A British Medical Association Lecture ON SOME MODERN ASPECTS OF NEPHRITIS.

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THE centenary celebration last year of the publication of Richard Bright's discovery caused his work to be re-examined with greater care. As with Darwin, so with Bright, a study of their own writings makes us realize how much more cautiously they expressed their conclusions than their followers have done. The disciple always tends to be more Royalist than the King. Aschoff says: "Bright himself, with characteristic caution, discussed the question of the extent to which all the symptoms described by him should be referred to primary disease of the kidneys or to primary lesions of other organs. It is, therefore, better to speak of *symptoms of Bright's disease in disorders of the kidneys* and not of Bright's disease of the kidney." He suggests limiting symptoms to the combination of toxic and inflammatory albuminuria with so-called renal oedema. This would exclude some forms of nephritis, such as granular kidney.

In general, nephritis is due to some toxic cause. I do not believe that mere exposure to cold causes nephritis in a healthy kidney, though it may exacerbate a chronic lesion which is already present. In the great war the epidemic of nephritis did not occur during the first winter when men were much exposed and badly housed; it occurred during the early spring of 1915, and there was no relationship between low temperature and the incidence of nephritis. It was then suggested that a great range of temperature was an exciting cause, but in the Boer war, when I saw the mirage at 2 o'clock in the afternoon and hoar frost at 6.30 on the veldt near Bloemfontein, cases of acute nephritis were almost unknown. On the other hand, in subsequent winters in the great war there was some agreement between low temperature and the onset of acute nephritis, because by that time there were a considerable number of men in the field whose kidneys had previously been somewhat damaged.

Adolescent albuminuria does not predispose to nephritis; MacLean tested the urine of 50,000 men in training camps and found that there was no relationship between the cases of albuminuria thus discovered and the onset of subsequent nephritis. The majority of men suffering from nephritis were free from albuminuria until a comparatively short time before symptoms of nephritis set in. We must remember, however, that some of the milder forms of toxic kidney may simulate adolescent albuminuria, so that a careful search should be made for toxic foci in those believed to be suffering merely from this condition—for example, in the tonsils, or the appendix, or tuberculous glands.

If the kidney is overwhelmed by a toxin there is a sheer necrosis affecting the convoluted tubules most, the loops of Henle less, and the glomeruli not at all. This is the "toxaemic kidney," where the kidney does not retain what it should excrete, but excretes what it should retain. If the toxic process is rather less severe typical acute nephritis results, in which the glomeruli share. If it is much less severe a chronic nephritis follows in which the interstitial tissues suffer more than the tubules. Geoffrey Evans has shown that even in chronic interstitial nephritis there is an inflammatory reaction. In general terms, then, the intenser the infection, the more the secreting epithelium suffers; the more chronic it is, the more the vessels suffer, and as the glomeruli are vascular tufts, they are specially involved.

Generally speaking, the toxins reach the kidney by the blood stream; if in addition to the toxin the actual infecting organisms, as in the multiple emboli of infective endocarditis, are carried to the kidney, a number of foci of

small-celled infiltration result, each of which starts an island of nephritis, constituting focal embolic nephritis.

Sometimes, especially after tonsillitis, boils, carbuncles, and staphylococcal infections generally, it is the perinephric tissue which is first involved—a metastatic inflammation which spreads via the lymphatics into the kidney. This is the type of nephritis in which pain in the back is most common. Again, the infection may spread upwards from the lower urinary tract—ascending nephritis—though here too, as Kenneth Walker pointed out, it is mainly, if not exclusively, through the lymphatics of the ureter that the infection reaches the kidney.

I shall adopt the following classification of nephritis, slightly modified from Aschoff.

1. DEGENERATIVE GROUP.

(A) Acute. *Toxaemic Kidney*—such as that produced by drugs (for example, corrosive sublimate and carbolic acid) or by the toxæmias of pregnancy.

(B) Chronic. *Amyloid Kidney*.

2. INFLAMMATORY GROUP.

(A) *Glomerulo-tubular*.

