joints in five; profuse perspiration and muscular twitchings in one; giddiness, loss of power in legs and general stiffness of the muscles, in one case.

Trismus was found present in six cases. The pupils were found dilated both in spasm and repose in two cases; contracted in one; in two cases the pupils were dilated in spasm and not affected in interval, while, in one case, there was present during the spasm, contraction of the pupils, but this was not observed in the interval; in one case the pupils were recorded as normal throughout. Opisthotonos was noted as present in thirteen cases, but in none of the others was any mention made of its presence or absence. Consciousness was reported perfect in eight cases; in one there was increased sensibility to light and sound; and in one sensation was described as being very acute in the interval between the spasms. In two cases the pulse was noted as weak and rapid; in one as hard; in one as hard and excited; in one as suspended in spasm, but in interval very feeble and rapid.

Spontaneous vomiting with pain in the epigastrium was noted in six cases. Dyspnœa noted as great in spasm and respiration as accelerated in the interval in seven cases. In one case the effect of nux vomica as a chronic, or, it might be a cumulative poison, was well illustrated. In this case, published in the *Lancet*, January 14th, 1856, 144 grains of nux vomica in powder were swallowed in sixteen days, and symptoms of poisoning did not appear till five days after the cessation of the administration of the poison, that is the twenty-first day after the exhibition of the first dose. In this case death did not occur till the twelfth day after the cessation of the use of the drug,

and not till the twenty-eighth day after the first dose was taken. The symptoms began with ringing in the ears, drowsiness and other symptoms referable to a disordered state of the cerebral functions. Vomiting and diarrhœa, followed by tremors, which gradually passed into tetanoid spasms, then appeared, respiration being suspended during the spasm but accelerated in the period of calm. The pulse was feeble throughout. The risus sardonicus was present, and trismus was well marked. The pupils were, in the spasm, dilated and sluggish. Patient died from exhaustion in the period of calm.

From these few remarks it will, I think, be seen that, as one would expect, the general outline of symptoms are common to nux vomica and strychnia, the same type would perfectly represent each, but still there are one or two very curious points of difference. The advent of the symptoms in cases of poisoning by nux vomica is less rapid than in cases of strychnia poisoning; there are more commonly found in nux vomica poisoning, symptoms of cerebral disorder; and, speaking generally, there seems to be, as far as from published cases I can judge, less of uniformity in the co-relation of symptoms than we find in cases of poisoning by the isolated alkaloid.

From a collection of cases such as I have made, other points of much interest and importance are attainable, and these points we shall now examine.

Thus, the total number of cases was 136, of which 65 were males, 51 females, while the sex of the patient was not stated in the others. Of the males, 32 recovered and 33 died; of the females, 26 recovered and 25 died; while of those in which the sex was not stated a fatal result ensued in 11 cases, and recovery was recorded in nine.

As to the form in which the poison was administered, vermin-killers, containing strychnia, were administered in 23 cases, in 16 of which recovery took place. In 15 cases the poison was exhibited in pill, and in eight of these death ensued; in eight the poison was administered in solution, and a fatal result followed in six. Strychnia proved fatal in three cases when administered in powder, the total number of cases in which this form was used being five. As sulphate it proved fatal in two cases, while recovery took place

also in two cases. There are also recorded two cases in which the acetate, and one case in which the nitrate were exhibited, but without fatal results, and one case in which both the nitrate and the pure powder were swallowed, and yet recovery took place. In 43 cases in which death occurred, and in 34 cases in which the patients recovered, the form in which exhibited does not transpire in the reports. In 92 of the cases the dose administered was stated, while in 44 no mention was made thereof. Of the fatal doses under one grain there are recorded 10 cases, of which $\frac{1}{16}$ of a grain proved fatal in one case, $\frac{1}{6}$ of a grain in one case, $\frac{1}{4}$ of a grain in one case, $\frac{1}{2}$ a grain in two cases, and $\frac{3}{4}$ of a grain in five cases. Of those cases in which a fatal result followed the exhibition of a dose of one grain and upwards, the absolute quantity administered amounted to one grain in one case, to one grain and a half in five cases, to one grain and three-quarters in one case, to three grains in eight cases, to four grains in one case, to five grains in three cases, to six grains in one case, to eight grains in one case, to fifteen grains in one case, to thirty grains in another, and to two scruples in another, while in one other case the fatal dose was divided into half a grain thrice daily for several days, thus constituting a supporting case for the theory of cumulative action. Of the thirty-seven cases in which recovery followed the exhibition of a dose greater than one grain, the following is the list:—Three cases in which the exhibition of one grain was followed by recovery, in one case recovery occurred after the administration of one grain and a half, in three cases two grains, in three cases two and a half grains, in thirteen cases three grains, in one case three and a half grains, in five cases four grains, in one case five grains, in two cases six grains, in one case seven grains, in two cases ten grains, and in one case twenty grains were exhibited, yet failed to produce fatal consequences, while in one case seventy grains were administered, in rather less than two months, without producing a fatal result.

The total number of cases in which the interval elapsing between the time of administration and the first accession of symptoms was forty-eight, and of these twenty-eight proved fatal. Of the cases in which recovery took place, the interval

was from two to three minutes in one case, five minutes in two, twenty minutes in five, thirty minutes in two, thirty-five in one, forty-five in two, one hour in two, one hour and a half in two, two hours in one, and two hours and forty-five minutes in one case. Of the fatal cases the symptoms came on in two cases five minutes after the exhibition of the poison, in one case in from five to ten minutes, in one case in ten minutes, in four cases in fifteen minutes, in four cases in twenty minutes, in six in half-an-hour, in one in forty-five minutes, in one in fifty-five minutes, in four in an hour, in one in an hour and a-half, in one in two hours, in one in two hours and a-half, and in one case in three hours.

The total number of cases in which the duration of the symptoms was recorded was thirty-three, and of these twenty-four were fatal. Of the non-fatal cases, the shortest duration was twenty-five minutes, and the longest sixty-two hours, while, between the two extremes, the duration was as follows :—In one case one hour, in one an hour and twenty minutes, in one two hours, in one four hours and a-half, in one five hours, and in two eleven hours and a quarter. Of the fatal cases the shortest duration recorded was five minutes, the longest six hours, while between these there occurred one case in which the symptoms lasted ten minutes, two in which the duration was noted as fifteen minutes, while of the others, the duration was in one case twenty minutes, in one thirty minutes, in one forty minutes, in one forty-five minutes, in one an hour, in three sixty-five minutes, in two an hour and a-quarter, in one an hour and a-half, in three two hours, in one two hours and a-quarter, in two three hours and a-half, in one four hours and forty minutes, and one five hours and a-quarter. As to the case above referred to as being peculiar in the duration of the symptoms, viz., sixty-two hours, it may be noted that this figure represented but the primary or tetanic effect of the poison, there being besides this a series of secondary effects ascribed to the action of the poison, which lasted fully six weeks ; while in another case, in which the duration of symptoms was not ascertained, there succeeded a train of dyspeptic symptoms of several weeks' duration, these symptoms being referred to the operation of the poison.

