A Clinical Lecture ON THE DIFFERENTIAL DIAGNOSIS IN CASES OF ALBUMINURIA.

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ALBUMINURIA is the term used to denote the passage in the urine of a pretein that is coagulable on boiling. More than one substance is included in the word "albumen" in this sense, and there are varying proportions of serum albumen and serum globulin in different cases. So variable may be the relative amounts of these, not only in different diseases, but also in different cases of the same disease and in the same patient at different times, that there is little useful clinical information to be obtained by dealing with the albumen and the globulin separately, at any rate so far as present knowledge goes. Nucleo-protein or nucleo-albumen comes in quite a different category.

Although a large number of different tests for albumen have been devised and advocated, for clinical purposes there is little need to trouble about more than the two common ones—namely, the acetic acid, and boiling for the cold nitric acid tests. It is true that each of these has fallacies; but the latter are not common to both, and there is at least one in the interpretation of one of the two tests that can readily be confused or otherwise by the other. It is alleged that more delicate tests exist; but there is such a thing as too great delicacy in a clinical method. One does not want to find albumen in minute traces where it does not matter, and it seldom matters until its amount is sufficient to give both the common tests.

The ACETIC ACID AND BOILING TEST.

A test-tube three parts full of urine—coagulated if need be by dilution—is held by its lower end, whilst its upper part is carefully heated to boiling point. It is best not to add any acetic acid before boiling unless the specimen is distinctly alkaline, in which case it may be just acidulated with a drop of acetic acid. After boiling, the tube should be held in a good surface light against a dark background, so that the edge of one's nose may be used to detect any opalescence which will be obvious at once, and there may be a dense white cloud. Except in very rare cases of Bence-Jones's albuminuria this cloud will be due to one or more of three things—namely, an impuety of magnesium carbonate, or coagulated albumen. One, two or more drops of acetic acid solution (B.P.) are now added; if the cloud disappears entirely, quietly, and at once, it was due to earthy phosphates, and no albumen is present; if it disappears entirely but with brisk effervescence, the latter is due to calcium carbonates amongst the phosphates, and no albumen is present; if, on the other hand, the cloud clears up but partially, or remains unaltered, or actually increases and becomes more flocculent, albumen is almost certainly present. There is only one serious fallacy remaining, and that is in regard to nucleo-protein; this is precipitated by acetic acid, and it is possible for a cloud of phosphates to be cleared up by the latter and yet for a faint cloud of nucleo-protein to come down in the place of the phosphates in such a way as to suggest that the original cloud was not wholly soluble in the acetic acid, and therefore that albumen is present when it is not. There are three ways of obviating this source of fallacy: the first is to add a single drop of dilute non-fuming nitric acid to the suspicious cloud that results after the acetic acid—is it due to albumen, it will persist or even increase, whilst if it is due to nucleo-protein the nitric acid will disperse it; the second is to perform the cold nitric acid test for albumen as described below—namely, to nucleo-protein will not give a definite localization of white ring with it; and thirdly, a control test may be done, acetic acid being added to another specimen of the urine without boiling, and the cloud due to any nucleo-protein compared with the cloud in the acidulated and boiled specimen.

Heller's Cold Nitric Acid Test.

About 1 c.c. of urine is poured into a test-tube, the latter is held much inclined, and colourless nitric acid is allowed to flow gently down the side, until about one-third as much as the urine has been added. The nitric acid is heavier than urine and goes to the bottom of the tube, forming a white ring at the junction of the two fluids. Some prefer to pour the nitric acid into the test-tube first and then to add the urine carefully with a pipette. It is important not to shake the tube on the acid and the urine will mix, and there will be no definite line of junction between them. Fuming nitric acid must be avoided, because the nitrous oxide fumes cause decomposition of albumen, and the resultant mix, at times there is bubbling even when the nitric acid is colourless, in which case this is due to CO2 set free from carbonates. The test is very delicate; if any large quantity of albumen is present, the ring appears at once; if there is only a trace, the white ring may not appear for a little; and the tube should be set aside and looked at again in a few minutes. Broadly speaking, it takes three minutes for it to develop when the amount of albumen is 1 part in 30,000. This test is open to more fallacies, however, than the acetic acid and boiling test, so that the nitric acid test should not be trusted alone, unless it is negative. In concentrated urines it is a delicate test, but in the latter is redish-brown, or violet-brown ring of colour at the junction. This is nothing to do with albumen; it is generally most marked in cases of indigocarmin. White urine, more or less like that due to albumen, may also be due to any of the following:

1. Resin.—If the patient is taking copalba resin, or other similar drug, enough of the resin may be excreted in the urine to form a diffuse white cloud above the nitric acid. This source of fallacy is best avoided by bearing it in mind and checking the nitric acid test by the heat test; this latter safeguard applies to all cases of suspected albuminuria.

2. Albumoses.—These generally occur in association with albumen; should they occur alone, the ring will disappear with warming, to reappear on cooling, and there will be no cloud with the heat test.

3. Bence-Jones's Albumoses.—This occurs without albumen, gives a ring with nitric acid that disappears on warming, to reappear on cooling; with the heat test a dense cloud appears about 50° C., to disappear on further heating to boiling point.

