THE LETTSOMIAN LECTURES ON SOME CLINICAL ASPECTS OF GRANULAR KIDNEY.

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LECTURE III. SYMPTOMS.

GRANULAR kidney may exist for a long time without appearing to affect the health or producing symptoms. When symptoms appear, no matter what their nature, the disease is far advanced and in its later stages. The symptoms are multifarious, and, unless there be intercurrent nephritis, in no way of themselves suggest renal disease. They fall into two groups—the cardio-vascular and toxæmic. Speaking generally, the cardio-vascular symptoms occur first, and the toxæmic subsequently, though both may be present together.

The cardio-vascular are important, because they often cause death earlier than might otherwise occur. The toxæmic always develop if the patient live long enough. They depend upon the wasting of the kidney, become manifest when it has reached a certain degree, and progress *pari passu* with it.

The cardio-vascular symptoms are more or less mechanical or accidental. The cardiac are summed up in heart failure. The vascular fall into two groups: the first is formed by hæmorrhage and its results; the second by chronic degenerative affections, especially in the nervous system, the result of imperfect nutrition through the diseased vessel.

A.—CARDIO-VASCULAR.

1. *Cardiac*.—Heart failure is often the first symptom to cause anxiety. Thus a little shortness of breath and palpitation on exertion, with, it may be, slight cardiac pain or some swelling of the feet, may direct attention to the heart, which is found hypertrophied or dilated, and that without obvious cause in the heart itself. The symptoms are usually gradual in onset, but may come on suddenly. The pain, though usually slight, may be severe enough to be called angina. In elderly persons these symptoms might be the result of atheroma, but in middle life and in the young granular kidney is the most likely cause. Cardiac symptoms are, however, not constant, even where the heart is greatly hypertrophied or the valves diseased.

I had a young man under my observation for some years with aortic regurgitation, who developed granular kidney, and subsequently died of uræmia, yet his heart gave him no trouble throughout.

Acute pericarditis belongs rather to the toxæmic group, but this is perhaps the most convenient place to refer to it. It is always a very serious complication, and even where it does not of itself cause death it is a warning that the end is near. It may produce few symptoms, and be detected only by physical signs, but the evidence of granular kidney is usually obvious enough. It may be the first sign of ill-health, as in a case I have recorded elsewhere.

2. *Vascular*.—The vascular lesions produce three sets of symptoms.

1. Those due to rupture and consequent hæmorrhage.
2. Those which result from nutritive disturbances in the parts supplied by the diseased vessels. This is especially met with in the central nervous system and in the eye.
3. Besides these, it is necessary to refer to aneurysm, and that not only of the small vessels, but of the main trunks.

I believe the connection of granular kidney with aneurysm of large vessels is a new point, but it is clearly shown in the *post-mortem* statistics from St. Bartholomew's Hospital (Woodbridge), for out of 219 cases of granular kidney the rupture of a thoracic aneurysm was the cause of death in 33, that is, in 6 per cent. There were, besides these, two cases of death from the rupture of small aneurysms at the base of the brain. To the possible causes of aneurysm, namely, laborious work, drink, and syphilis, must now be added granular kidney.

HÆMORRHAGE.

Hæmorrhage may take place in almost any part of the body, but it is in the brain that its most serious effects are

produced, and *post-mortem* statistics prove the remarkable frequency with which granular kidney is found associated with cerebral hæmorrhage.

Dickinson states that 41 per cent. of all cases of cerebral hæmorrhage were due to granular kidney, and Pye-Smith states that in 75 per cent. of the cases of granular kidney death is brought about by cerebral hæmorrhage. The St. Bartholomew's Hospital statistics only show about 15 per cent.

In elderly persons, of course, due allowance must be made for atheroma, but even elderly persons may have granular kidney and a little atheroma, while in middle life granular kidney is the usual cause, and in the young may explain cases of cerebral hæmorrhage which would otherwise present great difficulty.

Thus in Woodbridge's cases there was 1 at 19, 1 at 27, and 1 at 30, and 2 at 37.

Of course, many patients with cerebral hæmorrhage do not die of it, but are left with paralysis, of which the following is an instance.

A young man, aged 21, recently presented himself with left hemiplegia. The attack had come on suddenly in the midst of apparent health, and was evidently due to hæmorrhage. No cause was apparent until the thickened radial and high arterial tension suggested granular kidney, and albumen was found in the urine.