The next point worthy of notice is the total interval elapsing between the date of administration and the occurrence of recovery or death, this being a point of great practical importance. In all, this point was reported in sixty-seven cases, of which recovery took place in twenty-nine, and a fatal result in the residual thirty-eight. Of those cases in which recovery took place, the shortest time was half-an-hour, which was recorded in three cases, and the longest three weeks, excluding the two cases in which there appeared secondary phenomena, referable only in an indirect manner to the action of the poison. The other cases were reported, as to lapse of time between time of administration and recovery, one as thirty-five minutes, one as two hours and twenty minutes, one as three hours, two as five hours, one as five hours and twenty minutes, three as seven hours, one as eight hours, two as eleven hours, three as twelve hours, one as fifteen hours, two as twenty-four hours, two as two days, two as three days, one as four days, two as one week, and one as three weeks. Of the fatal cases, the shortest time was ten minutes, and the longest eighteen hours, the intermediate periods being one of fifteen minutes' duration, two of twenty minutes, three of thirty minutes, two of thirty-five, one of forty-five, two of an hour, three of an hour and a-quarter, one of an hour and twenty minutes, four of an hour and a-half, one of an hour and three-quarters, one of two hours, one of two hours and a-half one of two hours and three-quarters, four of three hours, one of three hours and ten minutes, one of three hours and a-quarter, one of three hours and a-half, two of four hours, two of five hours, one of six hours, and lastly, one of seven hours.

Such are the points which may receive elucidation from collecting and analysing a large number of cases, and while I might in a similar manner treat the cases of nux vomica poisoning, I refrain from so doing, believing that all the facts which would thereby be elicited are already thoroughly recognised. I therefore now intend to pass on to a consideration of the physiological effect of strychnia on the lower animals, to all of which, with the exception of the mite, it appears to be poisonous.

The exhibition of strychnia to animals is followed by a train of phenomena closely resembling that which attends its adminis-

tration to man. Stated generally, these phenomena consist of tremors, twitchings, and startings of the voluntary muscles, in part or in whole, followed by tetanoid spasms, emprosthonotic or opisthonotic, according to the species operated on. During these spasms the respiration is, as a rule, suspended, the heart's action accelerated, and consciousness apparently for the time obliterated. In the interval between the spasms the respiration and circulation generally become normal, and the consciousness returns, while there is also present the peculiar hyperæsthesia already noted in considering the type of physiological action in reference to man. Such cases may end in recovery or death; and should death occur, its immediate cause may be either asphyxia, syncopé from spasm or paralysis of the heart, or gradual exhaustion of the nervous system.

There are, however, in the various classes of animals, certain peculiarities, which may here be noted. And first, in the rabbit: strychnia, if administered by subcutaneous injection, kills generally within 15 minutes, if the dose exceed the 30th of a grain, the symptoms being similar to those already enumerated, and the spasms being, as a rule, opisthonotic. But if given by the mouth, such a dose will rarely prove sufficient to kill; nay, much larger doses may be given without producing any very marked symptoms; and generalizing from my own experience, I would say that death will not be found invariably to follow a dose of strychnia less than one-twelfth of a grain; by which I mean that I have never seen a rabbit recover from a dose of strychnia greater than one-twelfth of a grain, unless some reputed antidote were administered, while I have repeatedly seen a smaller dose followed by recovery.

The *post-mortem* appearances in the rabbit vary materially according to circumstances. Thus, it is not uncommon, after administering about one-eighth of a grain of strychnia by the mouth, to find patches of inflammation of the mucous membrane of the stomach; but this, though common, is not constant, nor does increase of the dose occasion any appreciable increase in the number of cases in which this pathological state is found. Then the appearance of the heart is very variable, it being in some instances firmly contracted and empty, while, in others, it

is very much distended by dark, fluid or clotted blood. The lungs are in some cases congested, while in others they are anæmic, and in some few quite natural. There is generally present congestion of the brain and its membranes, with effusion into the ventricles and subarachnoid spaces; but these phenomena are not constant. There is usually found also congestion of the spinal cord and membranes, with or without effusion in the sheath; but this also is not constant. The only constant phenomenon in my experience is the dark and fluid, or loosely coagulated condition of the blood; but as this is present in many other cases in which the death arises from other causes, some of which are perfectly natural, it is evident that the evidences derivable from the *post-mortem* appearances are of little, if any value, when taken apart from the symptoms and the chemical detection of the poison. Turning now to the sheep, goat, and hog.

In these animals the difference between the phenomena produced by small doses, administered by the stomach and by subcutaneous injection, is more marked than in the case of the rabbit; thus Despartes gave very large doses of nux vomica to a goat without producing any very apparent effect (Ainslie, Mat. Med., p. 320); and I have it on extremely reliable authority that in New Zealand, where strychnia is much used to kill diseased sheep, that doses amounting even to 10 grains, administered by the mouth, have frequently failed to produce any symptoms of poisoning whatever, although no vomiting occurred; whereas, if administered by subcutaneous injection, or applied to a wound, a single quarter or half-grain dose, of the same sample of the alkaloid, rarely, if ever, failed to cause death very rapidly. Again, in the case of hogs, Loss states that they may eat a large quantity with impunity, while Dr Christison has killed a wild boar with one-third of a grain in 10 minutes, by injection into the pleural cavity. Hence it would appear that in these animals there is brought about, during the digestive process, or during absorption from the stomach, some change, whether of molecular aggregation or of chemical composition of the alkaloid, whereby its physiological action becomes modified, and apparently entirely

destroyed, it being quite apparent, from the rapidity of action on its being introduced into the blood, that to no constitutional peculiarity of these animals is this anomalous fact to be ascribed. To Dr Young, Professor of Natural History in the University of Glasgow, I am indebted for an opportunity of testing the action of this alkaloid on an Abyssinian ram, weighing about 12 stone. To this animal half a grain of the acetate of strychnia was administered, by subcutaneous injection in the precordial region. In three minutes general twitchings of the muscles appeared, with staggering gait. The twitchings increased, and the swaying to and fro of the body became more marked, till five minutes after the administration of the poison, when a severe tetanoid spasm came on, the animal being thrown on its left side. There was present emprosthotonos, the breathing was rapid and stertorous, heart's action rapid, pupils widely dilated, and the muscles of expression around the mouth presented curious twitchings, not unlike the risus sardonicus. This spasm lasted three minutes, and was succeeded by an interval of repose of five minutes' duration, when a second spasm came on, more intense than the first; the emprosthotonos was more powerfully marked, the respiration was suspended, the pupils widely dilated, the eyeballs affected alternately with convergent and divergent strabismus, circulation rapid and weak, and sensation apparently abolished. This spasm lasted fully three minutes, and was again followed by a period of repose lasting one minute, the next spasm being induced by slightly touching the animal's tail, thus proving that the hyperæsthetic condition of the skin was present; this spasm passing off, was again succeeded by a period of repose of short duration, a fourth spasm rapidly following, induced apparently by clapping the hands close to the animal's ear, the sudden nervous impression causing the animal to start, and thus reflexly reinducing the accession of the tetanic state. The alternations of spasm and repose went on for 29½ minutes, when the animal expired in one of the periods of quiescence, death apparently taking place from exhaustion. Sensation in the tail and posterior extremities was destroyed in 24½ minutes after the exhibition of the poison, in the lower half of the trunk in 27 minutes, in the upper part of trunk, and in the anterior

extremities, and in the face, in 29, while the eye was still sensitive $29\frac{1}{4}$ minutes after the administration, and one quarter of a minute before death. Forty-eight hours after death *post-mortem* rigidity was present and well marked.

Post-mortem examination showed rapid advance towards putrefaction, congestion of the lungs towards their posterior surfaces; congestion of the liver, spleen, and kidneys; general darkness and fluidity of the blood; the heart was contracted with tolerable firmness, and contained little blood. The brain and cord were not examined, as such a mode of procedure would have interfered with the preparation of the skeleton. The liver, heart, and a quantity of the blood was removed for analysis, and shall be referred to hereafter.

