into the pleural cavity. If there are no adhesions artificial pneumothorax is not an unsafe method of treatment.

In a series of eight cases of simple abscess which I treated by artificial pneumothorax four patients made a good recovery and are still well. In two the abscess ruptured into the pleural cavity, but both recovered after drainage and are now well; in one the symptoms persisted and thoracoplasty was later performed; and in one the patient died after an operation for dividing the adhesions. I think, however, that if postural treatment fails it is on the whole safer to employ surgical drainage.

Aspiration through a bronchoscope has been performed and several successful cases described. This really may be regarded as an additional method of draining the abscess cavity medically, and if used should be combined with postural drainage. In certain cases it may be wise to give this method a trial, although if the abscess persists operation should not be too long delayed.

Surgical treatment consists in opening the abscess and draining. The operation should be performed in two stages; the first is intended to produce adhesions between the chest wall and the pleura over the cavity, and the second to drain the abscess. There are definite dangers, and the operation should be regarded as a serious one. Haemorrhage may occur later; cerebral abscess is perhaps slightly more common after operation than in cases treated medically, or infection may spread throughout the lung. It would appear that as methods of postural drainage improve this will be the treatment of choice in cases of abscess.

Intravenous injections of alcohol have been suggested, and 10 c.cm. of a 20 per cent. solution is that most commonly used. Sodium benzoate has been recommended for treatment of gangrene and abscess of lung: the dose advocated here is 20 c.cm. of a 20 per cent. solution, increased up to 50 c.cm., given daily. I have no experience of either of these methods.

In cases of gangrene good results have been recorded from an intensive course of treatment with arspenamine, the object being to kill the spirochaetes which cause the gangrene. It is certain that some of the cases in which the sputum is most offensive do quite well on simple medical treatment, and I have not convinced myself that improvement has been due to the arsenic. As the spirochaetes are sometimes found in the gums of normal people pre-operative dental treatment has been advocated, and it is claimed that this reduces the pulmonary complications.

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A new German quarterly journal, *Fortschritte der Erbspathologie Rassenhygiene und ihrer Grenzgebiete*, has appeared; it is published by Georg Thieme of Leipzig. The joint editors are Dr. J. Schottky of Hildburghausen and Professor F. von Verschuer of Frankfurt-a-M. The first issue is dated July, 1937, and in addition to an introductory editorial explanatory note contains an article on the transmission of intelligence and character which is contributed by Dr. K. Gottschaldt of Berlin, another by Dr. Wülker of Berlin on the investigation of natural selection, and a third by Dr. H. Schade of Frankfurt on the biological aspects of heredity. As indicated by these opening articles, the new periodical should appeal particularly to those who are concerned with the influence of heredity, particularly on the pathological side, racial hygiene, and related topics. The annual subscription is 16 RM.

A RAPID METHOD FOR ISOLATION OF ORGANIC POISONS PRELIMINARY NOTE

BY

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The standard method for the isolation of organic poisons from viscera, stomach contents, etc., is that described in the majority of medico-legal and toxicological textbooks as the Stas-Otto process. It is a slow, laborious, and often difficult method based on the repeated precipitation of proteins, fats, and similar interfering substances by alcohol, the organic poisons (alkaloids in the form of their salts) being retained in solution. Complete removal of the interfering substances involves repeated precipitation, each of which probably causes some loss of the substance sought. To minimize these losses thorough extraction of the precipitated material is required, and even with distillation *in vacuo* the evaporation of the relatively large volumes of alcohol (or aqueous alcohol in the early stages) is very time-consuming. On the other hand, if the Stas-Otto process is carefully carried out there is little likelihood of any of the commoner organic poisons, administered in lethal dose, being missed. It is not uncommon, for example, for morphine, given in medicinal doses, to be detected in the viscera post mortem.

It is obvious, however, that a shortening and simplification of the extraction process is very desirable, provided it can be achieved without any loss of power to detect very small amounts of poisonous substances. An alternative is supplied by Lloyd's process (Sydney Smith, 1936), which consists in preparing an acid-water-alcohol extract of the material as in the Stas-Otto process, and adsorbing any alkaloids present in this extract on fuller's earth. Adsorbents at this stage, however, are likely to take up many substances other than alkaloids, and, moreover, we have found fuller's earth to be notably inefficient in the adsorption of alkaloids.