Where the patient dies of apoplexy *post-mortem* examination may show the centre of the brain ploughed up by a large hæmorrhage of the common kind; but sometimes, without any extensive laceration of the brain, a large number of minute hæmorrhages are found of that peculiar kind known as milary aneurysms.

Where the small hæmorrhages are not numerous they may produce no pressure signs, but only localised symptoms of varying character according to their position. They probably explain the unilateral fits occasionally observed in uræmia. Even when death follows general uræmic fits of the ordinary kind multiple minute hæmorrhages are not infrequently found, so that the distinction between the hæmorrhagic and the toxic form of uræmia is not always possible. In the medulla a very small hæmorrhage of this kind may lead to death or to localised nuclear paralysees of special nerves. Pontine hæmorrhage is, of course, rare, but in many instances granular kidney is the cause of it.

Of hæmorrhage into the spinal cord below the medulla I have met with no example myself, and I do not know any recorded.

Epistaxis is common, and may be the first symptom of disease, and its importance be missed. Even in the young granular kidney must not be disregarded as a cause of repeated epistaxis.

Hæmaturia.—The next most important group of cases is that in which blood is found in the urine. Attention had not been drawn, so far as I know, to granular kidney as a cause of hæmaturia until I published some cases a few years ago, but the fact is now generally recognised. The blood is intimately mixed with the urine and is bright in colour, and for this reason I am inclined to believe that it usually has its origin in the bladder; at any rate, except when granular kidney is associated with intercurrent acute nephritis, and but rarely then, is the urine smoky or dark in colour. In a case recently reported to me the cystoscope showed blood passing by the ureters. It may be so red and bright as to look almost like pure blood, but even then there are hardly ever any clots. This form of hæmaturia has led to frequent mistakes, as, for example, to the diagnosis of calculus in the bladder, for which operation has been suggested and performed. The hæmorrhage is not often copious, but in slight amount it is common and recurrent. To this recurrent hæmaturia experience leads me to attach considerable diagnostic value.

Of hæmorrhage from other parts in connection with granular kidney I have myself recorded one case of hæmatemesis. I know of one of hæmorrhage from the bowels. Hæmoptysis is described, but I have never myself actually met with it; and similar hæmorrhage, though not in large amount, is described from the pharynx.

I have recently had to deal with a case in which very troublesome and persistent hæmorrhage occurred from the uterus. It was ultimately checked by full doses of ergot.

In the last stages of granular kidney the patient may pass into an almost hæmophilic condition, in which slight though continuous and almost uncontrollable oozing takes place from various parts of the body—from the gums, nose, tongue, lips,

vagina, or from any wound or scratch in the skin. A considerable amount of blood may be thus lost, and the anæmia from which the patient is already suffering be very greatly aggravated.

DEGENERATIONS.

The next group of cases to which I wish to refer is that in which, as a consequence of arterial disease, degenerative changes result in various tissues. The most delicate of these is the nervous system; to this Gull and Sutton long ago drew attention. The subject has not since they wrote received the attention it deserves. Bond has drawn attention to the remarkable frequency of granular kidney in *post-mortem* examinations of the insane in an asylum, and has shown that it is nearly double that in a general hospital like St. Bartholomew's; and he rightly concludes that there must be a close relation between the two diseases. Although some of the diseases of the nervous system associated with granular kidney may rightly be attributed to defective nutrition in consequence of the disease of the vessels, it must not be forgotten that they may also be toxic in origin.

B.—TOXÆMIC.

The toxæmic symptoms fall into two groups; in the one they are of acute onset and great severity, and usually lead rapidly to death; in the other they are of more gradual onset and of longer duration and of less apparent severity, and of a very indefinite character. They are respectively called acute and chronic uræmia, but as the groups stand in strong contrast with one another, it would be well if different terms were employed to denote them. For the acute cases uræmia in its ordinary acceptation might be retained. For the chronic group, on account of its varied and indefinite symptoms, chronic renal toxæmia would be the better term.

There are three main theories of uræmia, which may be termed the "retention" theory, the "perverted metabolism" theory, and the defective "internal secretion" theory.

The general cachexia which develops in some forms of granular kidney bears a striking and suggestive resemblance to the condition which is met with in Addison's disease or even in myxœdema, but there is no other proof so far of an internal secretion in the kidney.