1. *Acute—ordinary acute nephritis.

2. *Subacute—chronic parenchymatous nephritis; large white kidney.

3. Chronic—chronic mixed nephritis or contracting kidney.

It must be recognized that these may either follow one another in this order, or 2 and 3 may, apparently arise independently of 1.

(B) *Focal Embolic Nephritis*—as seen in infective endocarditis, when the nephritis is set up by multiple emboli from the heart valves.

(C) *Chronic Interstitial Nephritis*—the small red or granular kidney.

3. VASCULAR GROUP.

(A) *Hypertensive*.

(B) *Senile or Atheromatous*.

Only the starred members of this list really accord with the definition of disorders of the kidney with the symptoms of Bright's disease.

To my mind the position has only been made more difficult and obscured by Volhard's introduction of the term "nephrosis," which has by some writers been so extended as to include chronic parenchymatous nephritis. I consider this term should be limited to toxic kidney in which there are merely degenerative changes in the tubules without any inflammatory reaction. There is marked oedema, excess of cholesterol in the blood, and massive albuminuria, but there are no cardio-vascular changes or casts. The urea of the blood remains normal, as does the globulin, but its albumin content falls as the disease progresses. Nephrosis is part of a general toxæmia, and some observers claim that when it is experimentally produced the first protein to appear in the urine may be hepatic in origin. At the necropsy a large amount of cholesterol may be found in the kidney tubules, the so-called "myelin" kidneys. Death or complete recovery is the rule, but occasionally a toxic kidney may lead to chronic nephritis.

Of late the tendency has been towards a secretory rather than an anatomical classification. This is really an advantage since the anatomical basis can only be established after death, when the opportunity for treatment is past.

Broadly speaking, the kidney may excrete two classes of substances: (1) those which can be of use to the body—water, salt, sugar, bile, haemoglobin; (2) those which are purely waste products—urea and allied nitrogenous substances. Against the excretion of the first group the kidney presents a threshold; it does not attempt to excrete them until their concentration in the blood reaches a certain height, for it would not do for such substances to be drained out of the body. For the second group no such barrier is needed. The secretory classification is as follows:

1. *Hydraemic Nephritis* (which broadly corresponds to chronic parenchymatous nephritis).—Here the excretion of Class 1 is involved, particularly of water and salt. The output of urea may be normal, and there will not be any retention of it in the blood. Not so with chlorides, the content of which in the blood will be raised. Oedema may be very marked, but there will be little evidence of cardio-vascular change.

2. *Azotaemic Nephritis*.—Here there is gross failure of the concentrating power of the kidney, and since the great

work of the kidney in concentration is in relation to nitrogenous waste products, and as urea is the most abundant of these, we find not only a fall of urea in the urine, but a rise of it in the blood. There is a rise from the normal 20 to 40 mg. per cent. to 80, 100, or much more in severe cases. The cardio-vascular changes tend to be very marked.

3. Mixed Types.—As interstitial changes, which are chiefly associated with azotaemia, proceed more slowly than the parenchymatous, which are chiefly associated with hydraemia, the former gradually alter the picture. A chronic parenchymatous nephritis either dies of intercurrent infections or passes into the contracted stage with interstitial changes; the oedema subsides, the blood pressure goes up, and the heart hypertrophies. Both sodium chloride and urea are retained in the blood. If there is both nitrogenous retention and renal oedema the case must be a mixed one.

I shall next consider some clinical features and the treatment of three leading types of nephritis—the acute, the hydraemic, and the azotaemic.

ACUTE NEPHRITIS.

It is important to treat the cause of acute nephritis as soon as possible. The principal causes are:

1. Acute Specific Fevers, such as Scarlet Fever.—Recent observations show the great value of the administration of alkalis in scarlet fever as a prophylactic measure against the complication of acute nephritis.

