A Clinical Lecture ON GRANULAR KIDNEY AND ITS SURPRISES.

BEING AN ADDRESS DELIVERED BEFORE THE EAST SUSSEX
MEDICO-CHIRURGICAL SOCIETY.

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THE signs of granular kidney are usually obvious enough, yet there is no disease that is more often overlooked, even at the present time. The diagnosis is missed chiefly because the condition is not thought of. For this there are two special reasons:

1. That granular kidney is for a long time compatible with apparent health—that is, is associated with no striking loss of energy or strength.

2. That the symptoms when present may be most misleading, and point almost anywhere else rather than to the kidney.

Yet the pulse usually gives the indication if properly examined—not the pulse beats, for they may be unaltered; nor the pulse wave, for it may not be characteristic; nor the arterial tension, for this is not at all times high—but the artery itself, which is almost always markedly thickened.

Arterial thickening in early middle life is almost always due to granular kidney, and in the elderly to atheroma or to both conditions combined.

There is still another form of arterial thickening met with in young athletes. This is a physiological hypertrophy accompanying the hypertrophy which takes place in the heart, but, with this exception, arterial thickening in persons below 50 should always raise the suspicion of granular kidney, and the suspicion once raised is confirmed on further examination by the discovery of the characteristic changes in the urine, in the heart, and it may be in the eye.

If granular kidney, then, be so often overlooked, the diagnosis of it frequently comes as a shock and surprise to patient and doctor alike.

There are enormous reserves in the kidney as in every other important organ in the body. It has been shown that as much as two-thirds of each kidney may be removed in animals before life becomes impossible. So in granular kidney the wasting may go on to a very considerable degree before grave symptoms arise, but all this time, as the wasting of the kidney progresses, its reserves become less and less, until at last on some very slight extra demand, or even without any apparent cause at all, the limit may be reached, and the symptoms of renal inadequacy manifest themselves in more or less serious form. So it happens that no suspicion whatever may have been aroused until some grave condition arises which makes the diagnosis only too obvious.

It is with these surprises or unexpected first symptoms that I purpose to deal in this paper.

The morbid lesions of granular kidney are found in the kidney, blood vessels, heart and eye, and it is in connexion with these organs that the first group of surprises come.

The second group is probably toxic, and is composed of conditions which are often described under the heading of acute or chronic uraemia, or, as it would be better styled, acute or chronic renal toxæmia—for example, general cachexia, skin eruptions, violent vomiting or diarrhoea, cramp, gout, headache, epilepsy, and uraemia. This is a long list, but there is something of interest as well as of importance to be said about each item of it.

1. *Acute nephritis* may be the first serious condition to arise in what has obviously been granular kidney of long standing, for accompanying the ordinary signs of acute nephritis there may be found present arterial thickening, hypertrophy of the heart, and even eye changes of a degree or kind impossible in acute nephritis of short duration.

Just as in a child acute nephritis would suggest some recent specific disease like scarlet fever or diphtheria, so in the adult it should suggest antecedent chronic kidney

mischiefs, in all probability granular kidney, the evidence of which is obvious when looked for.

This relation of acute nephritis to granular kidney is both of theoretical and practical importance.

Acute parenchymatous nephritis, if it become chronic, may, of course, lead to interstitial changes, but even then not necessarily to granular kidney.

It is the common teaching of the day that granular kidneys are of two kinds—the white contracted kidney and the red; that the white is the end stage of chronic parenchymatous nephritis—that is, of the large white—but that the red is due to other causes. The two forms of contracted kidney exist, it is true—namely, the small white and the small red—but the difference is simply one of colour.

Anyway, the theory that the contracted or small white kidney is the terminal stage of the large white is a mere assertion, and is not supported by clinical evidence.

With two such common diseases, if acute nephritis often ended in granular kidney there ought to be abundance of clinical proof of it; but this is not so. *Per contra*, it is well known that cases of granular kidney rarely give any definite history of antecedent acute nephritis. Lastly, acute nephritis is, as I have stated, often found associated with the lesions of antecedent granular kidney. It follows, therefore, that the true reaction between acute nephritis and granular kidney is the exact opposite of what is commonly stated, and that granular kidney is far more often the cause of acute nephritis than the result of it.