The retention theory, which implies that the symptoms are produced by the retention of some of the ordinary constituents of the urine in the body, such as urea, creatin, creatinin, etc., is now discredited; so that the third theory only remains—namely, that which refers the symptoms only to perverted metabolism. According to this theory, the products of metabolism—that is, extractives, as they are usually called—are either produced in abnormal amount, or not properly elaborated, so as to be eliminated in the normal way. In either case they would be increased in the tissues, and this increase can be demonstrated. The symptoms of uræmia might thus be referred to "extractive" poisoning, or as it is sometimes called auto-intoxication.

There are many different extractives, and they have different physiological action, and thus the symptoms produced might vary according as one or other of this extractive predominated.

Clinically we know that the symptoms of uræmia are closely simulated by many conditions which at first sight appear to have nothing to do with one another; thus, the typhoid state which develops in many fevers is like some forms of uræmia, and Murchison did not hesitate to call it uræmic. Again, when the tissues are rapidly wasting—as in malignant disease—symptoms arise towards the end which, if they happened in a case of renal disease, would be called uræmic. So, again, in the later stages of cirrhosis hepatis, diabetes mellitus, the last stage of Addison's disease or myxœdema, and, indeed, in almost all slowly-dying persons. We might thus place them all under the one heading of toxæmia, and it is for this reason that I prefer to call uræmia "acute and chronic renal toxæmia," so as to bring it into its proper relation with other allied clinical conditions.

In the case of uræmia there are two ways in which the toxæmia may arise: either the metabolism may be normal and elimination defective or the metabolism may be increased or perverted, while the elimination is not deficient but may be much increased. In uræmia the tissues are enormously rich in extractives, even when elimination by the kidney is

active, and when elimination by the kidney is impaired they are still further increased.

If, then, we are thus led to associate the symptoms of chronic uræmia with chronic extractive poisoning—that is, with the presence of abnormal amounts of extractives in the tissues and the blood—we are tempted to refer the acute symptoms, which often develop with so little warning, to defective elimination by the kidney, and we might thus associate acute uræmia with the condition of the cells in the kidney, in granular kidney, just as we do in acute nephritis. It is to the chronic toxæmic group that most of the symptoms belong which bring the patient under medical observation.

The gastro-intestinal symptoms are often pronounced, and may be very misleading. Obstinate dyspepsia, especially if associated with pain, might suggest ulcer of the stomach, and this might be attributed, if there were much cachexia, to malignant disease, a suspicion which would be strengthened if hæmatemesis also occurred. As a matter of fact, hæmatemesis is rare, for the hæmorrhage is not likely to be profuse, and, unless it were profuse, the blood would not be vomited. Vomiting is often a source of difficulty, for it is very obstinate, and does not stand in relation to the taking of food.

In a man, aged 32, the diagnosis of pyloric stricture had been made and operation was proposed; the case proved to be one of granular kidney. In another instance, that of a man, aged 63, malignant disease had been suggested, but the diagnosis of granular kidney was confirmed by necropsy.

When to the vomiting retinitis is added, confusion with cerebral tumour is only to be expected. Morning vomiting, which is not rare, might suggest pregnancy, and I have seen cases confused with both these conditions. The symptoms in connection with the bowels are not, as a rule, so puzzling. Diarrhœa is common with any form of kidney disease, but there are cases in which diarrhœa is 'practically the only symptom, extremely obstinate, and almost uncontrollable. The dyspeptic symptoms are often associated with cramps. I have seen several cases in which cramps were the chief complaint.

Cramp leads naturally to the consideration of gout. The occurrence of chronic kidney mischief as the result of long-standing gout is well recognised, but it is quite possible that the opposite relation exists in many cases—that is, the patients are gouty because they have granular kidney.

The close association of chronic lead poisoning and granular kidney is interesting as supporting the view that granular kidney is the result of the circulation of some toxic substance in the blood, which like lead excites cirrhosis in the kidney with all its results, just as alcohol produces cirrhosis in the liver. On the other hand, it is also possible, considering that all persons who work with lead do not develop granular kidney, that the opposite relation may exist—namely, that they suffer so much from lead symptoms, just as others do from gout, because their kidneys are granular already.

