On granular kidney and physiological albuminuria: being the Lettsomian lectures delivered before the Medical Society of London / by Samuel West.

#### **Contributors**

West, Samuel Hatch, 1848-1920. Francis A. Countway Library of Medicine

#### **Publication/Creation**

London: Henry J. Glaisher, 1900.

#### **Persistent URL**

https://wellcomecollection.org/works/dpn9wcde

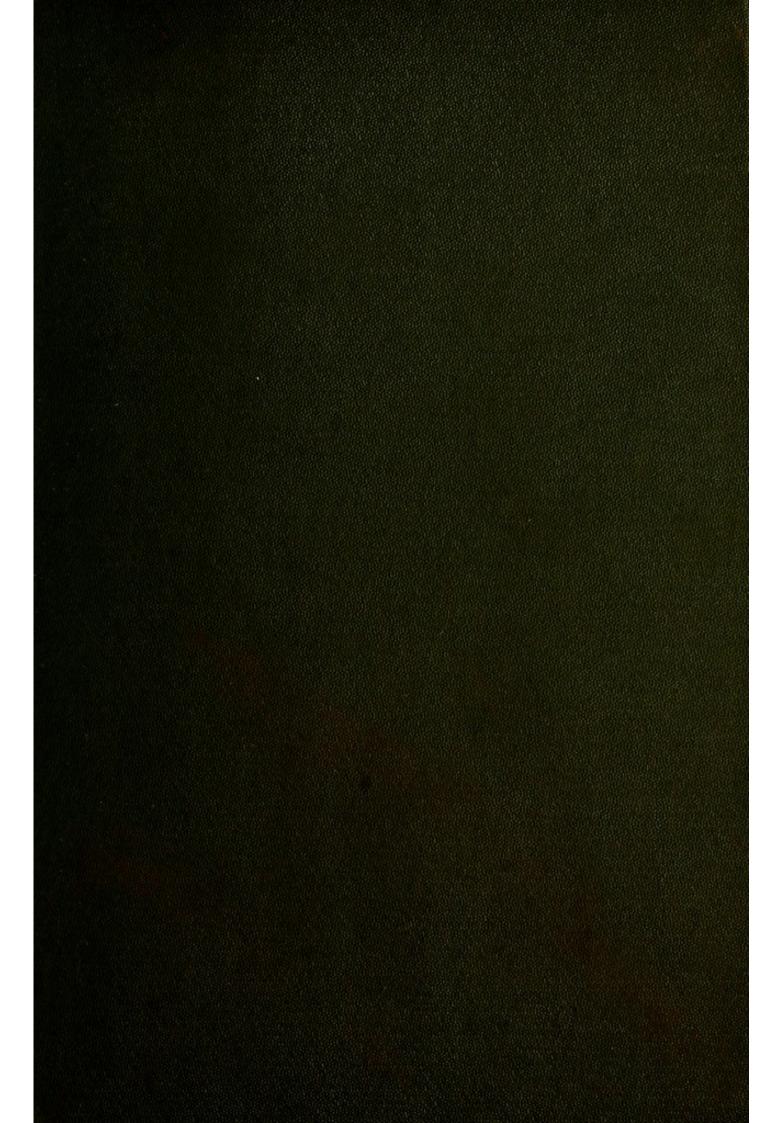
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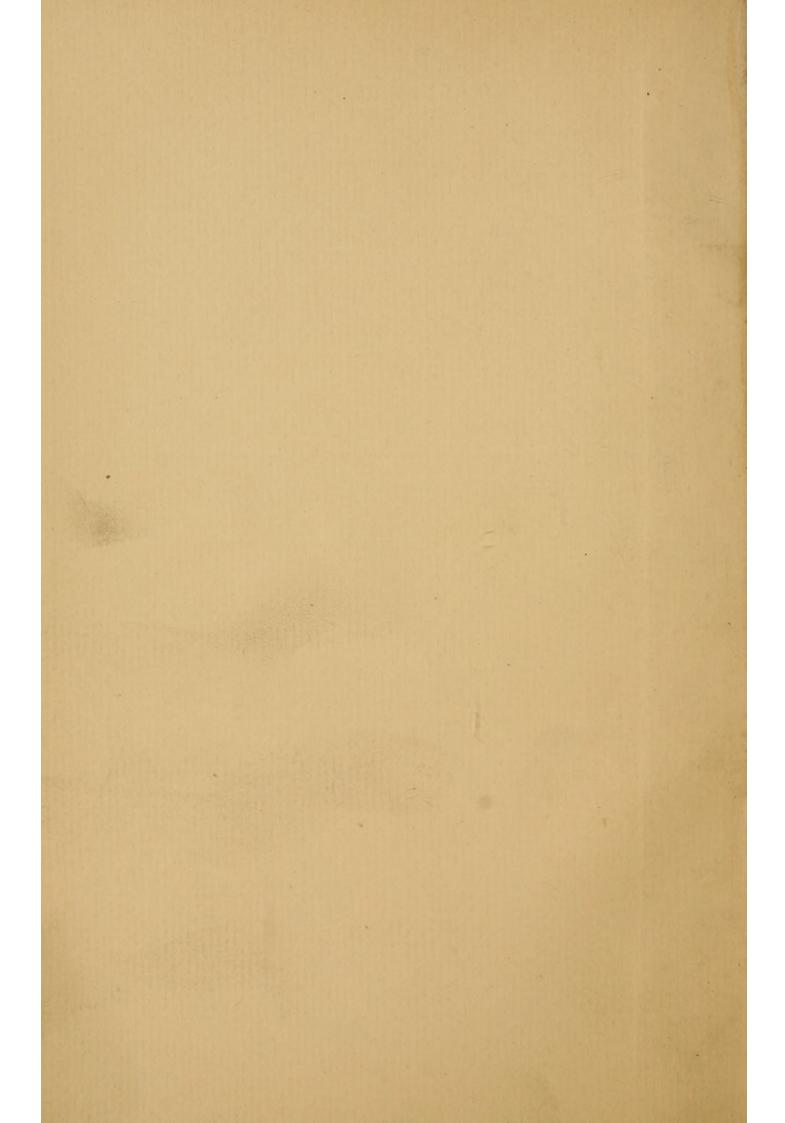