This relation is also of practical importance, for in such cases of association of the two conditions there can be no question of the acute nephritis recovering to such an extent that the albuminuria will completely disappear. At the best the patient can only be restored to the condition he was in before the acute nephritis developed. In this way the persistence of albuminuria and the recurrence of hæmaturia must be referred, not to incomplete recovery from the acute attack, but to the antecedent granular kidney. It follows, therefore, that long-continued treatment of these symptoms by rest in bed, rigid dieting, and drugs is as unnecessary as it often is injurious.

The relation between acute nephritis and granular kidney is best set out in the accompanying diagram, the dotted line showing the weak link in the chain of evidence.

A.N, Acute nephritis; LWK, large white kidney; G.K, granular kidney; C.W, contracting white; W, white; R, red; C, cure; +, death; C₂W, contracted white.

2. *Hæmaturia*.—A patient may be seized with an attack of hæmaturia for which no explanation seems forthcoming, and this may prove to be associated with nothing but granular kidney. The amount of blood may vary from a very little, just enough to suggest its presence to the eye, up to what is sufficient to give the urine a very bright red colour, almost as bright as arterial blood, and these attacks may be frequently repeated. In these cases a growth in the bladder or a calculus in the bladder or pelvis of the kidney may be suspected and even operations performed. If clots in the urine occur, the case cannot, I believe, be one of granular kidney only, for, however considerable the bleeding may be, the blood in the urine in granular kidney never seems to clot.

I used to hold that the blood in these cases came from the bladder, and I still think this is so usually, but with the cystoscope the blood has been seen passing from one

ureter, so that it may sometimes come from some source higher up.

Recurrent haematuria in small amounts of indefinite cause is in itself very suggestive of granular kidney.

3. *Epistaxis* in young people is common enough, and has little or no significance, but in middle life copious epistaxis is suggestive of serious disease, for example, aortic disease and degenerate arteries, cirrhosis of the liver, and very frequently of granular kidney.

Profuse epistaxis, requiring plugging of the nares, may be the first serious sign of granular kidney. The anaemia following is often extreme, and from it dates the rapid deterioration of health which may put an end to life from asthenia within, it may be, a few weeks of the initial epistaxis.

4. *Cerebral haemorrhage* is one of the great surprises which granular kidney provides, for it may occur without any warning in the midst of apparent health.

Granular kidney is the commonest cause of apoplexy in early adult life, and even up to the age of 60 divides the honours pretty equally with atheroma.

The diagnosis between apoplexy and some forms of uraemia is notoriously difficult, and this receives some explanation in the fact that though there may be no large haemorrhage ploughing up the brain, numerous small discrete haemorrhages are found scattered widely through the centrum ovale.

These little haemorrhages are of that peculiar kind to which the name of miliary aneurysms has been given, that is, small haemorrhages the size of a barley corn or less, not free, but situated in the sheath of the vessels. They are sometimes so numerous that if the brain substance be washed away by a forcible stream of water, the vessel may look like a string of small currants. The fact that they are so numerous makes it unlikely that they are spontaneous, for vessels rarely burst spontaneously in more than one place at a time. Still less are many different vessels likely to give way at the same time and to the same extent. It is therefore probable that these multiple ruptures are the result of the uraemic fits rather than the cause of them, though they may in part explain the coma by the increased intracranial pressure they would produce.

5. *Thoracic aneurysm* is not usually connected with granular kidney, yet the association is common enough to suggest a relation between them. Granular kidney, it is true, affects primarily the muscular or middle coat of the arteries, but the intima is ultimately involved too. In this stage the aorta is very likely to be affected and to give way, just as it does with atheroma or syphilis.

6. *Cardiac failure* is one of the commonest guises under which granular kidney presents itself. Cardiac symptoms develop without valvular disease; the arteries are found thickened and degenerate, and the cause is traced to the kidneys.