Not only alkaloids, but most other poisons usually classed as organic, are of such a chemical nature that one would expect them to be adsorbed by various earths, though not all under the same conditions. Hence a hopeful line of attack seemed to be available for the isolation of the poisons once the proteins and fats have been removed, and the problem resolved itself into two parts—(a) to find a rapid and safe method of removing such interfering substances as protein, fat, etc., with minimal loss of the poisons to be sought; (b) to find a suitable adsorbing agent and the conditions required for the adsorption and elution of the different types of poisons.

Since our first consideration was the detection of alkaloidal poisons we were concerned primarily with the possibility of adsorption from acid solution and with preliminary treatment which could be carried out completely at reactions below pH 7.

Precipitation by Trichloroacetic Acid

Of the various protein precipitants used in blood analysis some (like zinc hydroxide) function in an alkaline medium, others (like tungstic acid) involve little change in the reaction of the original material, and others again (like metaphosphoric acid or trichloroacetic acid) are strongly

* In receipt of a part-time grant from the Medical Research Council.

acid themselves and yield an acid protein-free filtrate. Only the last of these groups was of interest to us, and we found, in fact, that treatment of minced meat, liver, etc., with an adequate amount of trichloroacetic acid precipitated the whole of the protein, with which was carried down all or practically all the fat. By grinding the protein-and-fat-containing material with an equal volume of 10 per cent. trichloroacetic acid solution, allowing the mixture to stand for a few minutes, and then filtering through a Büchner funnel, we obtained a water-clear filtrate, which was to all intents and purposes free from protein and fat. The time involved, including the filtration, was about three hours, and the final solution was better for the purpose in view than that obtained by the Stas-Otto process in three days. The filtrate was acid, and would therefore be expected to contain any alkaloids present in the original material, along with any water-soluble but non-basic substances such as barbiturates and (most) glucosides. Qualitative tests showed that this expectation was realized, that added alkaloids were present in the trichloroacetic acid extract, and that no more could be recovered from the insoluble residue. Thus, so far at least as the substances we have as yet tested are concerned, the first part of the problem has been solved. In the extraction of alkaloids a method of preliminary treatment has been found which is superior to the Stas-Otto process. Further work in progress will decide whether it is of universal applicability.

Strychnine Adsorption on Kaolin

We wished to avoid the necessity for evaporating the acid filtrate obtained in precipitating proteins, etc., by trichloroacetic acid, and therefore concentrated our attention on the possibility of adsorbing alkaloids on a solid medium. For our preliminary experiments we chose strychnine as an alkaloid which is relatively stable and for which sensitive colour reactions are available. Of a number of substances tested, kaolin (British Drug Houses' "levigated powder"), franconit, charcoal (Merck's medicinal), and aluminium oxide (Merck's "nach Brockmann") were found to be very efficient in adsorbing strychnine from a slightly acid solution of its hydrochloride. When 25 c.cm. of a solution containing 50 mg. of strychnine hydrochloride were shaken for a few minutes with 5 grammes of any of these adsorbing agents and the mixture was then filtered, the filtrate did not retain enough alkaloid to be detected, after evaporation, by Mayer's reagent or by sulphuric acid and potassium dichromate. It had therefore been completely adsorbed. On the other hand, fuller's earth, like certain other brands of kaolin, charcoal, and aluminium oxide, was relatively ineffective.

Our choice of kaolin as the adsorbent to be used in further work was based on the finding that it adsorbed many other alkaloids with great ease and was much cheaper than either franconit or Merck's adsorbent aluminium oxide (which were, however, equally effective). Charcoal we discarded, since we feared that it might cause oxidation of some of the less stable alkaloids. Our impression of the efficiency of kaolin was confirmed while our work was in progress by the results of Mutch (1937), who was interested in the use of kaolin medicinally in cases of food poisoning.

Elution of the Strychnine

The next step was the elution of the adsorbed alkaloid. Certain facts suggest that, like many other substances, alkaloids are adsorbed as such by basic adsorbents although they are present as salts in the original solution.