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Fred'k O. Shattuck.



## GRANULAR KIDNEY

AND

## PHYSIOLOGICAL ALBUMINURIA,

BEING

### THE LETTSOMIAN LECTURES

DELIVERED BEFORE
THE MEDICAL SOCIETY OF LONDON

Fred'k C. Shattuck.
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#### London:

HENRY J. GLAISHER,

57, WIGMORE STREET, CAVENDISH SQUARE, W.

1900.

17 2 295

HARRISON AND SONS,
PRINTERS IN ORDINARY TO HER MAJESTY,
ST. MARTIN'S LANE.

#### PROLOGUE.

The invitation to deliver the Lettsomian Lectures before this ancient Society has been accepted in times past with full appreciation of the honour by many of the most distinguished members of the profession. The great names upon that list have aroused in me the natural fear that my ability may prove unequal to the task, yet I trust that with their example and your indulgence I may succeed in making the present Lectures not unworthy altogether of a place in the series.

In choosing granular kidney, I was guided by the wish to select a subject which should be of practical importance, and therefore of general interest, and at the same time one upon which I could speak from personal experience.

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#### PART I.

GRANULAR KIDNEY is a disease of great importance on account of its frequency, a frequency which is by no means adequately recognised. It is often discovered post mortem when not suspected. It is often in itself the cause of death, even of sudden death. It often explains why death has happened in other diseases which otherwise might not have proved fatal. During life it is often discovered unexpectedly if looked for; it is often overlooked if not suspected; and it often explains a case which has been a puzzle until granular kidney gave the key to its solution.

#### ITS FREQUENCY AND IMPORTANCE.

The general post-mortem frequency of granular kidney ranges from 11.8 to 18 per cent., so that it is a very common condition.

Thus the post-mortem records at St. Bartholomew's Hospital for a period of five years gives 13.2 per cent. (219 cases of granular kidney in 1,662 necropsies, children being excluded from the calculation).\* Of these, 132 were in males and 84 in females. Goodhart's statistics at Guy's yield 15 per cent.; Saundby's, at the Birmingham General Hospital, 18 per cent.