2. Diseases of the Respiratory Tract.—This applies particularly to the upper respiratory tract, especially the tonsils. I recently had a case of acute haemorrhagic nephritis associated with an infected antrum, drainage of which was followed by rapid improvement. But Sir Thomas Horder has also called attention to the importance of extended sepsis as well as of focal sepsis. Thus a widespread infection of the bronchial tubes can lead to troubles similar to those due to a small collection of pent-up pus. This is particularly well seen in hyperpiesis and nephritis.

3. Diseases of the Skin.—Since the skin is a part of the excretory apparatus the association between diseases of the skin and of the kidney is not surprising. Extensive burns are well known to cause acute nephritis, though here extended sepsis is probably the chief factor. I have recently had two cases of scabies causing a staphylococcal infection of the skin, which were followed by acute nephritis. Here ultra-violet rays helped to clear up the skin very quickly, and the nephritis rapidly improved when this was achieved.

4. Purpura.—Here presumably the purpura and the acute nephritis are both consequences of a common cause, but it is not infrequent for the nephritis to occur later than the purpura.

5. Epidemic Type.—This is the type encountered during the war, of which I have written elsewhere. It is sufficient here to point out that dyspnoea was an early symptom, and that Shaw Dunn found multiple thromboses in the lungs. So perhaps this is really a special instance of (2), though presumably due to some unknown specific infection. According to Aschoff the renal lesion is a pure glomerulitis.

In the treatment of acute nephritis I am strongly of opinion that the conventional milk diet is a mistake in the earliest stages. Far better results accrue from von Noorden's plan of giving nothing but fruit, fruit juice, sugar, and water. If there is much hunger I generally allow toffee as well. The question of diuretics will be dealt with under hydraemic nephritis. Later on, milk can be given and the conventional treatment followed. Sufficient alkalis to render the urine alkaline seems a wise measure, and it is well to keep the patient in bed until the centrifugalized urine shows no red blood corpuscles on microscopic examination.

HYDRAEMIC NEPHRITIS.

There has been much controversy as to the cause of the dropsy which is the outstanding feature of this type. Widal attributed it to the retention of sodium chloride, but the results of a salt-free diet have been disappointing. Moreover, as Izod Bennett points out, "the same kidneys which at first secreted a urine poor in chlorides will, a week later, when oedema is subsiding, secrete a urine containing abundant chlorides." In other words, if water is retained, salt must also be retained. But I do not agree with Bennett when he says that an increase in the blood

chlorides has never been demonstrated in this condition. Thus, in a recent case of mine, the blood chlorides were 580 mg. per cent., as against the normal 360 mg., and the urinary chlorides 150 mg. per cent., instead of 500 mg. I think that while retention of chlorides has been over-stressed in the past it may be a factor in renal oedema.

Epstein's explanation of renal oedema involves two main factors: (a) there is a serious drainage of blood proteins into the urine, which may mean that as much as 10 per cent. of these proteins are lost daily. In this way there is a fall in the osmotic pressure of the blood, with consequent retention of water in the tissues. Subsequent investigations on the osmotic pressure of proteins have supported this conclusion. (b) In hydraemic nephritis the lipoids, especially cholesterol, accumulate in the blood and tissue fluids, which he believes increases the tendency to oedema.

A recent case of mine showed a cholesterol content of 390 mg., falling to 250 mg. as the oedema subsided, whereas the normal lies between 100 and 190 mg. Bright himself called attention to the milkiness of the plasma and body fluids in nephritis with dropsy, and J. Maxwell has recently devoted attention to the subject. He showed that the cholesterol of the plasma is almost invariably increased in every type of renal oedema, and though not necessarily proportional to the amount of oedema its presence in increased amounts is prognostic of a chronic course. He did not think, however, that the cholesterolaemia and the oedema were related as cause and effect, but rather that both are the results of some toxic action on the tissues.

Epstein advised a high protein diet and very little fat in such cases. It is true that a high protein diet may sometimes greatly reduce oedema in hydraemic nephritis, but in part this is due to urea, the natural diuretic, which must be formed in large amounts from the amino-acids into which that protein excess disintegrates during digestion and before it is absorbed.