Cachexia.—Patients with granular kidney may for a long time preserve their normal appearance of health, and that even when the signs of granular kidney are well marked; but, as a rule, as the kidney disease advances the nutrition suffers greatly. Failure of health and strength in persons of middle life, without any evidence of malignant disease, should always excite the suspicion of granular kidney. The cachexia stands in direct relation to the kidney wasting, and when it is extreme is an indication that the destruction of the kidney substance has approached dangerously near to the limits compatible with life. The cachexia of granular kidney is characterised by anæmia and asthenia, and to some extent by loss of flesh, but emaciation is rarely carried to that degree which is met with in advanced malignant disease. It is often out of all proportions to the other symptoms, or may even exist alone. In some cases the anæmia predominates, and in others the asthenia. I do not know that the blood has been systematically examined in these cases, but in the few which I have examined the changes have been those of simple though extreme anæmia. The asthenia is often extreme, so that the patient can hardly stand or walk without assistance. Of this extreme asthenia I have seen two striking instances recently. One of these was under treatment for a skin affection, and will be referred to in another place. In this case, with rest and feeding the asthenia greatly improved. In the other case the asthenia was extreme and fatal. This case is so remarkable as to deserve record.

The patient, a woman aged 41, came under observation twelve months previously for general pityriasis. She had some albumen in the urine, and was so extremely feeble that I did not expect her to live. However, after a few days' stay in the hospital she insisted on going home, as I thought, to die. However, she lived on, and in the course of time lost the skin eruption. About ten months later she appeared again, more anæmic and ill than before. She was again admitted into the hospital, where she died two or three days later. I never saw a patient so feeble and cachectic with so little to show for it; she was like a patient dying in the last stage of malignant disease or of Addison's disease. I examined her with the greatest possible care to discover any other cause than granular kidney, but failed to find one. Even the diagnosis of granular kidney at that stage was difficult, for the tension was extremely low, and the artery but slightly thickened. There was a small amount of albumen in the urine, but not more than might have been due to her feeble condition, and the eyes showed nothing. When the *post-mortem* examination was made all the organs were carefully examined, and absolutely nothing found except granular kidney. The kidneys weighed only 4 ozs. together. The only history I could obtain was that the patient had been ailing in an indefinite way for about six years, but had been in fair health until the skin eruption appeared, three weeks before she was first seen. From the time when the skin eruption disappeared there had been no other symptoms except those of extreme anæmia and asthenia. The cachexia was so extreme that many thought that granular kidney was hardly sufficient to explain it, and that there must be some malignant disease which had escaped detection.

NERVOUS SYMPTOMS.

It is in connection with the nervous system that some of the most interesting conditions arise.

Headache which is so common a symptom, often occurs in such severe paroxysm as to closely resemble migraine. It is usually vertical, but may be frontal or occipital. When unilateral or localised as it may be, it is often diagnosed as neuralgia or tic douloureux. The vomiting is no doubt often central or nervous, for it stands in no relation with food, and is frequently periodical.

Renal Asthma.—The dyspnoea, which may be paroxysmal, is very often cardiac, and usually due to bronchitis and emphysema. The respirations in uræmic states vary much; thus they may be very slow—I have seen them as low as 10 in the minute—but they are deep, and there is no dyspnoea; or they may be rapid, noisy, and panting, not unlike that sometimes seen in diabetes. In this form, again, there is no dyspnoea. Cheyne-Stokes breathing is usually of cardiac origin. Where there is dyspnoea it is often cardiac, and, if not, is frequently due to emphysema and its attendant bronchitis, or the bronchitis itself may be of toxic origin. Any attack of the nature of true spasmodic asthma is very rare, and I must confess myself very sceptical as to its existence. I have certainly never met with it.

Peripheral neuritis is a rare condition in granular kidney. I have recorded a well marked case.

Epileptiform Convulsions.—Fits are, of course, the common form in which acute uræmia manifests itself, but epileptiform convulsions are not rare as one of the early symptoms of the late stage independent of uræmia. The fits occur in groups, two or three a day possibly, and last for a day or two; they may then disappear, and not recur for weeks or months, when a second bout of fits occurs with as little manifest cause as before, and so on. Before long grave symptoms of the usual kind develop, and the case passes into its final stage. In connection with fits may be mentioned the curious attacks of cerebral irritation, which are not at all uncommon. They may take the form of attacks of general nervous irritability, of emotional excitement, or of almost maniacal delirium. They may last a few days only, or be prolonged for some weeks, and in this condition patients have been certified as lunatics. These attacks, like the fits, are at first separated by long intervals, but gradually become more and more frequent, and finally end in a condition of chronic mental perturbation of either the excited or melancholic type.

SKIN AFFECTIONS IN RENAL DISEASE.

This subject has been but little written upon, and yet it is not without its clinical importance. The cases fall into two groups according as there is general œdema or not.