4. Nucleo-albumen.—The ring with this is not in contact with the nitric acid, but higher up and diffuse; it may be very local difficulty in cases where for it is acid precipitated by acetic acid, and may therefore give a cloudiness with the boiling test. The methods of avoiding this fallacy are mentioned above.

5. Ureas. The addition of a cloud near the nitric acid if the urine is very concentrated; the cloud will disappear on gentle warming, to reappear on cooling, so that it may also be mistaken for albumose; this fallacy may be avoided by diluting urine used for the nitric acid test is employed.

6. Urea Nitrate.—If the urine contains a large percentage of urea, a crystalline deposit of urea nitrate may form at the junction. As a rule, the crystalline nature of the ring is obvious on inspection, but in case of doubt the urine should be diluted and the test repeated. It does not matter which test is most relied upon when the result is negative, but before the positive deduction that a urine contains albumen is drawn, both the acetic acid and boiling, and the cold nitric acid tests should be positive.

In arriving at a diagnosis of the precise cause of albuminuria in any given case, it is essential that a microscopical examination of the centrifuged deposit from the urine should be made. Whatever else may be found, the first question to answer is—the urine albuminuric, as well as albumen, or not? All cases of albuminuria may be divided into two main groups, namely—(1) Cases with renal tube casts; (2) cases without renal tube casts.

RENAI TUBE CASTS.

When one speaks of renal tube casts in this respect, however, one has to bear in mind the fact that modern methods of centrifuging with electrical machinery have reached so high a degree of perfection that hardly anything that a given specimen of urine
contains escapes detection: technique has become almost too perfect, for when clinical methods become too delicate they begin to lose some of their clinical value. The result, in connexion with casts, is that even in a great many normal casesrenal tubule cast and an occasional red blood corpuscle are found; therefore, when one speaks of cases of "albuminuria with tube casts," one means "with enough renal tube casts to be pathologically." The observer experiences that when the "occasional" tube cast is inside or outside the normal limits. More than one examination may be required, and the urine should be as fresh as possible, for casts do integrate on standing, especially in hot weather and in alkaline urines.

Renal tube casts are of various sorts, and a certain amount of help can be derived from a knowledge of the particular kinds of casts present in a given case. Their matrix or foundation is a structureless material whose origin is obscure, though thought to be due to some kind of proteid coagulation. Sometimes the casts consist of this structureless matrix only, and according as they are thin less or more highly refractive they are spoken of as hyaline casts or waxy casts respectively. The hyaline form is commoner than the waxy, but neither is characteristic of any particular disease. Embedded in the hyaline matrix there may be various substances or structures, and, according to the main features of the embedded substance, the term epithelialleucocyte cast is given. If renal epithelial cells predominate, the cast is called an epithelial cast; if leucocytes or pus corpuscles, a leucocyte cast; if red blood corpuscles, a blood cast; if bacteria, bacterial casts; if granular, granular casts; if non-fatty granular débris, granular casts. It is not at all uncommon to find a long cast which in one part is simply hyaline, at one end is granular, and at the other epithelial—a mixed cast. Upon the whole, one may say that the hyaline casts occur in all forms of nephritic conditions, whether acute or chronic; that epithelial and leucocyte casts indicate acute nephritis; that granular casts tend to occur along with epithelial casts, but that when they occur alone or in association with hyaline casts, they are evidence of at least less acute mischief than are epithelial casts, while fatty casts come between the two. Blood casts may occur in almost any variety of renal haemorrhage, and by themselves they are not evidence of inflammation, though in association with other casts they indicate very acute inflammatory changes.

A. ALBUMINuria WITH RENal TUBE CASTS.

When it has been decided that there are a pathological number of renal tube casts as well as albumin in the urine, it is almost certain that there is an inflammatory lesion of the kidney. The next step in the diagnosis is to determine the pathological examination, whether pus is present also; in other words, the cases may be subdivided into two main subgroups—namely, (a) albuminuria with renal tube casts without obvious pus, and (b) albuminuria with renal tube casts and obvious pus. There are, of course, a few border-line cases in which leucocytes are present in excess and yet not in sufficient numbers to constitute pus. There will generally be other points about such a case that will lead one to decide whether it comes rather in the pyuria or in the pyuria group. The differential diagnosis of the former will be discussed in another lecture under the heading of pyuria, so that it only remains here the differential diagnosis of albuminuria with tube casts without obvious pus. The causes of this condition may be classified as follows:

1. The Various Forms of Bright's Disease:
   (a) Acute nephritis of a primary type.
   (b) Acute pyonephrosis upon an underlying chronic nephritis.
   (c) Chronic nephritis of young people.
   (d) Arising out of a known attack of acute nephritis.
   (e) Arising without any known previous attack of acute nephritis.
   (f) Chronic nephritis of old people, cirrhosis of the liver.
   (g) Arterio-sclerosis.
   (h) Gouty disease of the kidneys.