Mahomed's Table showing Relative Frequency of Granular Kidneys to Healthy Kidneys at different Age-Periods based on 336 Cases, of which 57 were above 50.

Ag	es.				
10-	-20	 	 	2.3	per cent.
4	30	 0	 	3.0	,,
	40	 	 	12.0	,, .
	50	 	 	38 .5	,,
	60	 	 	43.0	;,
Above	60	 	 	50.0	,,

In fatal cases of cerebral hæmorrhage Dickinson found granular kidney in no fewer than 41 per cent. In the St. Bartholomew's Hospital figures referred to the percentage was 21.5 (34 cases in 158).

As a cause of sudden death nothing will better prove the importance of granular kidney than the following statistics.

They were obtained for me by Dr. Horder,† as the result of an investigation made into the cause of death in persons brought into St. Bartholomew's Hospital dead or dying. The total number of such cases (excluding children under 5) was 79, in all of which a *post-mortem* examination was made. Of these, 64 were dead on reaching the hospital, and 15 died in the surgery.

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<sup>\*</sup> For these figures I am indebted to Mr. Woodbridge. They will be published in extenso in the 'St. Bartholomew's Hospital Reports.'

<sup>†</sup> This paper will be published in extenso in the 'St. Bartholomew's Hospital Reports' for 1899-1900. The short abstract now given of it is of the nature of a preliminary report only.

Table showing the frequency with which Chronic Interstitial Nephritis was found in the Bodies of Persons brought in Dead or Dying into St. Bartholomew's Hospital during the period of five years (1894–8 inclusive), Children under 5 excluded.

Chronic Interstitial Nephritis found to be	64 cases brought in dead.	15 cases dying in surgery.	79 cases together.
1. The actual cause of death in	13 cases = 20 · 3 %	2 cases = 13:3%	16.8%
death in 3. An accessory but doubtful cause of death in	19 cases=30% 6 cases=6 ·25%	2 cases = 13 · 3% 2 cases = 13 · 3%	9.77%
Totals	38 cases = 56 ·25%	6 cases=40%	48.17%

In 48 per cent. of these cases chronic interstitial nephritis was present. In 16.8 per cent. it was the only cause of death, and in 21.6 per cent. more it played its part either in producing death or in causing the lesion which led to death—that is, together in 38.4 per cent.

Nothing more is necessary to prove the importance and frequency of the disease.

Of the 21 cases in which granular kidney was the concomitant cause of death, in 13 death was due to hæmorrhage, to which the interstitial nephritis directly or indirectly led.

Of these, in one there was hæmorrhage into the pons varolii; in one pachymeningitis hæmorrhagica; and the remaining case was one of hæmoptysis.

In four cases aneurysm of the aorta was present, the rupture of which was the cause of death; and in the remaining three death resulted from the rupture of an aneurysm of the anterior communicating artery in one instance, and of the sylvian artery in two more.

The association of interstitial nephritis and aneurysm, both of the aorta and of other arteries, is remarkable, and, so far as I know, has not been clearly shown before.

In seven cases the cause of death was cardiac.

Acute endocarditis was found in .... 1 case.

Acute endocarditis with pericarditis in .... 1 ,,

Aortic incompetence in .... .... .... .... 3 cases.

Aneurysm of the heart in .... .... .... 1 case.

Failure of heart associated with atheroma of the coronary artery in .... ... ... 1 ,,

7 cases.

Of the remaining cases three had phthisis and one pneumonia.

The influence of granular kidney upon the prognosis of other diseases is well illustrated by acute pneumonia.

The association of pneumonia with any pre-existing disease greatly increases its gravity, even, according to Huss, to the extent of making it four times as fatal as in uncomplicated cases. In 100 fatal cases which I investigated, 23 showed some pre-existent chronic disease of the lungs or pleura, eight of the heart, and 10 of the kidneys.

Sturge's percentage was somewhat higher, namely, 15 per cent.

For all the reasons given, granular kidney is not only one of the most interesting of diseases, but also one of the most important.