In passing, why forbid eggs in albuminuria, as is so often done? Now that we know how completely protein is disintegrated before it is absorbed, how can it "run through" from the bowel to the kidney? D'Arcy Power's experiments on himself are often quoted apart from the context in justification of this restriction. It is true that he observed albuminuria in himself on three occasions after he had taken a large number of eggs, but it is also true that each of these occasions was after rowing a course. Now Collier found albuminuria in each member of the Oxford crew of 1906 after rowing a course, and strenuous exertion is now well known to produce a temporary albuminuria. But it was not known to do so at the time of those experiments. Again, raw eggs may cause a slight toxic albuminuria in those sensitive to them, but this does not occur after cooked eggs. I have deliberately added eggs to the diet of patients with hydraemic nephritis, and have found no increase in the albuminuria produced thereby.

• It naturally follows that the high protein diet is only applicable when it is certain that there is no urea retention. Mere estimation of the percentage of urea in the urine seems to me to be of little value, since so much of the urea is exogenous, coming directly from the disintegration of food proteins. Many patients with nephritis are already on a low nitrogenous diet, which will necessarily lower the percentage of urea in the urine. MacLean's urea concentration test is, however, of considerable value, since it shows whether, given a definite amount of urea to deal with, the kidney is capable of doing adequate work. I have often found that though the blood urea is normal, the urea concentration test gives too low a figure. This presumably means that the kidney can only just get along on its low protein diet, and that urea retention is just beginning. Such cases are not suitable for Epstein's treatment. There seems little justification for his embargo on fats, since it is only cholesterol that is concerned, and that probably not in causal relationship. Moreover, Epstein is not consistent in this, since he allows eggs, which contain cholesterol in fair amount.

It would appear, then, that Epstein's method is only of limited application to cases of hydraemic nephritis

proved to be free from nitrogen retention. Then a high protein diet may help to make good the excessive protein loss, while diuresis may be assisted by giving urea as such in doses of 40 to 60 grains three times a day. It is entirely non-toxic. Some thirty years ago it was given in large doses in tuberculosis. I doubt if it ever did any good for that disease, but it certainly did no harm, so that one need feel no scruples about using it in the type of case here described.

This brings me to the subject of diuretics in nephritis. They may act—

1. *By producing vaso-dilatation in the kidney.* The caffeine group act in this way. They probably act as direct stimulants to the renal epithelium, the vascular change being secondary.

2. *By increasing the cardiac efficiency.* The digitalis group apparently act as diuretics in this way.

3. *By increasing the quantity of circulating fluid:* (a) by absorption of water from the intestines, as by giving the patient large quantities of water to drink; (b) by increasing the osmotic pressure of the blood. The saline diuretics and urea itself act in this way, attracting water from the tissues into the blood stream.

How far are these methods applicable to hydraemic nephritis? The first breaks the physiological law of resting damaged structures; I believe all the stimulating diuretics are capable of doing harm in this disease. The second is presumably only helpful when there is cardiac insufficiency as well. The third can do no harm, and may do good.

A study of the etiology of renal oedema leaves us with the impression that it is "at once suggestive of pathological changes in tissues other than the kidney" (Bennett). This is the idea underlying the use of novasurol and cuphyllin as diuretics in nephritis, since they are believed to act on the tissues, enabling them to give up the water they are retaining. It is necessary to raise the hydrogen-ion concentration of the blood first by giving 1 to 2 drachms of ammonium chloride on each of two days, and then on the third day injecting 1/2 to 1 c.cm. of novasurol intramuscularly. Both parts of this treatment are usually repeated after a few days' interval. Some give larger doses of ammonium chloride and over a longer period. This plan may be adopted in obstinate cases, but it often fails. In acute nephritis I believe that 3 (b) is the only method that should be tried unless there is cardiac insufficiency as well, in which case digitalis may also be given.

Elimination by the skin as an alternative route of excretion has long been a common practice in nephritis. It is open to the following objections.

(a) Only 3 grams of nitrogen can be got rid of through the skin in the day, compared with 8 grams which can be more easily eliminated by the bowel.

(b) Physiological rest for the kidney is not secured by giving it a highly concentrated urine to deal with.