Where the subcutaneous tissue is distended with œdema the nutrition of the skin will naturally suffer, and from very slight local causes rashes are likely to be produced. Where there is no œdema the rashes are probably of a toxic origin.

1. *Rashes associated with Œdema.*—These are for the most part erythematous in nature, transitory in duration, produce but few symptoms, and when localised have but little clinical importance. If widespread the prognosis is less favourable,

and becomes the more unfavourable the more general the eruption is. Patches of erythema are often found on the inside and front of the thighs, and on various parts of the trunk, especially the lower part of the abdomen. As a rule they last but a few days, and then do not itch or burn or produce any discomfort. Sometimes the rash is of a papular lichenous character, and is then generally met with on the backs of the thighs and arms.

Eczematous eruptions are not at all uncommon if there be much œdema where the parts lie in contact with each other. If the skin is leaking, as after puncture or when blebs have formed and burst, various forms of rash occur; they are often eczematous, and produced by the irritation of the discharge, or erythematous, and spread in a way which closely resembles erysipelas or other infective eruptions, and are no doubt of septic origin.

As in diabetes so in dropsy—the tissues lose their resistance to pathogenic organisms, so that if infection occurs it will produce very grave effects. This used to be so far recognised that puncture or drainage of œdematous limbs was regarded as a very dangerous proceeding from the liability to phlegmonous inflammation, or even gangrene. Under the use of strict antiseptic precautions the danger has almost entirely disappeared.

2. *Rashes without Œdema.*—These occur almost exclusively in granular kidney. Generally widespread, or even universal, they are of great obstinacy and of grave significance. Localised eruptions similar to those already described occur also in granular kidney, but these are not of much importance. The general rashes vary in character. They may be described as: (1) Erythema; (2) pityriasis rubra; (3) dermatitis exfoliativa; (4) general eczema; (5) a discrete, papular eruption, sometimes lichenous, sometimes resembling chronic urticaria. I have myself met with instances of each.

In the few cases in which I have seen the initial stage, the rash has commenced as a localised, patchy erythema on the lower part of the abdomen, or on the inner and front parts of the thighs.

It is strange, considering the frequency with which hæmorrhage occurs in connection with granular kidney, that hæmorrhagic eruptions are so rare. I do not remember ever to have seen a case resembling purpura, nor, as a rule, have the skin eruptions a specially hæmorrhagic character.

These rashes, of whatever kind they are, occur only late in the disease and when the symptoms are well marked, so that the diagnosis of granular kidney is usually obvious, and this is perhaps the reason why they have been so long overlooked, or at any rate not described. In some cases, where the diagnosis of granular kidney is not so obvious, the patients come under treatment for the skin affection, and the essential disease is frequently overlooked, or if albuminuria is discovered it is regarded as the consequence of the affection of the skin, and its significance missed.

The association of a generalised skin eruption with albuminuria is of great importance, and justifies a more cautious prognosis than might otherwise be given. Evidence of granular kidney is often found if looked for, and then I believe the prognosis is very grave, and the end is not far off.

ACUTE RENAL TOXÆMIA: ACUTE URÆMIA.

The symptoms of acute uræmia have by no means that definite and uniform character which seems to be often assumed. The cases really vary very much from one another, almost as much as do cases of so-called diabetic coma. Fits and coma are the two most characteristic symptoms, and yet patients may not have fits, or at any rate no marked convulsions, and they need not be comatose. A patient may be comatose without any fits, or at most with but very slight twitching, and the condition may then closely resemble apoplexy. Patients in such a state nearly always die, but I have recorded a case of recovery in a man, aged 43, who is still living 12 months after the attack.

In some cases the condition almost resembles that of narcotic poisoning. In others, again, symptoms of the most profound collapse develop. The patient seems to have been suddenly poisoned, and presents symptoms very much like those met with in acute ptomaine poisoning.

Whatever the form acute uræmia may take the prognosis is as grave as it can be. If any one of the forms has a less

grave significance than the others, it is perhaps that in which there are epileptiform convulsions, for uræmic fits in granular kidney may end in recovery now and then, as they much more frequently do in acute nephritis.

Frequently signs of cerebral irritation develop, the patient becomes extremely restless, sleepless, and more or less delirious, and sometimes passes into a condition of noisy, active delirium, not unlike delirium tremens, with which I have seen the condition confused. At other times the patient becomes violently maniacal, and is for the time a raging lunatic. If the patient does not die during this stage the attack may subside, and in a day or two pass off. But even then, the general condition rapidly deteriorates, and other symptoms develop, which before long end in death.