#### AGE DISTRIBUTION.

Granular kidney is often said to be a disease of middle life, and this is true in the sense that the symptoms are usually evident then; in other words, the disease is then far advanced, and death may be near. The disease, however, must have commenced long before, perhaps years, so that even in these cases met with in middle life the onset of the disease is to be traced back, it may be, to youth.

Not only is the onset of the disease in many cases to be referred to early life, but the disease may even be advanced and fatal then. That granular kidney may occur in the young, even in children, is now generally recognised, but though rare it is still regarded as a much greater rarity than it really is. I have recorded an extreme instance fatal at the age of 18, and several instances in small children are recorded by Guthrie.

The following figures give the general age distribution above 20 years at the time of death:—

Age.	Dickinson.	Fagge.	Bartels.*	Galabin.	St. Bartholo- mew's Hospital (Woodbridge).†	Total.	
About 20	1	_	4	2	2	9	
20-30	17	_	4	6	10	37	
30-40	38	18	9	12	19	96	
40-50	73	39	4	19	43	178	
50-60	55	36	7	21	41	160	
60-70	43	24	5	16	28	116	
Above 70	15	4	_	3	10	32	

Table of Age at Death.

<sup>\*</sup> One death at 18, one at 19.

<sup>†</sup> One death at 19, one at 20.

Diagram constructed from the combined statistics given, showing the Age Distribution at the time of death.

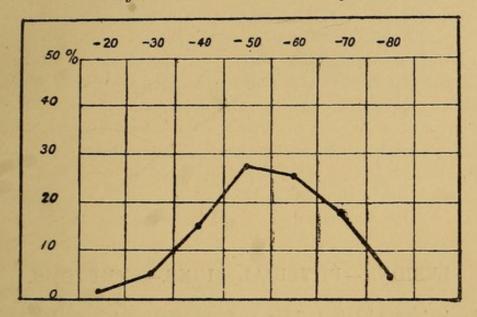


Table showing Age Distribution at the time of death of 206 cases at St. Bartholomew's Hospital.

20		20-30		30-40		40-50		50-60		60-70		70-80		
М.	F.	М.	F.	М.	F.	м.	F.	М.	F.	М.	F.	М.	F.	
3	3	6	9.5	-	14	33	26		14	27	9	7	5 2	

SEX.

The preceding table yields the relative frequency in the two sexes, and shows the remarkable preponderance of granular kidney in the male, viz., 129 males to 77 females: *i.e.*, a proportion of about 13 to 8.

#### LESIONS.—PHYSICAL SIGNS.—SYMPTOMS.

The lesions, physical signs, and symptoms of granular kidney all alike fall into two groups, the cardiovascular and the renal.

The physical signs are early, the symptoms late. When symptoms arise the disease has already existed for some time, and the lesions are far advanced. For the diagnosis of the disease in its early stages we must look to the physical signs and not to the symptoms.

#### THE LESIONS .- MORBID ANATOMY.

Granular kidney is a bilateral and to a great extent symmetrical affection, that is to say, both kidneys are similarly affected, though not necessarily to the same extent. The difference between the two, however, if there be any, is slight, and rarely exceeds an ounce.

The kidneys may be much contracted and greatly reduced in size, so that they may not weigh more than  $1\frac{1}{2}$  or 2 ounces each. Extreme contraction such as this is really rare. The kidneys are, it is true, usually reduced in size and weight, but by no means to the extent that seems generally believed; while in some instances, so far from being smaller than normal, they may be much above the average size and weight. In other words, there are large as well as small granular kidneys, just as there are large and small cirrhotic livers.

I have taken the weights of 140 cases, and put them in a diagrammatic form, in which the weights are indicated by the vertical height and the number of cases by the divisions on the base line.

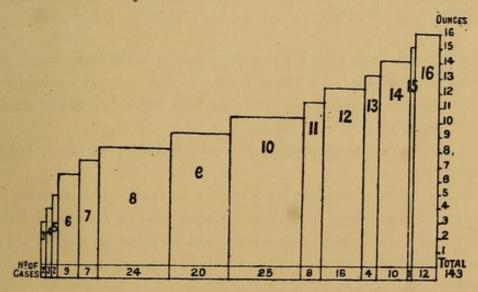


Diagram in which the weights in ounces of the two kidneys together are shown by the height of the vertical line, while the number of cases in which the kidneys were of the given weight is shown by the length of the base line.