(c) Diaphoresis is an exhausting process, and may depress the heart.

(d) The withdrawal of so much fluid without a corresponding removal of organic solids must increase the concentration of the toxins in the circulation.

It has been argued in support of this method of treatment that after a hot-air bath the patient may be actually covered with small crystals. These are, however, chiefly crystals of sodium chloride, though there may be some urea as well. Herein we have a clue to the type of case in which diaphoresis will be of service—namely, the one when there is salt retention as a factor in the oedema, as explained above. The elimination of salt may then be of indirect service by breaking a vicious circle. In cases of this sort I have actually seen diaphoresis followed by diuresis, which can only be explained in this way. I conclude that the hot-air bath is only suitable when dropsy is actually present. Another indication that the treatment is having a good effect is the occurrence of sweating at a lower temperature than the one originally required to evoke it.

Decapsulation was revived a few years ago as a method of treatment in chronic parenchymatous nephritis by Sir Thomas Horder. It had previously been advocated chiefly for chronic interstitial nephritis, and finally abandoned for this condition. In cases of parenchymatous nephritis the

following have been considered to be indications for this procedure.

(1) Persistence of the oedema for three months in spite of careful medical treatment.

(2) Absence of urea retention.

(3) Absence of cardio-vascular changes.

But even when all these indications are fulfilled the results are often unsatisfactory, and I cannot recommend this operation.

AZOTAEMIC NEPHRITIS.

When there is reason to believe that nitrogen retention is occurring the interpolation of two days of von Noorden's fruit juice and sugar diet, as mentioned under acute nephritis, may be of great benefit. I look upon this plan as comparable in value with the vegetable and egg diet in the treatment of diabetes in the pre-insulin days. After this a diet containing a restricted amount of protein should be given, and one which contains as little extractives as possible, since these give work to the kidney without providing a corresponding amount of nourishment. It is possible for an adult to maintain nitrogenous equilibrium on 1 gram per kilogram of body weight, and for a time less than this will suffice if there is nitrogen retention. This means that a man of 10 st. requires 66 grams of protein. During the epidemic of war nephritis I drew up the following two diets, the low nitrogen diet being given for the first week and the moderate nitrogen diet for the second and subsequent weeks as required. I am indebted to Miss Abrahams, dietitian to St. Bartholomew's Hospital, for recalculating these diets for me.

1. Low Nitrogen Diet.

Breakfast.—Milk 4 oz., porridge 8 oz., bread 2 oz., butter 1/4 oz. Fluids: Coffee 10 oz., milk 2 1/2 oz.

Lunch.—Bread 3 oz., butter 1/2 oz., lettuce or tomato 1 1/2 oz. Fluids: Milk 5 oz., barley water 10 oz.

Dinner.—Potato 4 oz., greens 5 oz., butter 1/4 oz., stewed fruit 4 oz., boiled rice 4 oz. Fluids: Lemonade, imperial drink, or barley water 12 oz.

Tea.—Bread 3 oz., butter 1/2 oz., lettuce or tomato 1 1/2 oz. Fluids: Weak tea 10 oz., milk 2 1/2 oz.

Supper.—Potato 4 oz., butter 1/4 oz., greens 5 oz., stewed fruit 4 oz. Fluids: Lemonade or barley water 12 oz.

This diet contains: Protein 49 grams; carbohydrate 358 grams; fat 35 grams. Calorie value, 1,992.

2. Moderate Nitrogen Diet.

Breakfast.—Egg 1 oz., bread 2 oz., butter 1/4 oz. Fluids as in No. 1 diet.

Lunch.—Bread 4 oz., butter 1/2 oz., tomato or lettuce 1 oz. Fluids as in No. 1 diet.

Dinner.—Mutton or fish 3 oz., bread (alternate days) 2 oz., butter 1/4 oz., stewed fruit 4 oz. Fluids as in No. 1 diet.

Tea.—Bread 4 oz., butter 1/2 oz., tomato or lettuce 1 oz. Fluids as in No. 1 diet.