The most interesting fact about uræmia in the course of granular kidney is that it may develop so suddenly, and with little or no warning, in the midst of apparent health, and carry the patient off. Granular kidney is not generally recognised as a cause of sudden death, and I may refer again to the interesting statistics of Dr. Horder on the subject, which I quoted in my first lecture.

What with uræmia and other acute symptoms to which I have referred, I think we may say of advanced granular kidney, as we can of diabetes, that the patient's life is hardly worth a week's purchase, so sudden may be the onset of acute symptoms, which may rapidly end in death. Yet, on the other hand, we know that though death may be sudden, yet in the absence of acute uræmia or serious hæmorrhage life may last for many years.

TREATMENT.

If we knew the causes of the disease we might take steps to prevent it; but not only are the causes unknown, but the disease is not even recognised in most cases until it is already far advanced. Little or nothing definite, therefore, can be done at present in the way of prophylaxis or prevention. But as it is in the early stages that we are likely to be able to do most good, the importance of an early diagnosis is obvious. Nor when the disease is far advanced can it be cured, for scar tissue cannot be removed from the kidney by therapeutic means any more than from the skin or from the liver.

But because we do not know at present how to prevent the disease developing and cannot restore the diseased organs to their normal condition, it does not follow that treatment is of no avail. If we cannot treat the disease we can at any rate treat the patient; if we cannot cure the lesion we can at any rate attack the symptoms. If we can relieve the patient of the symptoms which trouble him, he will care but little for the morbid lesion; if we can cure his disease, that is, discomfort, he will not mind the disease.

We cannot cure myxœdema but we now know how to relieve its symptoms. We may hope for similar success hereafter in the treatment of granular kidney.

The objects we should have in view in treatment are:

1. To prevent the disease getting worse if possible, and to relieve the damaged organ in every way possible. With this in view exposure must be avoided as well as fatigue of either mind or body; the general health should be kept at its highest level; the diet should be appropriate, and, where feasible, the winter should be spent in a warm, dry, and genial climate.
2. To guard against the accidents specially likely to occur. These are failure of the heart and rupture of vessels. With this object violent exertion must be avoided, as well as all excessive mental work and anxiety; the patient should lead an easy life, both physical and mental; and, where unavoidable illness arises, such as a severe accident or acute pneumonia, if the weak spots be remembered much may be done to diminish the risks.

3. To counteract or relieve symptoms as they arise. I have already drawn attention to the extreme variability of these symptoms, and the treatment must therefore be correspondingly various also; but it is often surprising when the cause upon which these symptoms depend has been recognised, that is to say, when granular kidney has been diagnosed, how much may be done to give relief.

Of drugs, I do not know of any more useful than nitrate of pilocarpin given in small doses two or three times a day by the mouth, or in urgent cases *sub cutem*. Thus the headache,

irritability by day and restlessness by night, vomiting and digestive disturbance, a foul tongue and a dry skin, may all rapidly yield to a dose or two of pilocarpin, and the patient be restored to comfort, or even threatening symptoms of uræmia be removed. There is one noteworthy fact about pilocarpin in chronic renal disease—namely, that it often does not produce the sweating which under normal circumstances and in similar doses it causes, and yet without the sweating its effect is striking.

There is one line of treatment to which I wish more particularly to refer, for it has not so far been investigated as fully as it deserves, and that is the treatment of chronic renal disease by means of renal extracts.

I have already said that there is no positive evidence at present of the existence of an internal secretion in the kidney; yet the cachexia which develops in chronic renal disease is not at all unlike that which is met with in Addison's disease or even myxœdema. Granular kidney also presents other resemblances with these diseases, in that the grave symptoms do not arise until the organ is very considerably diseased; in fact, as Bradford has shown, it is not until about three-fourths of the total kidney substance has been destroyed that life becomes impossible.

There was the same absence of conclusive evidence in the case of the thyroid gland until the administration of thyroid extract proved by its clinical effects that the symptoms depended upon the wasting of the gland. There can be no doubt clinically that the late symptoms of granular kidney depend upon the disappearance of the glands, and it is therefore not at all improbable that the kidney has an internal secretion, though absolute proof is not yet forthcoming.