Taking 11 ounces as the mean weight of the two kidneys together in the two sexes, or even including the cases in which the weights reached 12 ounces, it will be seen that in the great majority of cases the kidneys ranged between 8 and 10 ounces, and that in only 5 per cent. was the combined weight less than 6 ounces. On the other hand, in no fewer than 20 per cent. the combined weight was above the normal average, and in 12 cases reached as much as 16 ounces. In a few of these, no doubt, some allowance ought to be made for the fat deposited round the pelvis of the kidney, and in some others the weight was partly to be explained by the number and size of the cysts present. But in the majority neither cysts nor fat took any material part in the increase of weight, and in two instances in which the kidneys weighed 16 and 12 ounces respectively they were described in the post-mortem report as "large granular kidneys."

The kidneys, moreover, are not always granular on the surface, though microscopically the interstitial change may be marked enough.

It is also stated that the kidneys may be small and granular in appearance, and yet on section show no interstitial change. Such cases have been mentioned to me, but I cannot say that I have ever met with them myself.

As granular kidneys are not always granular, it might be thought some more accurate term could be found for its description, such as cirrhosis of the kidneys; but granular kidney is a term so well known and so generally accepted that it would be difficult to substitute for it any other which, though more accurate, would be likely to be adopted.

The typical granular kidney is small, contracted, hard, with a granular surface and often numerous cysts. On section the whole kidney is found to be cirrhotic and wasted, but the wasting affects chiefly the cortical region.

The changes consist in fibroid induration and cellular degeneration.

Though often described as chronic interstitial nephritis, it is an open question how far these changes are in reality of inflammatory origin. Certainly in most cases we have no more evidence of inflammatory processes in the cirrhotic kidney than we have in the cirrhotic liver.

#### THE FORMS.

Granular kidneys are sometimes described as of two kinds, the white and the RED, and the difference in colour is held by many to denote difference in origin, and they are accordingly called the contracted white and the contracted red. The small white is generally stated to be somewhat larger than the red, to be less granular on the surface, and to have more cells left, these cells being in a condition of fatty change, to which change the colour is referred.

None of these statements are, in my experience, absolutely correct; for small white kidneys are often quite as small and as granular on the surface as the small red, and may have quite as few or even fewer cells left, and these cells are often not fatty.

The term "contracted white" introduces confusion, and seems to assume what ought to be proved—namely, the different origin of the two forms. It suggests that the small white is but the later stage of the large white kidney. It assumes that every stage can be demonstrated between the large white kidney of chronic parenchymatous nephritis, through the contracting white to the contracted white.

If this were the usual sequence of events, it ought to be capable of easy clinical proof. Pathologically it is easy to show that chronic parenchymatous or the large white kidney presents interstitial changes of a contracting kind, but the weak link in the chain is between the so-called contracting form and the contracted form.

The two forms certainly exist, but if the distinction between the two forms is to be made it would be very much better to speak of them as small white and small red, or as white cirrhotic and red cirrhotic, rather than white and red contracted kidneys. For myself, I consider the difference is really one of colour chiefly. Microscopically I do not see that any clear distinction can be drawn. The colour does not depend entirely upon the condition of the cells as is usually stated, for the fatty change to which the white colour is referred is not constant, and such kidneys may be markedly white or pale, in which microscopical examination shows a remarkable absence of cells, while the cells that remain are not

so much fatty as granular. If pathologically the distinction between the two forms is open to question, clinically, so far as I can see, no distinction at all can be drawn between them; that is to say, with exactly the same clinical symptoms we may find the kidneys in the one case white and in the other case red.

It seems to be sometimes assumed that the small white and small red are but different stages or degrees, that is, that the white kidney would in time become red, but even that is not true. On the contrary, it might with equal justice be argued that the pale cirrhotic kidney is in some cases an accidental condition of the red, and that a red kidney would become pale if the cells became inflamed and degenerated.