3. Chronic Ascending Nephritis, leading to scorched corneal kidneys, the result of:
   (a) Obstruction to outflow by:
      (i) Urethral atresia.
      (ii) Enlarged prostate.
      (iii) Displacement of the womb.
   (b) Fibromyas, ovarian cyst, or other pelvic tumour.
   (c) Pregnancy.
   (d) Venous obstruction of the kidney and kinking of the ureter.
   (e) Rarities, such as abdominal aneurysm obstructing the ureter.

4. Lardaceous Disease of the Kidneys.

5. Infarction of the Kidneys, especially when the result of embolism in cases of tumoral endocarditis; but also due to thrombosis, as in some blood diseases.

6. Thrombosis of the inferior vena cava involving the renal veins.

7. New Growth of the Kidneys—some cases.

In many instances the diagnosis soon becomes obvious, but in some there may be great difficulty. These following cases may serve to indicate how such difficulties may arise:

A patient of middle age, who had not been strong for a long time, began to suffer from attacks of fever which increased and spread to her back, genital organs, thighs, and legs. She did not see a doctor at once; but within a few days her abdomen began to swell and she began to pass very little water, and what she did pass was the colour of blood. Upon examination the urine had a specific gravity of 1030 and was loaded with albumin and blood. In a few days there was an abundance of red blood corpuscles, renal epithelial cells, leucocytes, and epithelial, fat, granular, and waxy, or fatty, prussic acid, or crystals, or bacteria. It seemed almost obvious that she must be suffering from acute Bright's disease; but there was no oedema of the eyelids, and there was definite enlargement of the left supraventricular lymphatic gland. The discovery of the latter led to a very careful examination for malignant disease, and a latent and quite unsuspected carcinoma of the rectum was discovered. The diagnosis was carcinoma recti, secondary deposits in the retroperitoneal lymphatic glands, involvement of the inferior vena cava and of the renal veins, with consequent albuminuria, haematuria, and renal tube casts from nephritis simulating Bright's disease.

Another case was that of a girl of 16, who began to suffer from frequent attacks of lachanemia, shortness of breath, oedema of her ankles and face, and slight pyrexia. The heart seemed to be little enlarged, and there were soft systolic bruits that were regarded as secondary to the anemia. The urine contained blood and albumen, with renal epithelial cells and tube casts in abundance. Acetates were developed, with increasing general oedema, and a retinal haemorrhages and neuro-retinitis. The diagnosis of acute nephritis, however, was only in small degree correct; for she was really suffering from malignant endocarditis of a subacute type, the nephritis being due to infected emboli of the kidney producing inflammatory changes around multiple renal infarcts.

These two cases will serve to show how it may be impossible to arrive at a correct diagnosis except by a thorough examination of all the systems, by watching the case carefully, and by watching the history—giving evidence in the proper diagnosis at intervals. We will now deal with the main headings in the above table in their reversed order.

If there is no new growth in a kidney the number of renal tube casts is likely to be small; sooner or later a microscopic fragment of new growth will probably be detected in the centrifuged urinary deposits. Albuminuria will not be extreme unless the renal veins and the inferior vena cava become involved, the same applying also to the occlusions of the legs and trunk; haematuria is likely to occur at intervals, the attacks being separated by many weeks sometimes, and being relatively painless; there may be an increasing renal tumour; cystoscopic examination may show the blood-stained urine to be coming from one ureter only; and finally, when suspicion of new growth has been aroused, laparotomy may be indicated and the diagnosis thereby confirmed.

Thrombosis of the renal veins and inferior vena cava has been referred to above as a condition that may simulate acute nephritis. Points to lay stress on in arriving at the diagnosis are: (1) To make a thorough examination, including that of rectum and vagina, in order not to miss anything, such as some latent growth whose secondary deposits are obstructing the veins; (2) to inquire carefully into the history—a great many cases of inferior vena caval thrombosis are due to extension upwards from iliac or saphenous clots, in which case there will nearly always have been swelling of one leg only to
Differential Diagnosis in Cases of Albuminuria.

start with, followed later by extension to the back and to the other leg; (3) to note that, although the oedema of the legs and back may be extreme, there is a definite upper level to it and no swelling of the eyelids or scalp; and (4) to ask if there and often veins upon the abdominal wall the blood current in them has become reversed—to being from below upwards instead of from above downwards.

The kidneys may be either embolic or thrombotic. By far the commonest cause of embolic renal infarction is infected or fungating endocarditis. Each embolus gives rise to the sudden appearance of blood in the urine, which may have continued to a sudden marked increase in any existent haematuria; there may or may not have been a sudden pain in the back at the time. Around each infarct there develops acute nephritis, so that in some cases all the characters of the latter malady may be superposed upon those of the fungating endocarditis. If the patient is already known to have heart disease, the diagnosis is easy enough; the difficulties arise in cases in which, notwithstanding the fungating endocarditis, there is no bruise. If fungating endocarditis is suspected, the points that confirm the diagnosis are: Pyrexia, which may be of any type—though absence of pyrexia does not exclude the disease; enlargement of the spleen; cutaneous, retinal, or other haemorrhages; progressive anaemia; definite cardiac failure of the latter type; a radical change in their character, such as becoming musical instead of blowing, or vice versa; optic neuritis; and multiple embolism, for instance in the brain, spleen, or lungs. There is marked leucocytosis as a rule. Venous blood may be cultivated bacteriologically as a means of confirming the diagnosis.

