

Diagnosis.

The tumour itself may simulate any of the following: carcinoma, sarcoma, actinomycosis, excessive exudate caused by appendicitis, and a faecal tumour. From carcinoma the following points may be of use: the age of the patient, the length of the symptoms, and signs of a colonic tumour without blood and mucus in the stools. A marked tuberculous family history and the presence of tubercle elsewhere might be of some help. The finding of bacilli in the stools is of little practical use, as, if found, they might come from the lung or elsewhere. The diagnosis will usually be made at operation, or at necropsy, or by the course of the case.

Treatment.

The condition is usually not discovered till the peritoneum is explored at operation; and even then it may be difficult to decide whether the tumour is malignant or not, as even if familiar with this form of tubercle one would wish before giving an opinion to examine the cut surface of the gut wall, which would add considerably to the risks of the operation. The lesson to be drawn seems to be that extreme emaciation of the patient and the common occurrence of malignant disease in the colon should not deter the surgeon from an excision of a localised colonic tumour if there is nothing to make a diagnosis of malignant disease certain such as the presence of secondary deposits in the peritoneum or liver. If the tumour is malignant the patient will certainly die if nothing is done, whereas if it is tuberculous the patient may survive many years, even though excision be not complete. Conrath⁴ has collected 85 cases of localised tuberculosis of the colon of all forms treated by excision, with a mortality of 16·7 per cent. He enters fully into the different operations that might prove of service. These include excision with end-to-end or lateral anastomosis, short-circuit operations, artificial anus, and simple laparotomy as in general tuberculous peritonitis.

Apart from excision, or after excision, the treatment would follow that usually adopted for tuberculous lesions, perhaps combined with injections of tuberculin. In Case 3 the treatment adopted by Mr. Openshaw proved extremely effective—namely, bringing the tumour out on to the skin at the first operation, followed at a later operation by removal of the tumour. By this means all shock was avoided in a patient who could ill-afford to undergo a severe operation.

To sum up, one would urge that the existence of this condition should be kept in mind by those who operate on the large gut, so that the patient may reap the benefit of a correct diagnosis.

My thanks are due to Mr. Hutchinson, jun., and to Mr. Openshaw for permission to make use of their cases. I wish to acknowledge my indebtedness especially to the papers of Conrath, Lartigau, and Crowder, on whose work much of the latter half of this paper is based.

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THE LOCALISATION OF POTASSIUM IN MALIGNANT TUMOURS.

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THE method which I have employed is essentially that devised by Professor A. B. Macallum for determining the distribution of potassium in normal animal and vegetable cells. The reagent used by Macallum is prepared by dissolving 20 grammes of cobalt nitrite, obtained from the Baker and Adamson Chemical Company (Easton, Penna.), and 35 grammes of sodium nitrite in 75 cubic centimetres of dilute acetic acid. The solution is accompanied by the

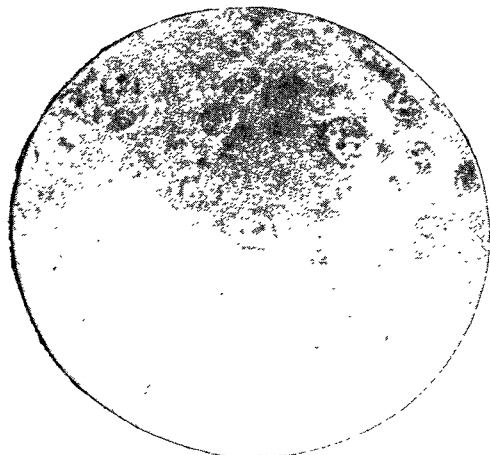
evolution of nitrogen peroxide. After standing for some hours the solution is filtered to remove the precipitate caused by traces of potassium present as an impurity and the filtrate is diluted with water to 100 cubic centimetres. This reagent produces, in the presence of potassium, an orange-yellow precipitate which consists of the hexanitrite of potassium sodium and cobalt. The precipitate is insoluble in dilute solutions of the precipitating reagent and in 80 per cent. alcohol. It is so sparingly soluble in ice-cold water that the excess of the reagent may be removed by water, without removing the precipitate, if care be taken to keep the temperature sufficiently low. After the removal of the whole of the excess of cobalt reagent, ammonium sulphide may be added to react on the triple salt and produce the black sulphide of cobalt. In this way the detection of minute traces of potassium is rendered more evident under the microscope.