Renal extracts have not been used except in quite the latest stages of granular kidney at a time when probably the disease is too far advanced to be amenable to treatment at all. The subject is, of course, surrounded with difficulties; and yet, if we are to do any good at all by this or any other method, we must attack the disease before it has reached its later stages, and before the nutrition and general cachexia is so pronounced. The renal preparations I have been using are tabloids made by Burroughs and Wellcome.

The first question is whether the administration of renal extracts by the mouth has any effect at all. I have already said that if nitrate of pilocarpin be given by the mouth or *sub cutem* to patients with granular kidney, the dose which under ordinary circumstances would produce free sweating often fails to produce this effect. The following experience is one which I have had on several occasions:

A patient with granular kidney who had been taking nitrate of pilocarpin regularly was given renal tabloids two or three times a day. The dose of pilocarpin had hitherto caused no sweating; but within twenty-four hours or so after taking the renal tabloids sweating became marked, and followed each dose to such an extent that on some occasions it had to be stopped. As soon as this was done the sweating ceased. After a short interval the pilocarpin was repeated and the sweating returned. The pilocarpin was then continued and the renal tabloids stopped and the sweating again ceased. The administration of renal tabloids, therefore, did in these cases modify nutrition in some way so as to permit the nitrate of pilocarpin to have its normal action.

The most striking instance of the effect of the renal tabloids occurred in the following case:

A girl, aged 13, was under treatment for what appeared to be acute nephritis. After some weeks' illness she began to develop uræmic symptoms; the amount of albumen increased considerably; the amount of urea fell to 0.8 per cent.; there was a good deal of vomiting and abdominal pain, some diarrhoea, and also some bronchitis. A little later headache set in, vomiting became more troublesome, and she began to have fits. Under treatment the fits subsided, and in the course of a week or so she was in much the same condition as before the fits commenced. As she seemed to be going downhill, I administered renal tabloids, giving her 5 grs. twice a day. Coincidentally with this she began to improve; the quantity of urine a few days after the first administration increased and reached 47 ozs.—the largest amount she had ever passed while under treatment, the usual average being not more than 15 or 20 ozs. With the increase in the urine the amount of albumen greatly diminished and the œdema began to disappear. In the course of a month the urine averaged 1.12 specific gravity, 40 ozs. in amount, and not more than 0.5 per cent. of albumen, and soon she was well enough to leave the hospital. Some months later she returned again in a condition of dropsy and chronic uræmia. She again took renal tabloids with great benefit, and left the hospital, except for the albuminuria, well. A third time she was brought to the hospital with uræmic convulsions, and died in a few hours.

I have had two or three other cases of the same kind, and in all the results have been the same, namely, an increase in the amount of urine and an improvement in the general condition. This improvement followed, and appeared to be due to the action of the remedy.

The use of renal extracts is still in a purely experimental stage. Judging by the analogy of myxœdema, it would be in the cases of chronic renal cachexia only that we should look for striking results, and this requires early and correct diagnosis. In acute uræmia there is so little time to act that recourse must be had to other and more active measures.

Sir, I have now finished the task you set me. My choice of granular kidney as the subject was inspired by the hope that what had interested me would prove of interest also to others. I trust I may not have misjudged. I have not hesitated to express my own opinions, even at the risk of appearing egotistic, though I trust with sufficient modesty to escape the charge of dogmatism. On a subject so full of difficult and contentious questions, I cannot expect that my views will commend themselves to all. Yet defined opinions challenge criticism, and criticism tends to advance knowledge.

THE MILROY LECTURES

ON THE

EARTH IN RELATION TO THE PRESERVATION AND DESTRUCTION OF CONTAGIA.

Delivered at the Royal College of Physicians of London

By G. V. POORE, M.D., F.R.C.P. LOND.,

Professor of Medical Jurisprudence and Clinical Medicine, University College; Physician to University College Hospital.

LECTURE III.¹

AGRICULTURE.

MR. PRESIDENT AND GENTLEMEN,—Enteric fever, diarrhoea, plague, and some other diseases are favoured by filth, although we are ignorant of the precise way in which filth favours the occurrence of these diseases. Some might say that a filth disease is a soil disease, and that there is no line of demarcation between the two. This is true, but it is nevertheless very necessary for practical purposes to distinguish the one from the other. We are all agreed that it is dangerous to allow the purlieus of a house to become sodden with liquid filth, but it might be equally dangerous to the public health to encourage the idea that it is dangerous to dung the land for fear of inoculating it with infectious disease.