In Cats.—These animals, whether from their proverbial tenacity of life, or from some other cause not yet explained, resist the action of strychnia to a degree totally disproportionate to their size. In them there is no material difference between the dose required to produce a fatal result when administered by the stomach and when subcutaneously injected, the latter, however, acting more rapidly, as we should expect. The symptoms produced are similar in kind to those which we have already recorded as regards the other animals: emprosthotonos is more common than opisthotonos. The *post-mortem* appearances are equally vague and unsatisfactory.

In Dogs.—These animals are affected with tetanic spasms perhaps more rapidly than the animals already noted, the interval elapsing between the time of administration and the period at which the phenomena begin being very short. The duration of the symptoms is however greater than in most animals, a dog rarely dying under half an hour, if the poison do not exceed, as a dose, the quarter of a grain given by the mouth. The *post-mortem* appearances are here also of little importance as evidences of the action of the poison. It has, however, been noticed by several experimenters that the arteries are much contracted.

In Mice and Rats.—There is variably produced opisthotonos and emprosthotonos, though, on the whole, especially in mice, emprosthonotic spasms may be said to preponderate. As the

symptoms and *post-mortem* appearances are very much the same as those to which attention has already been directed, no further remarks on these subjects are here called for. I may, however, state that, next to the frog, the mouse is by far the most sensitive to the action of strychnia of the small animals found in this country, and is, to the action of this poison, perhaps the most sensitive member of the mammalia; and not only is the ordinary grey house mouse, but also the white mouse, and the different species of shrews, approximate closely to each other in this sensitiveness to the action of this alkaloid. If the mouse be young and healthy, $\frac{1}{750}$th of a grain will generally be found to produce death after the lapse of about one hour.

In the Frog.—The frog, as first pointed out by Dr Marshall Hall, is an animal so sensitive to the action of strychnia that if $\frac{1}{1000}$th of a grain be dissolved in a drop of water, and be then placed on the skin of the back, previously dried, tetanoid spasms are produced in from a quarter of an hour to one hour. On this ground Dr Marshall Hall has proposed it as a test for the presence of strychnia in organic mixtures, and by Professor Traill, of Edinburgh, it was considered the most delicate and reliable test for strychnia then known, he having succeeded in detecting, by this mode of procedure, the $\frac{1}{5000}$th of a grain of the alkaloid (*Lancet*, July 12th, 1856). Dr Harley, writing in the *Lancet*, June 14th, 1856, considers the frog test the most minute and reliable of any test for strychnia, especially when injected into the thorax, he having succeeded, in very small frogs, in detecting the presence of the $\frac{1}{18000}$th of a grain of strychnia, by the tetanic phenomena produced after injecting of this minute quantity into the lungs.

From experiments which I have myself performed, I had some time ago become convinced that in a full-grown, healthy, vigorous frog it was possible to produce tetanoid spasms with the $\frac{1}{2000}$th of a grain of the acetate of strychnia, applied subcutaneously; and, further, it seemed to me that the smaller the frog, or the more lethargic its state, the more susceptible was it to the poison.

When such doses as the $\frac{1}{5000}$th, $\frac{1}{10000}$th or $\frac{1}{20000}$th of a grain were administered, I invariably found perfect recovery result,

provided the animal were covered by a wet piece of cloth, and kept under a bell-jar. This recovery took place generally within twenty-four hours, but in some cases there was some stiffness of the muscles of locomotion noticed even at the end of 48 hours. Nor was the $\frac{1}{500}$th of a grain the largest dose followed by recovery. In many cases I found that death did not result even after a dose as large as the $\frac{1}{75}$th of a grain, provided the skin of the animal were kept moist, and the surrounding water removed, and the animal as a whole washed occasionally with pure water. Apparently, if sufficient time be allowed, excretion of the poison is ultimately effected, and anything which has a tendency to accelerate this excretion has, of necessity, a powerful effect in tending to resuscitate the animal. One day, after having administered to a healthy frog the $\frac{1}{500}$th of a grain of strychnia by subcutaneous injection, and having obtained the usual tetanic phenomena, I covered it over with a moist cotton rag, placed it on a plate in which there was present about one ounce of pure water, and over it placed a bell-jar, to prevent the escape of the animal, provided recovery should take place. At the end of forty-eight hours, recovery was apparently perfect, and the animal was observed hopping about quite briskly within the bell-jar. Through inadvertence on my part, however, the animal was left for the next twenty-four hours under the bell-jar, on a dry plate, and on examining it at the expiration of that time, my astonishment was considerable when I found the animal, which the day before had quite recovered, now lying prostrate in severe tetanic convulsions. The damp cloth was at once re-applied, and in a few hours these spasms had entirely passed off. This experiment I then performed intentionally several times, and obtained a perfectly uniform result. It then occurred to me that the phenomena here witnessed might be due to the action on the system of the frog, of a quantity of the strychnia retained in the system, the quantity being, however, too small to sensibly affect the muscular movements, while it was in full health and vigour, but perfectly sufficient when the system was weak and exhausted by the deprivation of moisture, to produce the full physiological effect. I therefore argued that if this really be the cause of the phenomena witnessed, that by inducing in the animal an artifi-

cial weakness, debility, or exhaustion, by the deprivation of moisture, prior to the administration of the poison, that in this manner I might obtain results even more delicate. Accordingly, I obtained a full-grown, healthy frog, and placed it under a bell-jar, to hop about on several layers of blotting paper, which I conceived would suffice to remove the moisture from the animal with sufficient rapidity, and without danger to the life of the animal. In this I was not disappointed, and in twenty-four hours had the satisfaction of finding the frog very much exhausted, and on the $\frac{1}{20000}$th of a grain of the acetate of strychnia being exhibited by subcutaneous injection, found that in 15 minutes distinct and characteristic spasms were obtained. Gradually, then, reducing the dose, I have been enabled in this manner to detect the $\frac{1}{300000}$th of a grain diffused in water or blood. The application of this to the detection of strychnia, in cases in which such is called for, I shall hereafter discuss, but before leaving this part of the subject it is interesting to know that the supposition or theory which I had formed concerning the excretion of the strychnia by the frog into the circumambient moisture, gains considerable support from the fact that in that water I have of late frequently succeeded in demonstrating the presence of strychnia by the colour re-actions, and after concentration by its action on frogs, weakened as above described. In concluding the action of strychnia on animals other than man, we have seen that the general symptoms produced, as well as the *post-mortem* appearances are similar, that of themselves the symptoms are perfectly sufficient to stamp the real nature of the case, while the *post-mortem* appearances are but of little use in guiding to the formation of any clear idea of the nature of the case, and the cause of death.

The action on one other class of animals I might have mentioned, viz., the minnow. These small fish are very sensitive to the action of this alkaloid, and so also are trout parr. When placed in a solution containing about one part of strychnia in 150,000 parts of water, little is noticed for the first three or four minutes, they then become apparently alarmed, their movements become more rapid, and acquire rather a spasmodic character, and in twenty minutes at latest, death ensues, the animal being

curved laterally, and in at least 19 cases out of 20, the curvature is such that the concave surface looks to the right, the convex to the left. In these remarks it will be seen that I have strictly confined my remarks to my own observations, believing that no good would accrue to a mere recapitulation of the results previously known.