The arterial degeneration has caused cardiac hypertrophy; the hypertrophy has taken place at the expense of the cardiac reserves, and slight extra strain causes failure. This failure may be more or less gradual with the usual signs, or it may be sudden, sometimes with fatal cardiac collapse, but more commonly with attacks of more or less severe cardiac pain, which may culminate in angina.

7. *Pericarditis* may develop, but usually only in the course of manifest granular kidney and in its latest stages. It may in any case be latent or insidious and be detected only on physical examination, and come then as a complete surprise. It is always a very grave complication and may, by leading to rapid cardiac failure, be the cause of death.

8. *The Eye*.—It is in connexion with the eye that some of the most startling surprises come.

Some years ago I was called to see a gentleman who had been out hunting three weeks previously, and was then, as he thought, in vigorous health. The first thing he noticed was that he could not see the wire fencing, and in consequence had a fall, though he did not injure himself. From this time his eyesight failed rapidly, and he became very ill in himself. When I saw him he was in bed, with a very uraemic aspect, foul breath, and a coated tongue. He was almost blind, though he could still see a strong light. The most extreme double optic neuritis was found of the typical albuminuric type, with considerable exudation, numerous haemorrhages, and many white patches. He had also developed acute pericarditis a

few days before I saw him. He died uraemic about a week later, and within about a month of the day when he was out hunting.

I saw another very similar case to this a year or so ago. A gentleman was driving his motor from his house in Sussex to Oxford. As he came near London he found his sight becoming suddenly defective, so that he could not trust himself to steer through the traffic, and did not proceed beyond London. I saw him a day or two later. It was a typical case of granular kidney, with extreme and characteristic albuminuric retinitis. His sight failed very rapidly until, in a few days, he was quite unable to read. He returned home and died uraemic about a month or six weeks later.

Both of these cases were remarkable because until the sight failed both patients regarded themselves as in perfect health. Neither patients nor friends could understand or believed the grave prognosis which was given, and which the rapid ending justified.

The arterial changes in the eye are often very obvious in quite an early stage of granular kidney. The *silver wire* arteries, first described by Marcus Gunn, are quite characteristic, and occur in no other form of disease, for even the thickening of atheromatous vessels does not give it. They are a purely ophthalmoscopic sign, and associated with no eye symptoms.

The *bright glistening* white patches of degeneration too are pathognomonic, and therefore of the greatest diagnostic value.

The *exudative form of albuminuric retinitis* has little to distinguish it in itself from other forms of acute optic neuritis. In all cases alike the most extreme changes may be compatible with perfect vision for some time, but when once sight begins to fail it is rapidly lost, as in the two cases referred to above.

Haemorrhages, too, whether flame-shaped or irregular, may be numerous, and yet sight be little if at all impaired, unless they be of large size or in special parts of the retina, as in the yellow spot.

In all these cases alike, whether there be white patches, patches of exudation or haemorrhages, patchy defects in the field of vision may be complained of, as might be anticipated. In some cases coloured vision may be present—that is, a patient may in certain parts of the field or in certain portions of the eye see things green. This is, as it happens, the only colour I have myself known patients to mention. It is natural to suggest that this is due to the light passing through a haemorrhage, but this, simple as it seems, is in my experience not a sufficient or correct explanation. Large haemorrhages would of course make the patient blind in the affected eye. I have once seen the vitreous almost filled with blood, so that the haemorrhage was visible to the unassisted eye through the pupil. Such large haemorrhages are rare, but they would of course be accompanied with very sudden symptoms, pain, and loss of sight. Uraemic amblyopia or transient loss of sight without obvious cause in the retina is probably toxic in origin. It is similar in character to that which occurs with an attack of migraine.

Most of the remaining conditions to which I shall refer are of toxic origin.

9. *Cachexia and Asthenia*.—Many cases of granular kidney become so cachectic and asthenic as to suggest, if granular kidney has not been recognized, the diagnosis of malignant disease, as a rule, the anaemia is not so profound. The complexion is muddy or earthy rather than pale and white, and, though the asthenia may be extreme, there is usually not the expected degree of emaciation.