Infective organisms contained in dung have to run the gauntlet of many enemies—such as dogs, sparrows, rats, flies, maggots, beetles, earthworms, moles, sunlight, fresh air, innumerable saprophytes (both aerobic and anaerobic), and the chemical action of the roots of plants. Of course, there may be spores which emerge from these ordeals unharmed and still virulent, but it is evident that, being mortal as we are, they are likely to succumb before the digestive and disintegrating processes which they encounter. The bulk of the evidence goes to show that contagia must be largely destroyed in the soil, and that agriculture is really the corner stone of preventive medicine. It becomes of great importance, therefore, to devise means by which the fertilising material of our towns may be applied to the soil with safety and despatch.

I may be pardoned for reverting to the method of dealing with human excreta which I have practised now for twelve years in my experimental garden at Andover:

1. The excreta are moved every day so that there is no accumulation of filth near the dwelling.

2. They are put just below the surface of freshly-dug ground so that they are out of the reach of flies.

3. The ground is planted with plants of the cabbage order as quickly as may be, so that very soon there is no possibility of dust being blown off the surface of the ground, and the mass of living cabbage leaves freshens the air.

I cannot believe that dust from agricultural land is a danger in this country, whatever it may be in the tropics. In my

garden the ground treated in the manner stated, apart from the growth of cabbages, soon becomes coated with a green growth of alga. Mr. A. Gepp of the Natural History Museum, who visited my garden last summer, took some of this growth away and very kindly examined it, and he pronounced it to be an alga—"chiefly *vaucheria sessilis* (in good fruiting state) with a little *ulothrix*, a *gloeocystis*, and an *oscillatoria*." Such a growth effectually prevents the possibility of dust.

Dr. Samuel Hyde,² speaking on the Open-air Treatment of Consumption, says: "Sparseness of vegetation, like thinness of population, is a climatic factor favourable to the treatment of consumption. Where vegetable life abounds, there vegetable decomposition must also abound, and *vice versa*. Wherever there is life we have a corresponding amount of death accompanied necessarily by the products of decomposition." That is true, but it is also true that wherever there is death we have the potentiality of a corresponding amount of life. I believe that what I have called the circulation of organic matter is a beneficent fact from which there is no escape, and that whether we derive good or ill from the inevitable processes of death and decay depends very much upon ourselves. We must never forget that vegetation purifies the soil, freshens the air, rests the eye, and prevents dust, and these facts must be recognised as to a great extent counterbalancing the evils of dead leaves, and apart from the question of food supply, it is, I believe absolutely necessary to encourage agriculture in order that our race may be maintained in vigour. The strong contrast which exists between the agriculturist and the town worker in the matter of health is well known.

Agriculturists are amongst the healthiest in the community, and even the farm labourer, in the matter of health, is 33 per cent. better than the average.

THE MAINTENANCE OF THE FERTILITY OF THE SOIL.

There is much evidence to show that dung is absolutely necessary to maintain the fertility of the soil. In a paper by Sir John Lawes and Sir Henry Gilbert on the valuation of unexhausted manures,³ the difference between organic manures and mineral manures is well brought out. The lasting effects produced by farmyard manure (14 tons to the acre) are shown in the annexed table.

Experiments with Farmyard Manure on Permanent Grass Land.

	Unmanured every Year.	Manured 1856-63, Unmanured since.	Excess of Manured over Un- manured.
8 years, 1856-63 } 1st crops only {	cwt. 23½	cwt. 42½	cwt. 19½
12 years, 1864-75 } 1st crops only {	cwt. 19½	cwt. 32½	cwt. 13½
20 years, 1876-95 (1st and 2nd crops)	cwt. 25½	cwt. 29½	cwt. 4

In only one year—1893, a year of drought—did the manured plot give less produce than the unmanured. The authors say: "It is true that the application of 14 tons of farmyard manure per acre per annum for eight years in succession is an unusually heavy dressing; but it is of interest to know that the

Showing the Yield of Wheat in Bushels per Acre.

Period.	Mixed Mineral Manure.			
	Alone.	And NH ₃ 86 lb. N.	And NH ₃ 129 lb. N.	And NH ₃ 172 lb. N for first 13 Years (1852-64) Unmanured for last 19 Years.
	Plot 5	Plot 7	Plot 8	Plot 16
13 years, 1852-64 ...	18½	37½	39	39½
19 years, 1865-83 ...	13½	29½	34½	14½