Macallum placed teased-out portions of fresh tissues, or sections of fresh tissues cut with the freezing microtome, in the undiluted reagent, which was allowed to act for 20 minutes. The tissues were then washed with ice-cold water until the whole of the excess of the reagent was removed, when they were mounted in a mixture of equal parts of glycerine of 50 per cent. strength and concentrated ammonium sulphide solution. Animal tissues prepared in this way keep for two months, after which they deteriorate. In making up the reagent I have used a 20 per cent. solution of cobalt nitrite manufactured by Merck and also a solution manufactured by the Baker and Adamson Chemical Company, the strength of which was not stated but which was estimated at 12 per cent. Merck's solution is similar in colour to tincture of iodine. With it a reagent can be prepared which is of almost the same strength as that used by Macallum. The Baker and Adamson Chemical Company's solution is of a pale blue claret colour; with it a reagent of about one-half the strength of that used by Macallum can be prepared. No essential difference was noticeable in specimens prepared by the reagents made from these two different solutions of cobalt nitrite. A reagent prepared by adding acetic acid to a solution of the double nitrite of cobalt and sodium did not give such uniform results as the reagent prepared in Macallum's way. Two specimens of nitrite of cobalt and sodium were employed. One was prepared by Kahlbaum and the other was kindly placed at my disposal by Mr. T. B. Wood of Cambridge. In all cases a freshly prepared reagent was employed. It was found necessary to introduce certain modifications of Macallum's method in order to prepare thinner and more uniform sections than could be obtained by freezing fresh tissues. A more accurate study of the histological relationships of the various cell elements was thus rendered possible. Slices of tumour tissue, not exceeding two millimetres in thickness, were placed in the reagent for 20 minutes and were then washed for two hours in several changes of ice-cold water. They were then transferred to an ice-cold mixture of equal parts of glycerine of 50 per cent. strength and strong ammonium sulphide in which they were allowed to remain for 30 minutes. During the whole of this time the tissues were kept in a refrigerator. After washing in running water for three hours they were dehydrated in four changes of acetone. To the last change chips of paraffin were added. Finally the tissues were imbedded in paraffin, with a melting point of 45°C., care being taken to use only sufficient heat to keep the paraffin melted. One hour was found to be sufficient for the paraffin bath. The paraffin was changed three times during this time. The blocks were cut with a Cambridge rocking microtome and the sections were mounted in Canada balsam neutralised with lithium carbonate. Alcohol was also used as a dehydrating medium, but the necessity for subsequently infiltrating the tissue with a clearing agent and thus lengthening the imbedding process was a drawback. Attempts to combine the reagent with formalin or other fixing agents did not prove satisfactory. It was not found possible to obtain permanent specimens. After some months the precipitate of potassium disappeared from the greater portion of the sections. The malignant growths examined were: carcinoma (17), sarcoma (5), and rodent ulcer (1).

Preliminary experiments, made on fresh normal animal tissues, gave results agreeing in every detail with those described by Macallum, except that, in addition to the precipitation of potassium, the tissues were invariably stained a yellowish brown or dark brown colour. This staining was quite distinctive from the colour produced by the precipitation of potassium. It was not altered either in colour or

intensity by the subsequent addition of ammonium sulphide, showing that it was not due to a compound of cobalt. The distribution of potassium in malignant tumours, as revealed by this method, is exactly analogous to that found in normal tissues. The potassium is always extra-nuclear in growing cells (Fig. 1). It is frequently present in considerable amount

FIG. 1.