Thrombotic infarcts are less severe in their effects; they may produce no haematuria at all, and the albuminuria may be slight, and unaccompanied by tube casts. They generally arise in cachetic conditions, or in blo. d diseases such as leukaemia or porphyria anemia, in which case the infarction of the latter type may be accompanied by a marked leucocytosis as a rule. Venous blood may be cultivated bacteriologically as a means of confirming the diagnosis.

Lardaceous disease of the kidneys used to be common enough in the days of septic surgery, but it is decidedly uncommon now. It is a risky diagnosis to make, therefore, unless there is some obvious cause for it, such as long-standing suppuration in association with a spinal, hip-joint, or empyema sinus, bronchioclasia, phthisis with caviations, or the like; or else clear evidence of tertiary syphilis of the viscera with cachexia. There is nothing characteristic about the urine, although statements are made to the contrary. In the earlier stages there may be blood, which may remain in an encolphalorrhaphy, and may later the albumen increases, and it may reach very large amounts, such as 20 parts per 1,000, casts being very few in proportion, the total amount of urine increased, its colour being much normal, and the casts, if any, being very few. At this stage it is indeed possible, as a result of a superimposed nephritis, the amount of urine falls until only a few ounces may be passed each day, of high colour and specific gravity 1020 to 1035, loaded with albumen, and now containing hyaline, waxy, granular, fatty, and epithelial casts. Lardaceous casts may or may not occur, but they are not diagnostic, for they have also been found in cases of nephritis without lardaceous disease, hyaline casts are the rule, and in which there may be smooth, firm enlargement of the lower, moderate enlargement of the spleen, and more or less severe diarrhoea, to indicate corresponding lardaceous changes in the other organs that are generally affected as the same time as the kidneys.

Chronic ascending nephritis arises from precisely the same causes as acute ascending nephritis or surgical kidney, and may result from pyelitis, which heal, each leaving behind a smaller or larger scar, with the result that the course of months or years the kidneys are converted into a mass of irregular cavitations, which altogether change the other organs that are generally affected as the same time as the kidneys. It might seem that there could be little connexion between prolapus uteri and cerebral haemorrhage, but the latter may be due to the former by the following sequence of events: The displacement of the womb and bladder sometimes produces a spasm of the uterine arteries and a return of blood into the veins above their vesical ends; this obstruction, persisting for years, tends to produce chronic ascending nephritis. The fibrous changes in the kidneys that result from this may lead to thickening of the pericapsular sheath and to hyperpnoea, with tendency to apoplexy, just as other forms of granular kidney do. It is true that this sequence of events is not very common; but this is because the patient may or may be generally left untreated when it is of sufficient degree to cause the ureteral obstruction referred to above. Nevertheless, it is important to bear in mind that any cause of prolonged obstruction to the urine outflow may cause granular kidney with albuminuria, without pus, but with casts, and a pale and abundant urine of low specific gravity.

The diagnosis will generally be obvious when the obstruction is due to urachal structure; it is more apt to be overlooked in other cases, though if one bears in mind the kind of cases mentioned in the list above the method of diagnosis will generally be obvious. The diagnosis in particular that uraemia and displacements are a very common cause for slight albuminuria and a few renal tube casts in women; and that in men of 60 and over enlargement of the liver is a powerful indication of a similar condition long before there is any definite pyuria.

Chronic nephritis is sometimes spoken of as though it were an altogether different thing to nephritis of theBright's disease by type of view. I hold that Bright's disease has many different causes and many different types. It may be due to scarlet fever, in which case it is very possibly streplococcal; it may be due to pneumonia or empyema in which case it may be pneumococcal; it may be due to various micro-organisms; it occurs in some cases of cholera, and in severe secondary syphilis; it may be due to chemical irritation, especially phosphate of lime, or it may occur in any patient who has ever been exposed to any of these conditions; it is a very common cause of a slight albuminuria and a few renal tube casts in women; and that in men of 60 and over enlargement of the liver is a powerful indication of a similar condition long before there is any definite pyuria.

In all these cases the types of reaction on the part of the kidney are similar, and one can only regard pregnancy nephritis as a variety of non-suppurative nephritis in general. Very likely it is only a matter of degree whether it is non-suppurative or merges into the type in which there is pyuria as well as albuminuria—pyelitis of pregnancy. Pregnancy may cause a primary acute nephritis or an infarction or be associated with it, but it may persist as chronic nephritis; or it may seem to recover, when in reality it is merely latent, or even slowly and insidiously progressive; it may produce what seems to be a primary acute nephritis whose specific gravity—1015 to 1016—becomes superimposed upon a chronic nephritis that has been unsuspected; and very possibly it may produce nephritic changes which are not associated with definite symptoms at the time, but which ultimately result in what is spoken of as chronic interstitial nephritis. When, therefore, albuminuria with renal tube casts, but without pyuria, occurs during pregnancy, it matters little what name is given to the condition, provided it is of the same character as in Bright's disease in general in arriving at a conclusion as to whether the renal lesion is acute, chronic, or acute on chronic.