Such, then, are the effects produced on various animals by the action of strychnia, and it may now be interesting to inquire how it is that strychnia so operates, on what structure does it act, and, in that structure, what change does it induce in order to effect such a wonderful stimulation and distortion of the organic processes and muscular movements? This question is one of vast importance in the treatment of cases of poisoning by this alkaloid, besides having in it much of interest to the physiologist, consequently we find that it has been carefully investigated by such able scientific men as Professor Albert Kölliker, by Professor Meyer, of Zurich, by Magendie, by Addison and Morgan, by Brown Sequard, by Claude Bernard, by Dr Marshall Hall, and many others. From the results by these experimenters obtained, strychnia, it appears, acts by absorption into the blood, but does not operate either on the peripheral nerves or on the muscular fibre, facts which are easily demonstrable by dividing in a frog the nerve supplying a limb, while the circulation is left perfectly intact, either previous to the exhibition of the poison, or during the presence of the tetanic phenomena, when it will be found that the tetanic rigidity fails to appear, or, if present, at once passes off in the limb so treated. By analogous experiments the non-action of strychnia on the sensory nerves was also established, while it was further ascertained that in frogs muscular irritability and nervous excitability were almost destroyed, while in the mammalia both were much deteriorated. Limited by such restrictions, the question is by no means settled, and though now the belief in the action of the poison on the spinal cord is almost universally accepted, there are many theories advanced, some backed up by very interesting and ingenious experiments, to allo-

cate to one particular portion of the cord, or constituent thereof, or to explain in some collateral manner the changes therein produced, thus Dr Harley advocates the opinion that strychnia mainly acts on the blood, in which it induces some change, in virtue of which it becomes incapable of furnishing to the nerve centres especially, the proportion of oxygen requisite so to nourish these structures as to enable them to discharge in a healthful manner their several duties, or, in other words, the blood becomes so modified that it presents to the nerve centres oxygen in a form, or under circumstances that it cannot be perfectly utilized. Other physiologists tend rather to ascribe the effects produced by strychnia more immediately to a hyperæmic condition of the cord. In a paper read before the Medico-Chirurgical Society of Edinburgh on this subject, by Dr Alexander Ingram Spence, the theory is advanced that strychnia acts specifically on a certain class of cells in the nerve centres termed the intermediate nerve cells of Jacubowitsch, and therein induces a state of excitability such, that, when receiving any nervous impression from without, they agitate the motor nerve cells not only in their immediate vicinity but also further down the cord. For a full account of the experiments on which this theory is based, I must refer the reader to the *Edinburgh Medical Journal* for July, 1866; the method, however, in which the principal experiment was conducted, and the results therein obtained, are so much at variance with the results of Messrs Addison and Morgan, who ascertained that strychnia, applied to the substance of the brain or cord in a manner preventing its absorption into the systemic circulation, failed to produce its physiologlcal effect, in the face of this, I can hardly see how the proof can stand; while, if the intermediate nerve cells of Jacubowitsch exist, and really have arrogated to them the office of transmitting to the sensorium external impressions, and to the motor nerves, the impulse necessary to cause motion, the following is perhaps the theory which will best explain the mode of production of the tetanic phenomena witnessed in cases of poisoning by

strychnia, as also in explaining how, as a therapeutic agent, it is contra-indicated in certain cases, while in others its use is followed by great benefit to the health of the patient.

Strychnia, then, I would say, so acts on the nerve cells through which sensations are transmitted to the sensorium, that the impressions thereby transmitted are perverted, and in the sensorium causes, as it were, the registration of a sensation very different from that really applied to the extremities of the sensory nerves, and consequently induces the production, or, to carry out the simile of the electric telegraph, the sensorium issues an order to cause, through the motor nerves the muscular efforts required by the sensation transmitted. That the transmission of sensations to the sensorium is necessary to the development of the spasms, in other words, that the tetanic phenomena are in many instances purely reflex, receives confirmation from the fact that when strychnia is administered to a frog, and the animal remains, as in many cases it does, perfectly motionless, the spasms do not come on for a very long time, and in some cases I have seen the time elapse between the time of exhibition of the poison and the accession of symptoms reach two hours, and I have never yet seen the spasms come on in the frog unless some external impression were made on the skin, or the animal endeavoured to change its position, thereby causing itself the production of the sensation required to induce the spasm. The theory of the reflex nature of the spasm also receives confirmation from the fact that a frog perfectly tetanised by strychnia, if allowed to remain absolutely free from external impressions, and so surrounded by water as to facilitate the elimination of the poison, very shortly recovers, while if, by external impressions, the spasms be kept constantly present, the animal very shortly succumbs. Also from the fact, that if to a frog anointed with hydrocyanic acid—which paralyses sensation—there be administered strychnia, no spasms result as long as the action of the prussic acid persists, but as soon as this passes off, and any external impression is made, the spasms at once appear. Also from the fact that in man and the lower

animals, sleep and narcotics, both of which cause temporary suspension of sensation, tend very materially to prevent the accession of the tetanic phenomena. Yet, perhaps, one of the best arguments in favour of this view is that advanced by M. Claude Bernard, who, in advocating the theory of the action of poisons through the nerves, rather than through the blood, thus writes :—

"Let it (strychnia) be introduced into the circulating fluid—supposing all the posterior roots which arise from the spinal cord to have been divided, no convulsions, of course, would be produced; but let a single root be left untouched, and through this single channel the necessary impulse will be given; the blood which circulates throughout the system, and conveys the toxic substance into every part, brings it in contact with the extremities of that sensitive root which alone remains uninjured and still communicates with the spinal cord, and general effects are at once developed."

But does this not rather give force to the theory here advanced, that the transmission of an external sensation is necessary to cause the development of the full physiological effect of the poison. But while this theory may be quite satisfactory and sufficient in most cases, there may be a few in which the following theory may well represent the actual conditions, that instead of the nerve cells transmitting sensation, those rather which transmit the motor power are those affected, and in this manner we could account for the mere wish to change the position, being, as it were, the impression which induced the accession of the spasm, while, in a few cases at least, I think it possible that both these may co-operate, thus having a set of sensory nerve cells transmitting to the sensorium perverted sensation, and at the same time a set of motor nerve cells transmitting perverted orders with regard to the muscular efforts to be made.

In the preceding paragraphs, the physiological action of strychnia, in poisonous dose, has been fully discussed, but, in order fully to appreciate the *modus operandi* in medical doses, a short study of the physiological effects produced by small repeated doses of the alkaloid becomes necessary, and to these effects we propose now to direct attention, apart from the consideration of the various affections for the

relief of which strychnia, either simple or as a salt, has been proposed, and to which affections I do not intend to devote attention. The physiological effects observed in man to follow the administration of small repeated doses of strychnia may, for convenience, be divided into two classes, this division being, however, more arbitrary than real, and founded rather on the degree of physiological action produced than on any absolute difference in the phenomena observed; the former we may call tonic and stimulant, the latter spasmodic or convulsive. Strychnia, when given in small repeated doses, produces, by the influence which it exercises over the spinal cord and medulla oblongata, an increased tone in the various organs which are supplied with nerve power therefrom. Hence it is that small doses of strychnia increase the appetite, facilitate digestion, stimulate the liver, increase the secretion of urine, and cause its excretion to be performed more frequently, while it sometimes acts gently on the bowels, and occasionally acts as a sudorific. In larger dose, or when a slightly greater degree of physiological action is produced, it occasions phenomena indicative of interference with the digestive process, the appetite becomes impaired, the tongue rendered foul, and the other symptoms of dyspepsia appear. But, it may be asked, how is this state of affairs brought about? how does it occur that a slight increase in the degree of physiological action produces dyspeptic symptoms, while a less degree acts as a corrective of such, when pre-existing and arising from natural causes? If, as I have before pointed out, it be conceded that strychnia acts specifically on those cells in the spinal cord and medulla oblongata, whose office it is to conduct sensory impressions brought to them by the sensory nerves for transmission to the sensorium, and those which conduct from the sensorium motor impressions for transmission through the motor nerves to the periphery, it can, I think, be easily understood whence and how the benefit derived from the exhibition of strychnia arises. In this case strychnia would, theoretically, be beneficial in certain cases in which either the sensory nerve fibres convey