10. *Gastro-intestinal symptoms* are of common occurrence in any form of nephritis, and in granular kidney may be very intractable.

A young man, about 30 years of age, had been under treatment for some time with recurrent attacks of severe vomiting. He was thought to have gastric or duodenal ulceration, and an operation was suggested. The surgeon, however, was doubtful of the diagnosis, and asked my opinion. There were no signs of locomotor ataxy, so that the gastric crises of that disease could be excluded, and the signs of granular kidney were obvious. I advised against operation, suggesting that the attacks were connected with his kidney affection. This view was confirmed subsequently by the course of the case.

These attacks may be intermittent or recurrent; may last several days each time, and are obviously not of a simple gastric origin.

When vomiting is associated with optic neuritis, it may easily suggest a cerebral tumour, or, if it be morning vomiting, it may, in women of child-bearing age, suggest pregnancy. Instances of both these difficulties in diagnosis have come under my personal observation.

Diarrhoea may in the same way be paroxysmal and recurrent, and equally difficult to treat.

I saw some years ago what I now believe to have been a case of this kind, though I did not at first think so. The patient suffered with diarrhoea of a very obstinate kind, which was, for want of a better diagnosis, referred to colitis. The arterial thickening and the presence of albuminuria suggested the existence of granular kidney, but hardly, I thought, in sufficient degree to explain completely the intractable diarrhoea. In time the diarrhoea ceased, but the patient never recovered his health. About two or three years later I saw him again, when he presented all the signs of granular kidney in the advanced stage. The urine contained albumen in unusually large amount—sometimes more than one half. The heart was weak, and there was well-marked albuminuric retinitis of the mixed degenerate or exudative form. Extreme asthenia was the characteristic feature of the case, and of this he ultimately died, without any other definite symptoms. He had no diarrhoea after the first attack, but, on looking back, I think this was but the first of the long chain of granular kidney symptoms which followed.

With these gastro-intestinal attacks may be connected attacks of *cramp*, in the legs especially, often, it is true, associated with dyspepsia, but both alike the result of granular kidney. These are often diagnosed as *gouty*.

11. *Gout* is often stated to lead to granular kidney. Acute gout may be associated with very copious transient albuminuria, and gout when frequently repeated, or chronic as it is styled, may lead to renal degeneration and interstitial change. But the *gouty* kidney so called, and figuring as such in museums, is often not granular. The association of gout, and, it may be added, of chronic lead poisoning, with granular kidney is well established; but it does not follow that either gout or lead has necessarily produced the granular kidney, as is often assumed. It is at least quite as likely, and there is much clinical evidence to support this view, that the patients are so susceptible to gout, as they are to lead poisoning if exposed to it, because their kidneys are already granular, and therefore unable to eliminate as they ought.

12. *Skin Eruptions*.—Rashes form a very important group. I do not refer to small patches, for they are of little significance, but to generalized eruptions. They may be of various forms—eczematous, urticarial, erythematous, or polymorphic. The association of any of these general eruptions with albuminuria is important, but if the albuminuria be due to granular kidney the prognosis is very grave, for most of the cases are ere long fatal. The rashes are terminal eruptions, but may occur in cases which have not been previously recognized as granular kidney. One point deserves notice, namely, that in spite of the general tendency to haemorrhage in granular kidney, these rashes are rarely haemorrhagic.

13. *Headache* is perhaps the commonest complaint which brings the patient under observation; sometimes frontal, more often vertical, occasionally, but rarely, unilateral. The attacks occurring in violent paroxysms are often diagnosed as migraine, which they may closely resemble in many points, except that they are not as a rule hemispherical. When associated with vomiting and optic neuritis, the diagnosis of cerebral tumour naturally arises. I can recall so many cases of granular kidney in which the first and for a long time the only symptom was paroxysmal headache, that I now in such cases almost unconsciously look for signs of granular kidney, and very frequently find them.