It is possible, therefore, that after thorough washing of the kaolin plus alkaloid the latter might be removed by simple extraction with a suitable organic solvent. We have not yet tried this, since the removal of the last traces of the original acid solution requires very thorough washing; and, partly on account of the time involved and partly for fear of losses during the washing, we used a shorter process. We filtered off the suspended kaolin with its adsorbed alkaloid on a Büchner funnel, washed once with water, and ground with a little 10 per cent. aqueous sodium carbonate solution (using enough to make the suspension neutral or slightly alkaline). The paste so formed was then mixed, by grinding, with anhydrous sodium sulphate to give a dry powder, which was extracted with chloroform in a Soxhlet apparatus. Early experiments with this technique gave bad results, since a certain amount of coloured matter was extracted from the kaolin. Preliminary treatment of the kaolin by washing with alcohol, chloroform, and finally with ether, removed this difficulty and did not impair the adsorbing power of the kaolin. All kaolin used in subsequent experiments was treated in this way before use.

Using the washed kaolin, this method gave almost quantitative yields of strychnine from simple solutions of the hydrochloride. An alternative procedure, equally effective in the case of strychnine but less so with other alkaloids, was to suspend the kaolin plus alkaloid in dilute aqueous sodium carbonate and extract the suspension repeatedly with hot chloroform. The chloroform extract, however, did not separate very clearly, and in any case had to be filtered to remove particles of kaolin before being evaporated. The dry extraction method was therefore regarded as the standard procedure, although for *qualitative* purposes the wet extraction process is quicker and simpler.

The next step was to attempt the isolation of strychnine from a large excess of protein, fat, etc., using the method already described for removing the protein and fat. For this purpose a dilute solution of strychnine hydrochloride containing 50 mg. of the hydrochloride (equivalent to 41 mg. strychnine) was thoroughly mixed with 400 grammes of minced meat. After standing overnight this was thoroughly ground with 400 c.cm. of 10 per cent. trichloroacetic acid. After filtration on a Büchner funnel the well-pressed precipitate was again ground with 100 c.cm. of the trichloroacetic acid solution and refiltered. The two water-clear filtrates were combined and shaken with about 10 grammes of the washed kaolin. After an hour the kaolin was filtered off and submitted to the eluting process. In one experiment, using the wet extraction method, 36 mg. of strychnine were recovered (an 88 per cent. yield); in another, by the dry extraction process, 40 mg. of strychnine were obtained (a 97 per cent. yield). These yields were not exceptional, and the product was pure, as shown by melting-point, ignition tests, etc. Admittedly the quantity of strychnine involved in these experiments was large, but with as little as 5 mg. of strychnine hydrochloride present a recovery of 73 per cent. was obtained, and from only 1 mg. enough to give a strong qualitative reaction by the sulphuric acid-potassium dichromate test.

Results with Other Alkaloids

Using the same method equally good results—that is, recovery of 80 to 95 per cent. of the quantity added—were obtained when morphine or quinine in amounts as small as 10 mg. was mixed with minced meat. With nicotine and aconitine (triaconite *B.P.C.*) no quantitative experiments have been done as yet, but when minute

amounts were added to meat and the mixture was submitted to the process as described for strychnine, both alkaloids were readily detected in the final chloroform extract.

Experiments with atropine have, so far, been less successful. The substance is readily enough adsorbed by kaolin, but, probably because it is so easily hydrolysed, we have never succeeded in obtaining a recovery of more than 50 per cent. of the amount added to meat. Usually the recovery has been less than this. With 10 mg. of atropine originally added, however, we have never failed to detect the alkaloid in the final chloroform extract. This is disappointing, although the recovery of atropine is notoriously difficult with the standard Stas-Otto process. Further experiments will, we hope, enable us to obtain better results, and, in particular, experiments are to be made on the extraction of the kaolin without added alkali. It is a reasonable supposition that the process, if it can be suitably modified to give good results with the less stable alkaloids such as atropine, will be as satisfactory as the present method in dealing with the more stable ones.