Various Forms of Bright's Disease.

Of these, the hardest to diagnose with certainty is primary acute nephritis in the adult. The majority of severe cases that are labelled acute Bright's disease are really suffering, not from primary acute nephritis, but from an acute exacerbation upon the top of already existent, but possibly latent, chronic nephritis. The difficulty is to arrive at the diagnosis here, because there is a lag; since many of the points mentioned in textbooks as occurring in acute nephritis are really due, not to the acute attack, but to the subacute or chronic renal lesion which has then been the same for years.

The best examples of primary acute nephritis are to be seen in cases that are already under observation for some other disease, notably scarlet fever or lobar pneumonia.
Sometimes the onset of the nephritis is indicated by general oedema, especially of the eyelids and face, ankles, genital organs, and loins; but it cannot be too strongly insisted upon that oedema is not essential, many cases of acute nephritis without oedema, and many cases of chronic nephritis become evidences of the patient is already in bed when the kidney inflammation begins, as in scarlatina cases. If the urine were not examined, the renal lesion would often escape recognition, since chronic nephritis gives no clinical data that many, if it is primary acute nephritis do escape recognition in this way, coming under observation later, when they present symptoms of chronic nephritis, or an acute exacerbation on chronic nephritis.

The essential point in the diagnosis is urine examination. According to the severity of the nephritis there will be more or less diminution in the total daily quantity; it is common for less than 20 oz. to be passed in the twenty-four hours, and often the amount falls to 10 oz., 5 oz., or even to none at all for a while. The specific gravity is raised to 1025, 1030, or even to 1035, but rarely to 1040. The reaction is generally acid at first, but it soon becomes alkaline on standing. The colour is extremely variable, according as little or much blood is present; sometimes it is brown, sometimes yellow. More often than not there is some tingling with blood, varying from bright red to brownish, brown, brown-black, or to that peculiar blackish tint which is described as smoky. There is also evidence of the albumose, and on examining it deposits a heavy sediment which often has a dark brownish tint, owing to the phosphates carrying the blood pigment down with them. Microscopically, the centripetal filtrate contains partly to earthy phosphates, and to the disintegration of cells and tube casts; and one expects to find an abundance of red corporules, renal epithelial cells, variable numbers of epithelial or hyaline, albumose, leucocytes, an occasional crystal of calcium oxalate or uric acid, and irregular granular masses which are not definitely tube casts. It is noteworthy, however, that in the great majority of these cases the red renal epithelial cells are abundant; in such a case, tube casts will show themselves in a few days. It is important to note that each specimen should be examined as fresh as possible, owing to the tendency to alkaline reaction and disintegration of casts and cells on standing. In addition to red corporules there is often a considerable amount of free haemoglobin; the tinture of gaujacum test will be positive, and the spectroscope will show the bands of oxyhaemoglobin or of methaemoglobin.

Coagulable protein is generally present in abundance, the proportions of globulin and albumin varying greatly, but together, as compared with anything found in normal urine, per 1,000, often about 15 parts per 1,000 at first, rapidly dropping to less than the first few days of treatment, until at the end of a fortnight or a month it may be 1 part in 1,000, or less, or even 1 part in 1,000 at first. In some cases, however, there is very little coagulable protein but an abundance of albumose, so that the boiling test gives a faint cloud, whilst the nitric acid test yields a dense white ring, soluble on warming, reappearing on cooling. There is generally an excess of nucleo-protein also. The urea, chlorides, and phosphates all fall below the normal totals, though their percentages may be increased if the urine is very concentrated.

With this condition of urine there will be little doubt as to the presence of acute nephritis, the only question being whether it is primary or whether it is an exacerbation upon chronic nephritis. The fact is known that the urine was free from albumose up to the time of the attack; if the patient is known to have suffered recently from scarlet fever, pneumonia, diphtheria, secondary nephritis, or some other similar fever; if the heart is of normal size and its sounds natural, the blood pressure natural, and the respiration healthy. It may be that the patient himself may have been exposed to scarletina infection. Having said this much about acute nephritis, the association of feeling of the skin, or recent sore throat with enlarged glands in the neck, or otitis media, might suggest the diagnosis in these mild cases of scarlatina nephritis; but theolla evidence of the disease. The course of the malady will also assist the diagnosis; the albuminuria of primary acute nephritis may clear up entirely in from a fortnight to six weeks, though in unfavourable cases it persists, and chronic nephritis develops out of the acute. If, on the other hand, it is found that a disease of apparently resistant character with general oedema, haematuria, and the other urinary changes described above, there is cardiac hypertrophy with a prolonged first sound at the apex, a ringing second sound, a blood pressure of more than 150 mm. Hg, and possibly albuminuric retention, the probability is that the acute nephritis is not primary but an acute exacerbation of an unsuspected chronic nephritis. In such cases of former type of nephritis, the patients may be of any age, from childhood to past middle life. If the patient survives, one or other of two conditions usually results: either the albuminuria, and the scanty urine, and the tube casts pass away, whilst the patient remains watery-eyed until the end comes in a few weeks or months, or else the acute exacerbation subsides, and the clinical characters of chronic nephritis remain. Some of these, but by no means all of them, are examples of primary acute nephritis, persistent and becoming chronic.