14. *Fits*.—It is not generally known that epilepsy may be the first symptom in granular kidney, but it is so. By fits I do not mean uraemic fits, but ordinary epileptic attacks. Epilepsy commencing in adult life suggests a local lesion, or degenerative change in the brain, or some general disease, of which granular kidney is the most likely. In this relation the frequency with which granular kidney is found among the patients in asylums is important.

I suppose in many cases the fits are of toxic origin, but the transient attacks of paralysis or aphasia that are sometimes associated with them suggest a vascular cause.

15. *Uraemia*.—I have reserved to the last what I might have been expected to take first. By *uraemia* I mean acute uraemia, acute renal toxæmia—that is, uraemic coma and fits. Many of the other conditions already discussed are due to chronic renal toxæmia or chronic uraemia—such as the cachæxia, vomiting, and rashes. Acute uraemia is, like apoplexy, one of the most startling surprises, and often occurs quite unexpectedly in the midst of apparent health. A surveyor about 50 years of age walked to his office one morning and opened his letters. Then suddenly, without any apparent reason, he fell down upon the floor unconscious. The doctor was summoned, who bled him to 15 oz. or more at once, and sent him on to St. Bartholomew's Hospital. On his arrival he was semi-conscious, and had a little twitching of the limbs and face. Gradually he rallied, recovered consciousness, and was able to leave the hospital a few days later, feeling feeble but otherwise well; the signs of granular kidney were obvious. I have little doubt the free immediate venesection was largely instrumental in his recovery. A similar case occurred in a gentleman after attending an exciting political meeting. The diagnosis of granular kidney was obvious, but the uraemic attack was the first indication of illness. He, too, recovered quickly from the attack. In another case a gentleman was out shooting in apparently perfect health. He was shot in the eye. He suffered much from shock, and a day or so later developed uraemic fits, in which he very nearly died. The signs of granular kidney were definite, and to make the diagnosis certain the most marked condition of albuminuric retinitis was present. He slowly rallied, and after the removal of the eye became as well as he was before the accident. It is often stated, and quite truly, that acute uraemia may be recovered from in acute nephritis but not in granular kidney. These cases are interesting as rare exceptions to what is certainly true as a general rule.

Granular kidney is one of the most interesting of all the chronic degenerative diseases, not only because we have so much still to learn of its causes and real nature, but because, as I have endeavoured to show, of the many surprises it has in store. These surprises come for the most part in the late stages of the disease, when treatment can be little more than symptomatic. If anything is to be done to check or modify the course of the disease, the diagnosis must be made early, and it certainly could be made much earlier than it often is if it were carefully looked for. Many of the symptoms suggest from analogy defective internal secretion, and it seems fair to infer such a function in the kidney, though, so far, physiological proof is wanting. My own experience of the administration of renal extracts, I must say, has been distinctly encouraging, but the difficulty lies in the fact that the extracts must be made fresh as they are wanted. They will not keep, and no stable and effective extract has yet been prepared.

ON Wednesday, April 26th, the Senate of New York State refused to pass the Bayne Bill to investigate vivisection methods by 34 votes to 11.

THE Clapham Maternity Hospital's Dispensary for General Diseases has added to its work at its Battersea centre a branch for carrying out the tuberculin treatment of phthisis on Dr. Camac Wilkinson's method.

BURY Infirmary receives under the will of the late Mr. James Edward Renshaw of Poulton-le-Fylde a bequest of £1,000. The same will also set aside a sum of £500 towards the provision and maintenance of a seaside convalescent home for the use of Bury children.

THE report for 1910 of the Blencathra Sanatorium under the auspices of the Cumberland Branch of the National Association for the Prevention of Consumption states that at the commencement of 1910, 20 patients were under treatment, while during the year 91 were admitted; of these, 84 were discharged, leaving 27 patients under treatment at the end of the year. We can find no mention in the Medical Superintendent's report as to the mortality-rate of those admitted; this may be accounted for by the fact that only incipient cases are dealt with. He has been able to trace as alive at the end of the fifth year 193 out of 394 patients discharged, and of the 67 entered as not traced, several were found after the figures were compiled to be alive and able to work.