impressions which reached the sensorium in a form perverted by the modification induced during their transit through these nerve cells, or in certain cases in which the motor impressions are perverted during their transit through these cells from the sensorium to the motor nerve fibres. It may be noticed that in this statement I have limited the theoretically beneficial effects of strychnia to certain cases only, in which these cells are so altered as to lead to this perversion of their function—this inadequate performance of their duties. This differentiation is necessitated on account of there being two essentially different, nay, diametrically opposed conditions, which give rise to the production of the same phenomena, the one being associated with, but I do not believe solely depending upon, congestion, the other being associated with, but I do not believe entirely due to, a pathological condition of an opposite nature. In the former the exhibition of strychnia is useless, I may say in most cases highly prejudicial, while in the latter the results attending the administration of strychnia are, as a rule, highly satisfactory. This is well illustrated in the treatment of hemiplegia. Here we have an affection associated with congestion in certain cases, while in others this is absent. In the former strychnia invariably aggravates the disease, in the latter its exhibition is almost universally attended with success. Hence, then, it would seem probable that the action of strychnia is on those cells interpollated in the one case between the sensory nerve fibres and the sensorium, and, on the other hand, between the sensorium and the motor nerve fibres; that there are cases dependent upon perversion either of sensation or motion, or both, in which strychnia relieves, and others in which it almost invariably causes an aggravation of the symptoms, and that the mode of differentiation of these is by the absence or presence of congestion, and that while in these cases strychnia really does good, it is still capable, when adminstered in health, of producing in those very cells over which, in disease, it exercises a favourable influence, a condition similar to, if not identical, with the diseased state.

Mode of death.—Such being the explanation of the production of the symptoms, I have now to consider the manner in which death is produced, and here, again, is a much contested point. There has been advanced the theory of nervous exhaustion—that of nervous paralysis—that of paralysis and spasm of the heart—that of asphyxia, each and all of which have their firm advocates; some, however, stating that several of these may co-operate. But there is no doubt in my mind, from the experiments which I have made, that death may, nay, does occur in all these different ways.

Apart from physiological distinctions, there are two great classes into which fatal cases may be divided, according to the mode of death—the cases in which death occurs during a spasm, and the cases in which a fatal result occurs during the state of repose. Of the cases which I have collected, twenty died during the spasm, and ten during the repose, while the fact of the occurrence of death was merely stated in the others.

Post-mortem appearances.—Here, as in the consideration of the physiological effects of this poison, I shall present my view of what constitutes a typical combination—supposing the examination to be made from 24 to 48 hours after death. The face is pale and tranquil, the eyes closed, pupils dilated, cadaveric rigidity is present to a marked degree, with opisthotonos, arching of the soles of the feet, clenching of the hands, and flexion of the arms across the chest. The dependant parts of the body livid—lungs congested, especially towards the posterior surface—the heart contracted, firm, and empty—the blood viscid, dark, and containing a few loosely formed coagula—liver, spleen, and kidneys slightly congested, bladder empty, mucous membrane of stomach congested in patches—brain and spinal cord, together with their respective membranes, much congested, with effusion into the ventricles and subarchnoid spaces. Such are the *post-mortem* appearances which may be regarded as typical; but the variations are considerable.

Thus, in 36 cases in which careful notes of the *post-*

mortem appearances were accessible, the face was recorded as pale, and the features calm and placid in four cases; in seven the face was described as congested; in one case the appearance of the face presented characters very like those looked upon as distinctive of death by strangulation; in one case the expression was determined; in one case it was livid and swollen, and in one œdematous; in two cases slightly congested, while the features were placid; in one case the face was pale, but the lips livid, and in another the face was livid, and the tongue protruded. In six cases the jaws were shut and fixed; in one fixed but half open; in two half open and lips covered with bloody froth; in two open and lips covered with a whitish froth; in three cases the teeth were firmly closed, with dark frothy saliva issuing from mouth and nostrils; in one the jaws were rigid, with bloody froth; and in one case a white froth was described without reference to the rigidity of the jaws. In two cases the eyeballs were protruded, in two cases the eyeballs were prominent—and in one case bright, but not prominent. The pupils were dilated in seven cases, semi-dilated in two cases, and natural in one case. The eyelids were open in two cases. Opisthotonos was present in six cases; the feet were arched in eight cases. In one case feet natural, while in four cases the feet were incurved, and in one case the toes were widely drawn apart. The fingers were clenched firmly in twelve cases; in one case the arms were akimbo, and in three cases the arms were flexed. The state of the heart seems to vary exceedingly. Thus, it was healthy in structure, empty and flaccid in five cases; small, contracted, and empty in two cases; dilated in one case; in one relaxed; in two contracted; in one tonic; while in three it was perfectly natural; empty and unnaturally atonic in two; flaccid in one case; large, flabby, collapsed, and empty in one. In three cases the heart was described as flabby, the right ventricle containing dark fluid blood partly, but loosely coagulated; while, besides possessing these features, another was noted as having air bubbles mixed with the fluid part of the blood. In two

cases the right ventricle was distended with dark fluid blood, while the left contained only a small quantity. In one case all the cavities of the heart were described as containing dark fluid blood, there being, however, more in the right than in the left side. In one case the right ventricle was empty, while the left contained two drachms of fluid blood. In one case the heart was noted as filled with clotted blood; in another the organ was healthy and flaccid, with blood in all its cavities; and in one case the muscular fibre of the heart was darker in colour than usual. Pericardial effusion was noted as present in three cases. In most cases the blood was reported as fluid and dark, but in one case there were recorded as floating about in the fluid blood fine coagula; in other two cases the blood was described as clotted; and in three cases as partly coagulated and partly fluid.

The lungs were unchanged in four cases, in four were slightly congested, and in six were described as congested, the blood being very dark in colour. In one case they were noted as containing much fluid blood, while the larynx was stained with dark blood; in one case they were very much congested; in another voluminous, but congested with dark blood, in three as healthy; but gorged with fluid blood; in one as healthy and bloodless; in one as infiltrated in patches; and in one as emphysœmatous, with the tubes filled with frothy mucus. In one case an apoplectic state of both lower lobes was recorded; in two cases the lungs were highly congested, there was present pulmonary apoplexy, the mucous membrane of the trachea was of a dark plum colour, and covered by a dark mucus; in one case there was noted the presence of blood in the air passages, while the lungs were apoplectic; in one case the lungs were œdematous, but contained little blood; and in one case they presented a violet colour from engorgement, and this was accompanied by effusion of bloody serum into the cavity of the pleura.

In four cases the bladder was empty and firmly contracted; in two cases it was recorded as empty; in one case as containing a considerable quantity of urine; in three cases as

full; in one case as containing twenty fluid ounces of bright amber-coloured urine; and in one case as containing ten fluid ounces of urine. In eight cases the kidneys were reported as healthy and natural; in two as dark in colour and gorged with blood, while natural in structure; in seven cases there was present congestion of the kidneys; and in six cases the right kidney was more congested than the left, while in one case the congestion was limited to the left.