It must, however, always be very difficult, and indeed almost a matter of opinion in many cases, to decide whether a patient is suffering from a chronic nephritis which is the result of a primary acute nephritis that has not cleared up, or from a chronic nephritis which was present but unrecognised before the acute nephritis drew attention to it; but my own view is that many cases in which young adults seem to develop acute nephritis from no more definite cause than exposure to damp or cold, are really anonymous dikes of a primary acute Brown's Bright's disease. The albuminuria in these cases does not clear up, and it is a mistake to restrict the diet or the daily occupation after the acute exacerbation has subsided. In fact, if they are examined, these patients do best if they are given iron and allowed to go about their ordinary avocations; they have diseased kidneys, and they will not live many years, but there is no need to adopt stringent rules about the diet, or the amount of work. As the acute exacerbation subsides in such cases, the amount of urine rises rapidly to 60 or 70 oz. or more per day, and remains increased even after all oedema has passed away; the specific gravity falls to 1012, 1010, or 1008; the albumen persists to the extent of anything between 0.5 and 8 parts per thousand; blood is absent, though an occasional red corpuscle may be seen under the microscope, and there are moderate numbers of hyaline, granular, or even fatty casts, with an occasional renal epithelial cell. It happens not infrequently that a young patient suffering from chronic nephritis undergoes observation for shortness of breath, palpitations, anaemia, or for inflammation of one or other of the serous membranes, without ever having had any symptoms of acute nephritis at all. The diagnosis is often made on account of the granular contracted kidneys of older people in that they are pale instead of red. They are pale, granular, contracted kidneys, precisely similar to those which may result from a long antecedent acute nephritis that has not entirely cleared up. When they develop without any known preceding attack of acute nephritis, they have been referred to as Rose Bradford kidneys. It is by no means impossible that they are really the results of a preceding acute nephritis which escaped recognition because there was no oedema to attract attention to the need for urine examination. The patient may be of any age, though generally between fifty and thirty-five. There may be no sign of anything wrong until acute uraemia, with convulsions, leads to rapid death. On the other hand, in a typical case, in addition to the urine changes mentioned above, one expects to find some of the following symptoms or signs: a great increase in the size of the left ventricle, and outwards and onwards into the sixth left intercostal space below and outside the leath, may be heard, may be heard over the neck by stethoscope, in the left upper quadrant, or may be the sole evidence of the disease. The course of the malady will also assist the diagnosis; the albuminuria of primary acute nephritis may clear up.
maximum systolic blood pressure of 175 mm. Hg or more, sometimes to over 300 mm. Hg, even when the pulse feels comparatively soft to the finger; albuminuric retinitis; a tendency to haemorrhages, especially to epistaxis; headache; insomnia; breathlessness on exertion; and inability to work with the usual energy, either mentally or physically.

The chronic nephritis of old people is diagnosed more often than in the main symptoms of interstitial fibrosis alone, by the appearance of albuminuria or of albumin, or the other signs of renal failure. In some cases the albuminuria is very slight, and the albumin possibly undetectable; in those cases in which the albuminuria is more pronounced, it is often an intermittent one, which may be so extreme as to have caused difficulty in delivery; the bilateral cystic tumours can be felt, and the diagnosis in extreme cases is by no means difficult. Minor cases of this disease may be detected by the appearance, in large series of young adults, of prolapse of the kidneys, or of the renal pelvis, if the bars of the kidneys have reached an extreme degree; the enlargement of the kidneys in these cases is very much less than in young persons, where the lesion is probably congenital, and the examination and diagnosis of the cases is more difficult. In such cases, the kidneys may be easily palpated, and the determination of the specific gravity and other characters of the urin is often necessary, and often of great importance.

When pus is present in the urine, along with albumin and renal tubal casts, the differential diagnosis resolves itself into that of pyelitis; it is essential, therefore, to be able to distinguish between the two conditions. The first step is to ascertain the character and amount of the albumin and casts, and the presence or absence of pus in the urine. The presence of large quantities of albumin, and of casts of the same character as those found in cases of nephritis, is suggestive of pyelitis, but the absence of the latter is by no means of small importance. The presence of albumin in the urine, with casts and pus, is suggestive of pyelitis, and the presence of pus alone is suggestive of pyelitis.

The differential diagnosis of the cases of albuminuria so much as might be expected; the occurrence of much blood with much albumin and many renal casts and tubal casts indicates acute nephritis, but by itself does not decide between pyelitis and nephritis, or the effects of embolic infarction in cases of malignant endocarditis. Renal growths, calculi, or tuberculosis may all cause haematuria and pyuria with albuminuria, and a variable number of granular, hyaline, fatty, epithelial, leucocyte, and cell casts. It is, therefore, not possible to distinguish between these and acute nephritis. Their differential diagnosis was discussed in a previous lecture on haematuria.

C.-ALBUMINURIA WITHOUT TUBE CASTS.

