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

ammonium urate is collected and washed with a saturated solution of ammonium nitrate until free from chlorides and decomposed after solution in distilled water by adding in excess a known amount of a volumetric solution of silver nitrate. After filtering off and washing the precipitate of urate of silver, the amount of nitrate of silver in the filtrate is determined by means of a standard solution of thiocyanate of potassium, the filtrate being first rendered acid with a few drops of dilute nitric acid (1 in 3), a few drops of saturated solution in iron alum being used as an indicator. 3. "C," a gasometric process, in which the washed ammonium urate is decomposed by hypobromite of sodium in a specially devised apparatus which can also be used for the determination of urea, &c. (See Fig. 2).

FIG. 2.

General preliminary treatment for all three processes.—The precipitate used in the three foregoing processes consists of ammonium urate which is obtained by adding ammonium chloride or ammonium nitrate to urine which has previously been rendered slightly alkaline by the addition of 1 per cent. of lithium carbonate and subsequently boiling, the precipitated phosphates, &c., being removed by filtration. The method employed is as follows. Take 100 cubic centimetres of clear urine (warm if necessary to dissolve uric acid or urates) and place in a conical flask (Erlenmeyer) of about 400 cubic centimetres capacity, add one gramme of lithium carbonate, and boil the whole for three minutes. If frothing occurs it can be checked by blowing on the upper portion of the outside of the flask. Filter the liquid whilst hot and wash the precipitated earthy salts with a little distilled water until the filtrate measures 100 cubic centimetres at 15.5° C. In tropical countries a convenient and inexpensive method of cooling to the required extent is by means of immersion of the ordinary vessel in a mixture of sodium sulphate one part and water four parts.

Process "A."—To 50 cubic centimetres of the filtered alkaline urine, which contains the uric acid as lithium urate, add five grammes of ammonium chloride and shake the flask until solution occurs. After three minutes warm the contents of the flask to 50° C. so as to secure a uniform aggregation of the precipitated urate of ammonium. Now pour the whole into a tube graduated in parts of uric acid per 100 and allow deposition to take place and take the reading after 24 hours have elapsed. If the urine does not contain a high percentage of uric acid the reading can be taken in four hours. If any ammonium urate adheres to the surface of the glass the tube should be gently rotated.

Process "B."—The ammonium urate is obtained as follows. To 50 cubic centimetres of the filtered alkaline

urine add 15 grammes of ammonium nitrate and shake the flask until solution occurs. After three minutes warm the contents of the flasks to 50° C. as in Process "A." Transfer the whole to a beaker and allow to stand for two hours. Collect the precipitate on a filter paper of 5.5 centimetres diameter and wash with about 10 cubic centimetres of a saturated solution of ammonium nitrate until no trace of chloride is indicated by the addition of a few drops of a solution of 5 per cent. of nitrate of silver acidulated with nitric acid. After washing the precipitate with about 5 cubic centimetres of distilled water to remove excess of ammonium nitrate, transfer it with the filter paper to a beaker with about 40 cubic centimetres of hot distilled water; solution being effected, pour off from the filter paper and wash the latter with two successive quantities of 5 cubic centimetres of distilled water: to the 50 cubic centimetres of solution thus obtained a measured quantity of the nitrate of silver solution is added—e.g., 10 cubic centimetres or 15 cubic centimetres. Add about half a gramme of powdered talc and stir the whole well, filter into a flask previously rinsed with a little distilled water, and wash the precipitate with about 10 cubic centimetres of distilled water. Add to the filtrate in the flask a few drops of dilute nitric acid (1 in 3) and a few drops of a saturated solution of iron alum and titrate with a standard solution of thiocyanate of potassium. The number of cubic centimetres thus obtained is subtracted from the number of cubic centimetres of nitrate of silver solution originally used and this gives the exact amount of nitrate of silver required for the uric acid in solution. Solutions required for Process "B": standard

silver nitrate solution— $\frac{n}{20}$ solution silver nitrate, 500 cubic centimetres; distilled water, 20 cubic centimetres; one cubic centimetre of the above equals uric acid 0.005 gramme. Solution of potassium thiocyanate of equivalent strength to above; dilute nitric acid, 1 in 3.

Process "C."—Dissolve 31 grammes of ammonium chloride in 100 cubic centimetres of urine previously treated with lithium carbonate and decant off the clear portion as shown in Fig. 3, and transfer the remainder with the

FIG. 3.