Photomicrograph $\times 250$. Carcinoma of mamma. Potassium extra-nuclear, chiefly immediately external to the nucleus.

immediately external to the nucleus. It also occurs in intercellular spaces and to a lesser extent in cell walls. The concentration of potassium in the cytoplasm adjacent to the nucleus is sometimes so marked as almost to obscure that body, but careful examination fails to give any evidence that potassium ever enters the nucleus of a growing cell. Potassium is present in greater amount in the cell cytoplasm of the more actively growing portions of a malignant tumour than in older and less rapidly growing portions. In degenerated and dead tumour tissues potassium is sometimes found in abundance both within the cells and in the intercellular spaces. In such cases potassium may impregnate any cellular element, including the nucleus. Usually it is not revealed in such fine particles as are found in growing cells. A similar distribution of potassium is seen in the fully cornified cells of epitheliomata (Fig. 2). These cells

FIG. 2.



Photomicrograph $\times 500$. Highly keratinised cells over epithelioma of cheek. The whole of the cell elements are impregnated with potassium.

cannot be regarded as growing. In them the potassium is found in fissures in the keratin and also in the central portion of the cell which represents the remains of the cytoplasm and nucleus. The potassium precipitate in these cells does not differ in its arrangement in any essential detail from that found in the stratum corneum of the normal epidermis.

The distribution of potassium in dead tissues is irregular and must be regarded as an impregnation of elements which no longer possess any bio-chemical selective power. The possibility of the sulphur in keratin causing a precipitate of cobalt sulphide, and simulating the appearance produced by the presence of potassium, is negated by the fact that in

epithelial tissues treated by the cobalt reagent alone the precipitate is universally of a golden-yellow colour which only becomes black on the addition of ammonium sulphide. Dr. Martha Tracy has employed Macallum's method in the study of malignant tumours without being able to confirm Macallum's results and has arrived at the conclusion that the method is not sufficiently reliable to be of any real value. Dr. Tracy found evidence of potassium only in the cell nuclei. It is possible that this difference of opinion may be due to different interpretations of the two different actions of the cobalt reagent—the staining action, which affects both cytoplasm and the nucleus, and the precipitating action which affects only potassium. When the nucleus is deeply stained an appearance is not infrequently produced which closely resembles that of the potassium precipitate.

I wish to express my indebtedness to Professor A. S. F. Grünbaum for much advice and help and to the honorary surgical staff of the Leeds General Infirmary for the supply of valuable material.

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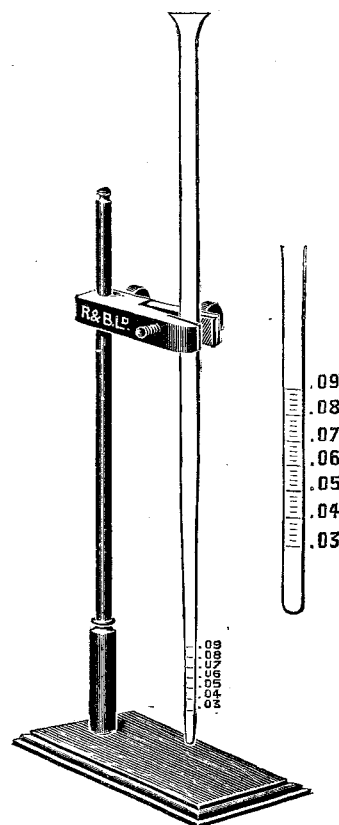
SOME NEW METHODS FOR THE DETERMINATION OF URIC ACID, INCLUDING A SIMPLE CLINICAL PROCESS.

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WE have been engaged for a considerable time in comparing existing processes and in originating new methods for the determination of uric acid in urine. Of the processes which we have devised preference is given to the following.

1. "A," a measuring process, in which a precipitate of

FIG. 1.



ammonium urate is measured in a tube specially shaped and graduated in parts per cent. of uric acid (see Fig. 1).

2. "B," a volumetric process in which a precipitate of