Turning now to the question of the occurrence of albuminuria without renal casts, we find that the fact that more than one microscopic examination may sometimes be required, for if the urine is alkaline, or has stood for any length of time, casts originally present may have been decomposed, and the examination of the urine with definite nephritis, there may be very few casts at one time, may at another. This applies particularly to the very acute cases on the one hand and the very chronic on
the other. Assuming however, that no cast, or not more than a very occasional cast, is found, the chief conclusion that can generally be drawn is that the albuminuria is not necessarily related to other renal disease.

The cases may, then, be subdivided into: (1) Those in which the urine presents some other definite abnormality besides albuminuria, especially (a) pyuria, (b) haematuria, (c) leucorrhoea, or (d) given in which, were the albumen removed, the urine would be normal. 1. These cases need not be discussed further here; the differential diagnosis comes under the heading of pyuria, haematuria, leucorrhoea, and, the role of Microscropy.

2. These are clinically of importance in that, until the absence of casts has been determined, the absence of organic renal changes cannot be concluded. Even when casts have been found or albuminuria decreases, this may be the first evidence in elderly persons of enlargement of the prostate, chronic interstitial nephritis or arteriosclerosis, or in younger persons of chronic ascending nephritis, the result of such things as gonorrhoea, repeated pregnancies, uterine prolapse or other displacement, chronic vesical catarrh, or urethral stricture. The chronic effects on the kidneys of interference with the urinary stream are apt to be overlooked; if they are borne in mind they are generally easy of diagnosis.

The following are a number of other conditions which may cause slight degrees of albuminuria without tube casts, be it noted, some, or else diagnosed by other obvious symptoms or signs: Burns, scalds, chronic alcoholism, cirrhosis of the liver, diabetes mellitus, exophthalmic goitre, lead poisoning, mumps, secondary syphilis, malarial, or other fevers such as Raynaud's disease or anogenital neuritis, obstruction to the vena cava inferior by thrombosis or by external tumours, the pressure of considerable ascites, ovarian cysts or tumours, pregnancy, subphrenic abscess, or lymphadenoma, lymphosarcoma, lymphatic or splenic medullary leukaemia, splenic anaemia, phegmphysis, phosphorus poisoning, chronic arsenical poisoning, pregnancy, severe anaemia the result of syphilis, congenital, malarial, or tuberculous, or phthisical cachexia, ankylostomiasis, or infection with other parasites, such as Bothrocephalus latum, or Trichina spiralis.

There remain three other groups of conditions in which albuminuria and its differential diagnosis are often important, and these are: (1) Febrile conditions; (2) heart-failure conditions; and (3) so-called "physiological albuminuria of young males.

1. Febrile Conditions

In nearly every fever there is some cloudy swelling of the parenchyma of various visera, especially the kidneys; consequently most fevers may sometimes be associated with albuminuria, and, broadly speaking, the higher the pathogenic virulence of the disease the greater is the liability to albuminuria. The amount of albumen present is generally not great. We need not enumerate all the various fevers in this connection, nor discuss the causes of hyperpyrexia. Suffice it to say that albuminuria is relatively common in scarlatina, diphtheria, variola, erysipelas, pyrexial phthisis, cholera, dysentery, Weil's disease, severe malaria, and yellow fever; not so common in lobar pneumonia, broncho-pneumonia, typhoid fever, and erysipyis; and relatively uncommon in other febrile conditions, such as acute rheumatism, influenza, meningitis, measles, German measles, follicular tonsillitis, and so on. The albuminuria in these cases may be already present in a person who develops an intercurrent fever; the diagnosis then depends upon considerations mentioned above.

If, on the other hand, the albuminuria is known to have developed together with the febrile illness, it is the chief point to decide will be whether it indicates actual nephritis or not. Many consider there is an essential difference between "febrile albuminuria" and actual nephritis. This difference will not, however, be so easily difficult to be sure of the distinction clinically. It may be urged that—to take scarlet fever as an example—the albuminuria of the first few days is "febrile," whilst that of the latter part of the week is "nephritic.": In fact, in not a few cases in which death has occurred in the first week the "febrile" albuminuria has been associated with large motile acute nephritic kidneys, even when there was no oedema, no haematuria, and no very large numbers of renal tube casts. Probably there are all degrees of acute nephritis from very slight and transient to very severe and possibly fatal; and it is a mistake to decide, and make a distinction in the great majority of cases of albuminuria during fever recovery completely; some seem to recover, but come under observation years later with pale granular contracted kidneys; others die leaving the albuminuria or nephritis, and this distinction is not a direct measure of the renal changes unless the amount of albumen is large; a small amount of albumen does not necessarily indicate trivial nephritis. Absence of oedema and clinical examination of the cutaneous uriniferous deposit is essential: the more the renal epithelial cells, red corpuscles, lencocytes, and various renal tube casts, the more conclusively can some degree of actual or acute nephritis be decided.

When doubt lies between scarlatina and measles or German measles, or between diphtheria and other forms of sore throat, the existence of albuminuria sometimes assists in arriving at the diagnosis of scarlatina in the one case, or of diphtheria in the other.