precipitate to a narrow cylindrical jar of about 25 cubic centimetres capacity. In a few hours the precipitate will be ready to transfer to a small filter paper 5.5 centimetres in diameter. Care must be taken that any precipitate adhering to the vessels used is detached and washed out on to the filter paper with some of the clear urine. Wash the precipitate and edges of the filter paper carefully with distilled water, the precipitate being disturbed as little as possible so that the wash water may percolate through it. The washing of the precipitate may be performed in the following manner. Allow the liquid to drain from the precipitate, then fill the filter paper with distilled water by means of a wash bottle with a fine jet. Repeat this operation a second and a third time. Test some of the filtrate with a 5 per cent. solution of nitrate of silver, acidulated with nitric acid, 5 per cent. Only a very slight precipitate should be given, indicating the absence of any appreciable amount of ammonium chloride, but should the filtrate still contain this salt wash with a small additional amount of distilled water. Place the precipitate with the filter paper in the generating bottle of apparatus (Fig. 2), fill the tube up to the mark (25 cubic centimetres) with the hypobromite solution, and lower it into the bottle by means of string. The temperature of the solution should approximate to that

of the room in which the operations are carried out. This may be easily attained if the hypobromite solution is immersed for some time in the water vessel in which the generating bottle is placed. Now place the cork in the generating bottle and plunge the bottle in the vessel of cold water of a similar temperature to that of the hypobromite solution. After two minutes adjust the water level in the measuring burette to zero and then close the tap and observe if the water level remains constant. In order to test if leakage occurs in any part of the apparatus alter the water level in the measuring burette; any defect is then easily seen. Finally, lift the generating bottle and allow the reagent to flow out of the tube, and shake so as to promote the reaction between the sodium

obtained by Process "A" by J. H. Gough in four hours was 0.053 per cent.; by Process "B" by Dr. Dimmock, 0.052 per cent.; by Process "C," by F. W. Branson, 0.055 per cent.; and by the Gowland-Hopkins method by the Clinical Research Association, 0.056 per cent. One of us (A. F. D.) also obtained on different dates the following average results (15 samples being used), the specific gravity of the samples ranging from 1.013 to 1.028, the average specific gravity being 1.021; uric acid parts per 100, Process "A," 0.053; Process "B," 0.054

Conclusions.—Process "A" is a very convenient method and gives approximately correct results in a short time. Process "B" is a quick method and gives very concordant results. Process "C" is suitable for proportions of uric

FIG. 4.

hypobromite and the ammonium urate. After ten minutes, during which time the bottle should be shaken at intervals, adjust the level in the two tubes and read off the percentage of uric acid, as indicated by the nitrogen evolved. The hypobromite solution is prepared as follows:—

Soda solution { Caustic soda, 41 grammes.
Distilled water to measure 100 cubic centimetres.

Bromine solution { Bromine, 1 cubic centimetre.
Potassium bromide, 2 grammes.
Distilled water to measure 10 cubic centimetres.

For use mix equal volumes immediately before being required and cool.

To correct a reading for atmospheric pressure and temperature a calculating scale has been devised (a portion is represented in Fig. 4). 1. Read on the scale the observed number of cubic centimetres of nitrogen obtained. 2. Follow the horizontal line along the point of intersection of the vertical headed by the observed barometric pressure, reading between the lines where necessary. 3. From this point of intersection follow the oblique line to the right or left to the point where it intersects the vertical of 760 millimetres. 4. Follow the horizontal line to the point of intersection with the vertical of observed temperature. 5. Continue again along the oblique line to the left to the vertical number 0°C. The reading of cubic centimetres obtained at this point is the volume of gas corrected to normal pressure and temperature, and the amount of uric acid which this represents is shown in the last column to the left—e.g., 6.6 cubic centimetres N. at 1°C. and 780 millimetres Hg = 6.4 cubic centimetres of gas = 0.05 per cent. uric acid.

A large number of analyses on duplicate samples have been made in order to obtain comparative results with the different processes. The following are selected to illustrate the general concordance obtained. Dr. Nierenstein obtained by process "C" 0.049 per cent. and by the Gowland-Hopkins process 0.049 per cent. The Clinical Research Association reported as regards the same sample 0.05 per cent. The following comparative results were also obtained by four independent workers, the methods used being the "A," the "B," and the "C," and the Gowland-Hopkins method, portions of the same bulked urines, specific gravity 1.023, being used in each case. The amount of uric acid

acid ranging from 1 in 1000 to 1 in 5000. Urea is also easily determined by means of the uric burette, one cubic centimetre of urine (carefully measured by means of an accurate pipette) being used, in place of the collected precipitate as in Process "C."

BRONCHIECTASIS IN CHILDHOOD, WITH SOME OBSERVATIONS ON THE CONDITION KNOWN AS HONEYCOMB LUNG.

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In order to confine these remarks on bronchiectasis in childhood within reasonable limits those cases which are due to the presence of foreign bodies or to the pressure exerted by enlarged glands on the bronchial tubes are not considered. It will be most convenient to start with an investigation of the pathology of the ordinary form of the affection and then to consider the clinical manifestations and treatment of the disease.

The lungs of children, and sometimes of adults, occasionally present a peculiar cystic appearance well designated by the descriptive and non-committal term "honeycomb lung." In some cases the condition is bilateral and universal, in others it involves parts only of the lung or may be limited to one lobe. Whatever the distribution, the cavities in all cases present a similar appearance. They are multiple, more or less spherical, and generally larger towards the periphery and smaller towards the centre of the organ. Observers with great unanimity describe them as "varying in size up to the diameter of a pea." More often than not the pleuræ are not adherent and the superficial bullæ project, in the recent state, as small transparent blisters beneath the pleural envelope. The cavities are lined by a smooth whitish lining