As to the condition of the stomach, great varieties are met with; thus, in eight cases there was recorded congestion appearing in patches; in two cases the bloodvessels were noted as distended; in two cases slight congestion was reported; in two cases it was stated that there was present slight congestion but no inflammation; in one case there was present some congestion at the cardiac extremity, accompanied by yellow specks on the mucous membrane; and in one case the stomach was noted as congested, while there were also present a few dark brown patches. In one case the mucous membrane was noted as rugose, of a dark reddish brown colour, at the greater end a patch of congestion, covering three quarters of an inch, with lividity at both ends and diffuse redness; in two cases the mucous membrane was of a deep red colour from congestion, this being accompanied by a thin layer of extravasated blood; in one case there was noted a yellow spot at the pyloric extremity; in one case there were reported patches of congestion near the cardiac end, with a white powder adherent thereto, while the organ was otherwise natural; in one case the mucous membrane was softened, and of a dark brown colour, from effusion of blood between the inner and middle coats; in four cases the stomach was reported as pale; and in eight cases as healthy, and presenting no unusual appearance. The duodenum was reported as natural in five cases, while in one case there was present congestion affecting both it and the jejunum.

The small intestines were recorded as natural in five cases; as red from congestion in eight cases; as dotted with patches of congestion in two cases; and as containing a bilious fluid in one case. In one case the mucous membrane of the

pharynx and gullet presented a peculiar violet colouration. In one case the veins of the omentum were reported large.

The spleen was reported natural in five cases, and as in five cases congested. The liver and gall-bladder were noted as healthy and natural in eight cases; the liver as large and firm in one case; as congested in one case; as dark and soft in one case; as large and congested in one case; and as large and cirrhotic in one case. In one case the right lobe of this organ was reported as larger than usual; in one case the left lobe was larger than the right, and the gall-bladder was in one case reported as containing one fluid ounce of bile.

The contents described as being found in the stomach were as follows:—In one case, one fluid ounce of a thick greyish-looking substance, of a slightly acid reaction; in one case there was reported present some ounces of a brownish fluid; in another case the contents measured four ounces, while crystals of strychnia could be seen between the folds; in one case the contents were of a reddish brown colour, and measured seven ounces; while the contents in another case present similar characters, though the quantity was not noted. In three cases the contents were grumous, the quantities recorded being respectively ten, eleven, and thirty ounces. In one case, while the character of the materials was not described, the quantity was reported as two-and-a-half ounces, while some particles of powder were found adhering to the mucous membrane. In two cases the contents were like coffee-grounds, though of a dark greenish colour; and in one case the contents were of a pale greenish colour, and measured three ounces.

As to the condition of the membranes enclosing the encephalon, these were in six cases congested, the congestion being general, and accompanied by effusion of serum; there was present serous effusion into the ventricles in six cases; and in one case the effusion was bloody. In one case the membranes were tinged with blood of a dark colour; in two cases the arachnoid was opaque and thickened; in five cases the dura mater was congested; in one case the pia mater was thickened and opaque; in one case the lateral ventricles

contained two drachms and a-half of dark fluid and loosely clotted blood; in one case there was reported remarkable congestion; in three cases the vessels of the membranes were gorged with fluid blood; in two cases the vessels were tinged with blood; and in one case *post-mortem* examination revealed patches of old lymph effused beneath the arachnoid. As to the brain substance proper, this was reported natural in eight cases; in nine cases as congested; as presenting bloody points in one case; as congested at the base in one case; as congested and softened in one case; in three cases there was reported congestion, a dull dusky colour of the choroid plexus; in one case the cerebellum was soft; and in one case there was reported the presence of an apoplectic clot in the right corpus striatum around which the brain substance was softened.

As to the conditions observed in the membranes of the spinal cord, these were reported natural in three cases; as generally congested in six cases; as presenting venous congestion in one case; as congested at posterior part in one case; as gorged with fluid blood tarry and dark in one case; as congested at its upper portion only in one case; and as tinged with dark coloured blood in one case. In one case there were reported four patches of extravasation external to the arachnoid covering, and opposite the last dorsal and first lumbar vertebræ; in one case the canal was noted as full of serum, and in another case as full of bloody serum. The membranes were rather vascular in one case; presented effusion beneath arachnoid in one case; and in one case it was stated that the arachnoid was reddish in colour, and that at the root of each nerve there was noticed a patch of extravasated blood.

The substance of the cord was reported natural in six cases; congested in three cases; soft and vascular in one case; softened in its upper part almost to a pulp in one case; softened opposite the seventh cervical vertebra in one case; and as pale and somewhat softened throughout in one case; while in another the veins were reported congested.

Detection of the Poison. — Having now considered the

physiological effects of, and the *post-mortem* appearances found in, cases of poisoning by strychnia, and having seen that these may be, if typical, nearly conclusive evidence of poisoning by this substance, but that no conclusive evidence can be founded on them in every case, let us now consider what alone can be absolutely conclusive evidence, viz., the detection of the poison in the body, its tissues or fluids, or in material administered to the patient.

It is always necessary to employ, first of all, a separating process, by which the alkaloid in a pure state is obtained. For this end many different modes of manipulation have been proposed and advocated, each experimenter having his own peculiar process; and as a review of these in full would occupy much space, I shall briefly state that which to me seems the most correct and simple, and which I have found the most efficient, and shall then make a few remarks on some of the other processes proposed.

To the suspected matters reduced to a pulp with distilled water by bruising in a clean mortar, acetic acid is added in excess, and the materials allowed to digest for 24 hours, at a temperature of about 70° Fah. The materials are then thrown on a dialyser and permitted to remain for 48 hours floating in ten times their bulk of pure distilled water. After the lapse of this time the dialysing frame is removed with its contents, and the clear fluid surrounding it evaporated to the bulk of one drachm, and then tested with blue litmus paper; if acid, it is agitated for five minutes in a test-tube with twice its bulk of pure chloroform, which dissolves the pure alkaloid, but not its salts; but if not acid to test paper, a slight excess of acetic acid is added, and it is then agitated with the chloroform. By this means everything soluble in chloroform, especially fatty matters, is removed from the fluid, and, being the heavier, the chloroform gradually subsides, and can be removed by a pipette; or, better still, by pouring the mixed fluids, immediately after agitation, into a tube fitted with a glass stop-cock at its lower end, care being taken to have a small quantity of pure chloroform at the bottom. Then, by turning the stop-

cock, after the liquids have perfectly separated, the chloroform is removed, and there is left behind the clear fluid containing the acetate of strychnia. This may be again treated in the same manner with chloroform, till, on evaporation of the chloroform, no deposit is obtained; and then, after being again separated, it is treated with ammonia in slight excess, and at once agitated, for five minutes, with four times its bulk of chloroform. The chloroform now contains the free alkaloid. The chloroform is again separated as before, care being taken to allow it to fall drop by drop on a clean watch-glass or slip of glass plate, each drop being allowed to evaporate before another is allowed to fall, thus ensuring the accumulation of the alkaloid on one point of the glass. A sufficient amount of the alkaloid having been obtained on one slip, another piece of glass is substituted, and so on till the chloroform is exhausted. This process, as a separating process, is certainly as simple as any one can desire, and the success attending its adoption has with me been perfectly uniform. There is thus obtained on the glass a spot, it may be whitish, or in some cases mere wavy transparent elevated lines, the appearance of which, by transmitted light, is very similar to mother of pearl; and in order to determine the nature of the residue, a drop of pure, strong, sulphuric acid is added, and allowed to remain in contact with it for a short time. Should the spot not become dark, there is added a small crystal of bichromate of potash, and should strychnia be present, there is developed a beautiful violet colour, passing into purple, then red, then reddish brown. This is a test which, if it succeeds, is perfectly distinctive of the presence of strychnia, as no other substance, under similar circumstances, develops the same colour reactions. But should there be a slight darkening of the spot on the addition of the sulphuric acid, due to the presence of extraneous organic matter, another drop or two of sulphuric acid should be added, and heat applied, till complete charring takes place, and, after neutralization with ammonia, the strychnia should be separated by agitation with chloroform, and then treated as above described.