Supper.—Greens 2 oz., potato 3 oz., bread 4 oz., butter 1/2 oz., stewed fruit 4 oz. Fluid: Milk 5 oz.

This diet contains (on average): Protein 63 grams; carbohydrate 407 grams; fat 91 grams. Calorie value 2,772.

These diets have proved suitable in the experience of other observers also. Alcohol is certainly undesirable in azotaemic nephritis.

It is generally recognized now that there are decided dangers in lowering the raised blood pressure in azotaemic nephritis by means of vaso-dilators. The rise of blood pressure is compensatory and should only be treated by such methods as help in eliminating the toxins whose action is forcing the pressure up. For this purpose I find the internal administration of tincture of iodine as useful as anything. Sometimes a small dose, say 1/2 grain, of thyroid extract twice a day will help this. Gentle exercise in the open air will also assist in the physiological lowering of blood pressure.

The necessity for a raised blood pressure in this type is illustrated by the case of a man admitted under my care with chronic interstitial nephritis and much dyspnoea. His blood pressure was 160 mm. systolic and 100 diastolic. On 15 minims of tincture of digitalis three times a day his blood pressure rose to 200 mm. systolic and 125 mm. diastolic, while his blood urea fell from 100 to 40 mg., and his general condition greatly improved. Evidently his blood pressure on admission was too low for due elimination of nitrogen by his defective kidney, and it had fallen

through cardiac insufficiency. When the condition of the heart was improved by digitalis it was able to cope more successfully with the necessities of the situation. In such a case to lower blood pressure is to court disaster.

A case of azotaemic nephritis may terminate through failure of the pump, the tubing, or the filter; in other words, through heart failure, rupture of a vessel as in cerebral haemorrhage, or uraemia.

Uraemia.

What signs and symptoms can rightfully be included under this heading? Personally, I should exclude the diarrhoea and vomiting, which may be regarded as alternative methods of excretion. I have already pointed out that 8 grams of nitrogen can be eliminated by the bowel in this way; and Graham has shown that considerable quantities of ammonium salts are present in the vomit of a uraemic patient. The skin rashes I should also look upon as an attempt to excrete toxins. This leaves us with three groups of symptoms which can be fairly classed as uraemic, but I would urge that these groups are due to different toxic substances and are of different significance.

1. *Convulsions and Amaurosis*.—Though very dramatic symptoms, these are really of less serious significance than the others. Patients may recover not only from the attack, but actually from the nephritis. They may occur also in eclampsia and toxæmic kidney, both conditions from which recovery may be complete. In my series of 160 cases of war nephritis convulsions occurred in 8. They all recovered and escaped without permanent damage to the kidney. It has been suggested that these symptoms are due to some toxin acting on the liver rather than to the kidney lesion. On this view I am in favour of treating such patients with insulin and dextrose, since a hepatic toxæmia is best helped by providing an ample store of glycogen in the liver. But there is no doubt that the best and most rapid relief can be given by prompt venesection. Bennett ingeniously compares the convulsions to tetany, pointing out that there is a reduction of blood calcium in both conditions.

2. *Uraemic Asthma*.—The sufferer from this has been graphically described by Rose Bradford as "a drowsy patient, with hissing respirations and bleeding gums." I believe that the cause of this distressing syndrome is acidæmia from failure of the kidney to excrete acid sodium phosphate. The hydrogen-ion concentration of the blood is consequently raised and the dyspnoea is an attempt at compensation for this by washing out carbon dioxide from the lungs. A compensated alkaline defect may exist without dyspnoea, but an uncompensated alkaline defect will cause dyspnoea and calls for free administration of alkalis. De Wesselow finds that a rise of blood phosphates and a fall in calcium content go together.