Need for Further Tests

It is evident that, although it promises well, the method of adsorption on kaolin requires much further testing and possibly modification in detail before it can be applied confidently to the detection of organic poisons in medico-legal work. To be of the greatest possible use it must be applicable to many substances besides alkaloids. Into this field we have not yet ventured very far. Antipyrine, however (as one would expect from its structure), behaves like the alkaloids. Veronal, tested as an acidic substance in contradistinction to the basic alkaloids, is not adsorbed by kaolin, fuller's earth, franconit, or alumina from acid solution; it is, however, readily adsorbed by animal charcoal (Merck's carbo medicinalis), especially easily from a warm solution. After adsorption on charcoal it is readily eluted by ether, though not by chloroform. For the elution the charcoal was moistened with acetic acid and extracted with ether. The ethereal extract was filtered to remove suspended particles of charcoal and evaporated. The purity of the recovered veronal was shown by determination of its melting-point. The recovery varied in different experiments from 75 to 90 per cent. of the amount used (20 mg.).

When both strychnine and veronal were added to minced meat it was found possible, after treatment with trichloroacetic acid, to adsorb the strychnine on kaolin, from which it was later recovered by the chloroform extraction method previously described. The trichloroacetic acid extract from the kaolin still contained the veronal, which was then removed by adsorption on charcoal and elution with ether. Both strychnine and veronal were recovered in good yield and in pure state.

Summary

It is shown that in the extraction of alkaloidal poisons from viscera the laborious and time-consuming Stas-Otto process may be replaced by treatment of the minced material with trichloroacetic acid. This at once yields a water-clear filtrate free from protein and fat, and containing the whole of the alkaloid originally present.

From this filtrate the alkaloid can conveniently be removed by adsorption on kaolin, from which after neutralization it is eluted by hot chloroform. After removal of the alkaloids veronal can be adsorbed on charcoal and eluted with ether.

The method is being tested further and extended to other organic poisons.

We wish to take this opportunity of thanking Mr. J. Whittaker, senior technician in the biochemical laboratory of the Edinburgh Royal Infirmary, who has carried out a number of analyses using the method we have described, and has independently obtained results similar to those reported in this note. We have also to acknowledge a grant from the Moray Research Fund of the University, which covered the expenses of the work.

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AFFECTIONS OF THE EYE WITH RELATION TO SKIN DISEASES *

BY

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There is no lack of evidence to prove that the care of skin diseases is in many ways closely linked with ophthalmic practice. Some overlapping of these specialized branches of medicine is necessitated by the mere fact that the eyelids are covered by skin; and this skin, like that of the rest of the body, may be afflicted by a large number of different lesions—for example, eczema, gangrene, gumma, and lupus. But the amount of actual overlapping is far greater than can be explained by any such simple fact. Dermatologists and ophthalmologists have many other reasons for pooling their clinical experience and acknowledging common interests. In the first place, the eyelids are one of the favourite starting-points for rodent ulcers and various other diseases; secondly, the skin in this situation is loosely attached and exceptionally sensitive; thirdly, there are certain skin diseases with important eye complications; fourthly, ocular treatment may require to be modified owing to the state of the adjacent skin; and incidentally the eye must be safeguarded in applying certain remedies to the upper part of the facial skin.

Oedema of Eyelids

Since they form part of the face and are continually exposed to view, the eyelids are rendered conspicuous by slight changes such as would hardly be noticeable if they occurred elsewhere. Their skin, being thinner and more delicate in texture than that of any other part, is remarkable for its rapid distensibility by oedematous fluid. Thus in some cases of disordered renal function the eyelids are puffed out in the absence of any evident swelling elsewhere. The eyelids also respond with rapid swelling not only to the inflammatory processes involving their immediate anatomical relations, such as styes, conjunctivitis, or acute infection of the tear sac, but also to abscesses that are, relatively speaking, remote. One case recently sent for ophthalmic treatment was a boy whose right eyelids showed considerable oedema. Noticing that the whole of his right cheek was unduly prominent, I asked him to open his mouth, whereupon he was immediately seen to be suffering from an upper bicuspid abscess.

The sudden enormous swelling of the eyelids that is so well known in ordinary "black eye" from a blow with a fist finds an inflammatory counterpart in the dramatic

* Read in opening a discussion in the Section of Ophthalmology at the Annual Meeting of the British Medical Association, Belfast, 1937.