Concerning this part of the subject, much diversity of opinion exists among chemists, and it may be well to consider briefly a few points which seem worthy of notice. And first, it has been said by various authorities that oxalic acid, tartaric acid, sulphuric acid, hydrochloric acid, are preferable, but acetic acid is preferable because it has the peculiar property of coagulating casein and other albuminous materials. It does not tend to cause the conversion of starch and farinaceous matter into sugar, its excess is easily removed, and the acetate of the alkaloid is one of the most soluble of its numerous salts. Hydrochloric acid should especially be avoided in this process, as it tends to induce some change in the strychnia, the exact nature of which I have been as yet unable to make out, but a change by which its power of producing tetanoid phenomena is considerably impaired. This is best shown by digesting together strychnia and hydrochloric acid for some time, when the fluid, at first clear, becomes slightly smoked and ultimately brownish, while its power of producing physiological effects of a tetanic character becomes deteriorated. The experiments on which this statement is founded might be detailed at length, but as they would occupy considerable space, I merely mention the deductions from them, and I may add that these quite agree with the experience of Prof. Rainy.

The material by which the alkaloid is to be dissolved out from the fluid has also created considerable discussion, some preferring ether, others benzole, but for my part I prefer chloroform, because strychnia is very soluble in it, and, owing to its greater density, it can easily be separated from the supernatant fluid, while its density also allows of its concentration on one part of the glass, thus permitting the effect of the colour-test to be more visible. Besides this test, by which the colour reactions are produced by sulphuric acid and bichromate of potash, others have been recommended on the same principle, the bichromate of potash being replaced, as the case may be, by peroxide of lead, peroxide of manganese, ferricyanide of potassium, iodic acid, chromic acid; but, as before stated, after many

comparative trials with these, I find that that which affords most uniformly a successful result is the bichromate of potash, next to which chromic acid, peroxide of manganese, and peroxide of lead may be ranked in order of delicacy of result.

Should the quantity then admit, the modification of the colour-test, called by Dr Letheby the galvanic test, already mentioned, should be tried, as also the test proposed by Dr Guy, already discussed, the sublimation test, the carbazotic acid and the bichromate of potassium tests. It is also important to obtain a solution of the acetate in water and test with ammonia, by means of which a crystalline precipitate is obtained, while another portion is treated with sulphocyanide of potassium, when the characteristic crystalline precipitate is thrown down. Precipitates obtained by the addition of the other reagents alluded to in a preceding paragraph do not seem to me to be sufficiently distinctive to demand constant adoption.

These chemical characters then, conjoined with the death being due to a convulsive affection, are sufficient to designate the case as one of poisoning by strychnia; but in the absence of the history of symptoms observed during life, it would be necessary to prove that the blood contained strychnia in an active condition—that is, that it was not present as one of the addition compounds of strychnia which have been so fully investigated by Messrs Crum, Brown, and Frazer. These addition compounds yield the same chemical reactions as strychnia, but their physiological action is very different. The one, strychnia, produces effects powerfully convulsive, while the others, like curari, produce an opposite condition, viz., paralysis of the muscular movements. By the application of the frog test of Dr Marshall Hall, modified, as already stated, this differentiation becomes very simple and easy, since by a great number of experiments I have ascertained conclusively that the degree of saturation of the blood with the poison required to produce death in the mammalia is such that every ten drops contains at least the $\frac{1}{200}$th of a grain of the alkaloid, a

quantity quite capable of producing the tetanic phenomena in an exhausted frog. This holds in all mammiferous animals with which I have experimented, as in the Abyssinian ram already mentioned, in the dog, cat, rabbit, guinea pig, and rat, and, from the following statement, I think it extremely probable that in man the same may be found. The quantity of blood in the human body being taken as 16 lbs., and the smallest recorded fatal dose as one quarter of a grain, it follows that each pound might be expected, were all the poison absorbed, to contain the $\frac{1}{64}$th of a grain, each ounce rather less than the $\frac{1}{1000}$th of a grain, and every ten grains by weight about the $\frac{1}{10000}$th of a grain. Now, this amount is easily capable of producing the tetanic phenomena in frogs, and the mere deprivation of ten or fifteen drops of the blood, while, if successful, conclusively demonstrating the nature of the case, has the manifest advantage of consuming but a very small quantity of material. From my own experience I should also be inclined to say, that putrescence of the blood does not interfere to any great extent, if at all, with this experiment; thus, in one case, I poisoned a rabbit with the $\frac{1}{30}$th of a grain of the acetate of strychnia, and after its death removed the heart, lungs, and as much of the blood as possible, preserving them in a stoppered bottle for eighteen months, and in another case a similar procedure was adopted, and the materials kept for two years, and when ten drops of this blood were administered to a weakened frog, the spasms resulted very speedily. To ascertain whether putrid blood alone might produce this result, I have frequently injected blood far advanced in decomposition, into the bodies of frogs of all stages of growth, development, and strength, yet never were there produced any phenomena liable to mislead the most casual observer into the belief that the symptoms presented any resemblance whatever to poisoning by strychnia.

It is then in my opinion necessary, in order to prove the presence of strychnia in the body, to remove by the separating process already alluded to, a substance yielding with sulphuric

acid and bichromate of potassium, the characteristic play of colours, a substance which, when dissolved in a dilute acid, yields with ammonia and sulphocyanide of potassium respectively, crystalline precipitates, with carbazotic acid and bichromate of potassium, the results already enumerated, and at the same time a substance which administered to a frog produces the characteristic spasms. On this evidence alone do I believe the analyst justified in ascribing the death to the physiological action of strychnia on the animal economy.

Then, as to the estimation of the total quantity present, this, I believe, may best be accomplished by the use of the separating process modified as above, described from Stas' method, and by actual weighing of the alkaloid so separated. If morphia or any alkaloid belonging to the natural order solanaceæ be present, then the former might be removed by dissolving it in solution of potash, in which strychnia is insoluble, and the latter might be decomposed by heating them with the same substance, and then the strychnia might be separated again by chloroform, and the weight of the residue determined. The process recommended by Messrs Graham and Hoffman, for the separation of strychnia in beer, answers the purpose well, and with perfect efficacy, but I am convinced that the process first mentioned answers the purpose quite as well, and in the case of detecting the poison in the tissues and complicated organic matters generally, that this end is by it more simply, and at a less expense of time, attained.

The process more recently proposed by Professor Cloetta, viz., the separation of the albuminous substances by heat, and the subsequent precipitation of other extraneous substances by basic lead acetate, filtration, and agitation with ammonia and chloroform, does not appear to me, after careful trial, to afford results nearly so satisfactory as the process described at length already, as by it the strychnia obtained, though comparatively pure, is not sufficiently so to yield the colour reactions perfectly, when small quantities only are concerned.

As the other separating processes, those in which it is proposed to substitute ether and benzole, have already received consideration, I shall not further dilate upon this subject, but pass on to the treatment of cases of poisoning by this alkaloid.