In pneumonia, albuminuria has become much less frequent since blistering with antihistories has gone out of fashion in treating this disease.

2. Heart-failure Conditions.

The right side of the heart may fail owing to many different causes, the most common being those which may be arranged under the headings as follows: (a) Valvular disease; (b) obstructive lung affections; (c) myocardial affections; (d) granular kidneys and other high blood pressure conditions. Each of these may be associated with albuminuria to a marked degree, and not be repeated in detail. Any one of them may result in albuminuria, though the amount of the latter is extremely variable, some cases of severe heart failure exhibiting no albuminuria at all, others may have as much as 10 parts per 1,000 or more.

The first step in the differential diagnosis is to exclude primary renal conditions by negative microscopic examination of the urine, examination of the casts, examination of the retina, and exact determination of the blood pressure. Curiously, even with feeble, irregular pulses, such as are found in pitting cases of mitral stenosis, the blood pressure is considerably higher than normal, doublet owing to partial asphyxia; so that merely finding a systolic blood pressure of 150 or 160 mm. Hg is no proof of granular kidney or arteriosclerotic; sometimes, however, the reading is as high as 200, 250, 300, or even 350 mm. Hg, and then the diagnosis of one or other of the latter is almost certain.

The renal and arteriosclerotic conditions can be excluded, the diagnosis lies between the two main groups. The cardiac bruits, the history of growing pains, chorea, and acute rheumatism, the youth of the patient, the family history of heart disease, the history of rheumatic fever, the association of other rheumatic affections, such as rheumatic fever, subcutaneous nodules or erythema, will often serve to point to primary valvular disease and its nature; in older patients, especially in men between 40 and 50, there may be aortic disease and a history of syphilis, and not of acute rheumatism. In severe heart failure in children under puberty the result of mechanical difficulty with the circulation, an adherent pericardium is generally found, and clinically the heart is large out of proportion to the general physical signs.

When there is a definite history of recurrent winter cough in an elderly person with a prominent and overexpanded chest, the likelihood of emphysma and bronchiectis will at once suggest itself. Similarly fibroid lung, or fibroid lung and bronchiectasis, as a cause of heart failure and rapid pulse, is excluded. At a mention of the diagnosis generally being obvious from the physical signs, the clubbed fingers, and, in the bronchiectatic cases, the abundant, intermitent, and frequently foul, expectoration. Myocardial affections, such as fibroid, fatty, or primary alcoholic heart, are generally diagnosed by guessing at these when other causes of heart failure can be excluded. The patients are generally middle aged, with precordial failure and oedema, and quite a frequent mention among their cardiac symptoms; there may or may not be a high blood pressure, the albuminuria is not associated with renal tube casts, there is often no cardiac bruit, or at most a more or less localized blowing systolic...
Clinical Observations

On the Use of Digitalis in Heart Disease and Dropsy with Fibrillation of the Auricles (Nodal Rhythm).

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In the present paper I propose to illustrate the use of digitalis in cases of heart disease with dropping, in which the auricles are in a state of "fibrillation" and functionally inactively—a condition present in a large proportion of cases of severe heart failure, whatever the nature of the underlying lesion may be. Cases of this kind constitute a definite group, and their diagnosis is of great clinical importance both for treatment and prognosis.

It has always been recognized that benefits from digitalis in cases of heart disease is variable, even when classical indications for its use are present. In some patients, improvement is rapid and maintained; the heart decreases in size, and dropsy quickly disappears; in others, it shows a steady improvement up to a certain extent, and comes to a standstill; in others again, particularly cases of acquired stenosis with regular pulse, and those resulting from arterial disease, the result is often disappointing and may be even harmful—the heart continues to dilate, and dropsy increases under its use.

An example of such a case is the following:

Case I

A girl, aged 13, under my observation for some time with a compensated double mitral lesion of rheumatic origin. In August, 1909, severe dyspnoea with marked cyanosis came on after exertion, and a severe attack of dropsy. A prompt recovery followed, and the patient was quite recovered from, but later compensation gradually failed, and at the end of October the severe dropsy reappeared. The pulse was quick but regular; heart enlarged to right and left; mitral presystolic, systolic, and diastolic murmurs were present. Although digitalis was well tolerated and given for over a month in full doses, with occasional remissions of a day or two, it had very little influence on the rate of pulse (Fig. 1). For a time there was some improvement in the general condition; but subsequently the heart further enlarged, dropsy manifestly increased, the amount of urine diminished, and eventually the lungs became oedematous, death, which occurred two months after the onset of dropsy.

The fact that digitalis often fails to do good in the later stages of heart failure, when the pulse is rapid and regular, was known in the early days of its use. It was recognized that the drug slowed the pulse in some cases more than others, and that to a great extent improvement was proportionate to the degree of slowing which ensued; and, further, that the most marked slowing and rapid response to treatment usually occurred when the pulse was irregular, but it was also recognized that these results were not constant in all cases with irregular pulse.

There was no explanation of this discrepancy forthcoming until MacKenzie differentiated the various forms and causes of irregularity of the heart by means of the venous pulse. He established the fact that in cases which...