3. *Headaches; drowsiness; twitchings; hemiplegia; monoplegia; neuralgias; formication; pruritus*.—All this group of symptoms appear to be associated with nitrogen retention. The actual cause of the symptoms seems to be exudate of lymph and even of actual blood through the capillary wall, especially into the cerebral and the subcutaneous tissues. Small punctiform haemorrhages are commonly seen in necropsies on uraemic patients, and large or small purpuric areas in the skin are not infrequent. Canti considers that a blood urea of 300 mg. is a sure portent of a fatal issue; and I should agree, though I have had one case with a blood urea of 500 mg. reduced to 70 mg. under treatment, and sufficient clinical improvement for the patient to leave hospital. He died, however, about six weeks later. In this case, as there was no dyspnoea, the plan of giving hydrochloric acid was adopted, and the improvement certainly appeared to follow this. It has been suggested that in this way toxic amino-acids are converted into ammonium chloride, but I am not convinced that this is chemically sound. But, as already pointed out, dyspnoea implies an acidæmia calling for free administration of alkalis, under which I have also seen some slight fall in blood urea.

In connexion with nitrogen retention I should like to call attention to the different results given by the hypobromite and urease tests for non-protein nitrogen in the blood. The former method gives the amino-acids as well as the urea, the latter the urea only. Now in health 92 per

cent. of the nitrogen given by the hypobromite test comes from the urea, but it must not be assumed that a similar proportion exists in disease. I have, indeed, found the hypobromite test yield twice as much nitrogen as the urease test in uraemia. In other words, in uraemia there is a large increase in the relative and absolute amount of non-protein nitrogen other than urea, and it is presumably this "unknown" amino-acid fraction which is toxic, since urea is a harmless substance. If only one method is going to be used it is better to employ the hypobromite test. But using both gives most useful information as to the amount of toxic material.

This is well illustrated by the great rise of blood urea, sometimes accompanied by tetany, in cases of pyloric obstruction and in toxic conditions severe enough to produce anuria; here the hypobromite and urease methods may give identical figures showing that the rise of blood urea is merely secondary to failure of excretion; there is not, at any rate at first, any excess of amino-acids produced by altered metabolism. Pyloric obstruction presumably acts by preventing ingestion of fluids into the blood stream, so that there is not sufficient for the kidney to function properly. The combined use of the hypobromite and urease methods is a useful way of recognizing such conditions and of proving that they are not primarily renal in origin.

It will be seen that I do not subscribe to the doctrine sometimes advanced that the symptoms of uraemia are due to one specific toxin, albeit of unknown nature. On the contrary, it seems to me that the three different groups of symptoms above detailed are much more likely to be due to different chemical poisons.

CONCLUSION.

In conclusion, I am conscious that these more recent investigations appear to have had a destructive rather than a constructive effect on treatment. This must be admitted, but new aids to treatment will surely spring from a sounder pathology. In the meantime, our patients will do all the better and be more comfortable if we realize that many of the methods formerly recommended in the treatment of these diseases are impotent where not actually harmful.

FURTHER OBSERVATIONS ON THE MACROPOLYCYTE.

BY

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THE statement that megakaryocytes are not infrequently found in the peripheral blood continues to be repeated in papers and in textbooks, but while not denying that the megakaryocyte may be found in the blood stream, its presence must be extremely rare. I have never seen, in blood films, a cell which faithfully resembled the multinucleated giant cell of the marrow; nor have I seen photomicrographs or drawings of the cells so described that are at all convincing. There is every probability that the vast majority of the so-called megakaryocytes found in blood films belong to one or other class of macropolycyte.

DEFINITION.

The term "macropolycyte" (1927) is applied as a descriptive title to the large or giant polymorphs found in certain conditions. The normal neutrophil polymorphonuclear leucocyte, for brevity called the polymorph, measures 10 to 12 microns in diameter in fixed and stained films. (Plate I and Plate II, Fig. 1.) The title "macropolycyte" is given to the large cells of the polymorph type having a diameter of more than 14 microns. It is of this cell which this paper treats, but for its better appreciation a few details concerning the polymorph may be recounted.

THE POLYMORPH IN HEALTH AND IN INFECTIONS.

The polymorph enters the blood stream from the marrow with a single-lobed nucleus, and as its life in the circulation continues, the nucleus becomes more lobulated until