Treatment and Antidotes.—The first procedure which ought to be adopted is the perfect evacuation of the stomach, and for this purpose emetics should be administered freely, and their action aided by the free use of demulcent liquids, as milk, gruel, or warm water; the animal temperature should be well sustained by warm applications externally, while, after the evacuation of the stomach, a mild laxative, as castor oil or magnesia, should be given. Great attention should be paid to the respiration, and should any tendency to asphyxia appear, artificial respiration should at once be begun, and continued, till respiration is properly re-established, or till it entirely ceases. Much discussion has taken place on the part of various writers on this subject as to the antidote for this poison, and there have at various times been proposed, woorara, tobacco, chloroform, charcoal, camphor, hydrocyanic acid, tannin, iodine, bromine, chlorine, morphia, codeia, aconite, albumen, kermes mineral, iodated-iodide of potassium, lard, and, latterly, the Calabar bean, and hydrate of chloral. Of these agents, those which demand special attention are woorara, chloroform, tannin, Calabar bean, and hydrate of chloral. I have at various times performed experiments with all these save tannin, but certainly from these experiments it appears extremely doubtful whether they possess any efficacy if administered subsequently to the accession of the tetanic spasms. Thus with woorara, chloroform, and Calabar bean, I have frequently succeeded in retarding the appearance of the spasms, and, as I thought, in mitigating their severity when produced, but in every experiment a fatal result ensued, apparently either from deficiency or excess of the supposed antidote. After the administration of hydrate of chloral the animal at once becomes flaccid, but very shortly thereafter the tetanoid spasms reappear, and the animal eventually

dies either from the effect of the strychnia or of the chloral, but in no case in my experiments did a successful result attend its exhibition.

While examining the contributions on this subject, it occurred to me that nitrite of amyl might, from its physiological action, prove an antidote, this idea being strengthened by the results which were obtained by Messrs Brown & Frazer in their experiments on the modifications produced on physiological action by chemical addition. With this agent I have made several experiments, which were confined to rabbits, as being the most easily obtained. The result, I may briefly state—twenty rabbits being operated upon. Of these ten died in the first spasm, and consequently the nitrite of amyl was not administered. In the others, the remission after the first spasm having appeared, the nitrite was exhibited in six cases by inhalation, in two by subcutaneous injection. Of these the symptoms were prolonged for 40 minutes in one case, for 43 minutes in another, for one hour in another, for one hour and 10 minutes in another, these, however, ending fatally. The other four recovered, one after the interval of one hour, another after an interval of one hour and a half, another in two hours, while the last, to which, during four days, a dose of the sulphate of strychnia, amounting to ten grains, had been given in divided doses, recovered perfectly. With the exception of this last, the dose administered to the others was a quarter grain each of the acetate, irrespective of the size of the animal. To the two others there was administered a mixture of half a grain of strychnia, with 12 minims of nitrite of amyl, and in neither case did any marked symptoms appear, although carefully watched during three hours. There was at first a slight amount of apparent depression, but after the lapse of half an hour this had entirely disappeared, and perfect recovery ensued.

Operating then on dogs, I found that in all the cases in which I used the nitrite, the symptoms were temporally mitigated, while in about half the cases recovery took place. The number of dogs used for these experiments was ten,

and in five of these perfect recovery followed the use of the nitrite, it being administered after the first spasm had passed off. In the case of one of the dogs the nitrite was not administered at all, owing to death occurring in the first spasm, and in the others the animals died after the lapse of one hour, one hour and a quarter, one hour and twenty minutes, one hour and a half, and two hours respectively, these being all examples of rather long-continued duration of symptoms. With the chloride of amyl, which I then tried, the general results were the same, so that though very useful in some cases, it is quite patent that we have not yet any perfectly reliable antidote, though I should be inclined to trust more to the amylic compounds than to any other reputed anti-spasmodics, still, however, adopting all the other methods of procedure noticed in the first few sentences of this part of the subject.

The last point, then, to which I would allude is to the mode of differentiation of the symptoms of poisoning by strychnia, from the symptoms found in ordinary cases of traumatic and idopathic tetanus, from rabies, and from epilepsy.

In traumatic tetanus there is a well-defined relationship to a wound, which may be and often is of a very slight character, but which generally present an unhealthy aspect. In idopathic tetanus there is usually a history of exposure to cold and damp, or other causes, which lead to the development of this form of disease. In rabies there is always the history of a bite from some animal in a state of great excitement or rabid. In epilepsy the history supplies the account of previous attacks, and there is no relation capable of definition between the disease and any external apparent cause. The symptoms of poisoning by strychnia have, then, no connection with any wound, but have usually, if not invariably, a pretty constant relation to food or medicine swallowed. In tetanus in both forms, the premonitory symptoms are painful sensations of contraction, and tension in the region of the loins, and the nape of the neck, accompanied by stiffness of the muscles of the neck and of the

jaw; in the case of traumatic tetanus there may be a dull numb feeling in the wound, or it may suddenly become painful. In rabies there is felt a peculiar painful sensation in the cicatrix, extending thence in the course of the nerve to the back of the larynx and chest; if the wound be not perfectly healed the pus becomes unhealthy, while if cicatrization has taken place, the scar becomes livid and tumified.

In epileptic convulsions the premonitory symptoms are very slight, and of short duration; thus the aura, as it is termed, may consist in a peculiar creeping sensation in the hand or foot, which rapidly extends to the trunk, and the person then falls down in the fit; or it may consist in a peculiar sense of taste in the mouth, or a peculiar sound heard in the ear, and many other slight symptoms such as these.

In poisoning by strychnia the premonitory symptoms are at first slight, but rapidly deepen in intensity, and in a few minutes at most terminate in the tetanic spasms. In tetanus the spasms are slow of advent, they take a long time to develop in their full intensity, and when present are tonic, that is, the spasm is constant, but subject to exacerbations and remissions, the consciousness is generally perfect in such cases, though sometimes, in the intensity of the spasm it may for a few seconds be lost. In epilepsy consciousness is always lost, and there is rarely more than one spasm in each fit, though this is not absolutely constant, and the spasms are not, properly speaking, tetanic, neither are they in rabies. In strychnia poisoning, the spasms are cloric, that is, they are subject to complete intermissions, during which the patient is perfectly quiet, and free from all convulsive affection; consciousness is rarely affected.

In tetanus, trismus is constant, early in accession, and perfect, so that the jaws, even by force, cannot be separated. In rabies and epilepsy trismus is very rare, and if present, is only so to a very slight extent. In strychnia poisoning, trismus may be present, but is usually very late, and may, by slight force, be overcome. External impressions deepen the symptoms in tetanus, induce a spasm in strychnia

poisoning, but have no effect in cases of rabies or epilepsy. Strychnia spasms are developed always within three hours of taking the poison, and usually within an hour. The spasm in idiopathic tetanus come on generally three or four days after exposure to the cause. In traumatic tetanus, in from eight to ten days from time of reception of the injury. In rabies symptoms may come on weeks, months, or even years after the bite.

The symptoms in epilepsy last only a few hours at most, and generally terminate in recovery. In rabies the symptoms last about seven or eight days, and almost invariably terminate fatally. In tetanus, generally last three to eight days, and not a few cases recover. In strychnia poisoning, the patient, if he is to die, does so within sixteen hours, certainly, and generally perfect security of recovery may be felt if death does not occur within ten hours.

By these prominent and distinctive features, I believe it quite possible to differentiate these cases perfectly, though there may be, I grant, some cases in which much difficulty would be experienced in the diagnosis.

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