If this did prove to be the case it might explain why in the course of granular kidney acute symptoms so often develop suddenly as they do, and lead rapidly to death—the few active gland cells left in the wasted kidney becoming suddenly inflamed and degenerate, with the result that the kidneys cease entirely to do their work, and life is brought rapidly to an end.

We might thus possibly connect the sudden onset of acute uræmia, i.e., acute renal toxæmia, with the condition of the renal cells, just as in cirrhosis of the liver we associate the sudden onset of acute hepatic toxæmia with acute degeneration of the liver cells.

Granular kidney is often described as chronic interstitial nephritis, but all forms of chronic interstitial nephritis are not necessarily granular kidney.

First of all must be cut out of the category of granular kidney all those cases in which the lesion is unilateral, for example that which results from obstruction to the ureters.

The first effect of obstruction to the ureters is felt by the cells in the kidney, which lose their vitality, and ultimately atrophy and disappear. The ultimate results may be two—either fluid continues to be secreted and a condition of hydronephrosis is set up, or the fluid ceases to be excreted and the kidney shrinks. In the latter case fibrotic change occurs, and in the end the kidney may become greatly contracted and typically granular. Extreme changes of this kind consequent on obstruction, can, of course, only occur on one side.

Again, all cases of patchy fibrosis—for example, the results of infarcts or gummata—even if both kidneys are involved, must be excluded, for they do not produce the clinical symptoms of granular kidney.

Even when the lesions are bilateral, and both kidneys are affected, I should still exclude from the category of granular kidney certain forms of chronic interstitial nephritis, which are often included pathologically, though clinically they are distinct. I refer to the degenerate kidneys met with in connection with advanced atheromatous disease, or with the chronic gout of elderly persons; in fact, the kidneys which used to be commonly called senile or gouty. These kidneys are often markedly interstitial, and there is a good deal of fatty and cellular degeneration, giving the surface a mottled appearance, but they need not necessarily be granular, and are usually large. Moreover, the case need not, and indeed does not generally, run the clinical course of granular kidney.

Eliminating these various forms we are left with a pathological group of cases of interstitial nephritis of definite character, which we commonly recognise by the term granular or cirrhotic kidneys.

#### CAUSE OR ORIGIN.

Granular kidney being a bilateral affection must ultimately depend upon some general cause, acting no doubt through the intermediation of the blood, for there is nothing else except the nerves which could explain the symmetry of the disease.

Whatever the ultimate cause, the fibrotic changes in the kidney might arise in connection with some primary affection of the gland cells or some primary affection of the non-glandular parts; for example, the connective tissue itself or the structures contained in it, namely, the arteries, veins, lymphatics, or ureters.

Of primary affections of the connective tissue itself nothing is known, nor is anything known of primary affections of the lymphatics of the kidneys, though this much is known, that they are secondarily involved in all forms of inflammation, whether acute or chronic. We have no evidence that venous obstruction can produce cirrhosis in the kidney any more than it does in the liver. In considering, therefore, the causes of granular kidney, we have only the arteries and cells left as the primary sources of the disease.

In most recent writings granular kidney is divided into two forms, the arterio-sclerotic and the renal. These are often dealt with in different places, the one form under diseases of the vessels, the other under diseases of the kidney, so that in order to gain a complete view of granular kidney as a disease it has to be read in different chapters. This is very inconvenient and confusing, and suggests a marked difference between the two forms which, clinically, does not exist. It has, however, one advantage in that it fixes attention upon the question which is still at issue, namely, whether it is in the vessels or in the kidney itself that the primary causes of the disease are to be sought.

I shall now consider, as briefly as possible, the relation in which granular kidney appears to stand, on the one hand to inflammatory affections of the kidney, and on the other to the degenerative disease of the vessels.

# THE RELATION OF GRANULAR KIDNEY TO ACUTE NEPHRITIS.

Acute nephritis attacks the cells primarily and chiefly, but the interstitial tissues are always involved to some extent, and the more so the longer the disease has existed. It is by the lymphatics that the products of inflammation to a great extent are removed, and in passing they appear to set up some irritation, so that in course of time a small-celled infiltration is found, in parts at any rate, following the lymphatics and surrounding the blood vessels. This small-celled infiltration may in time end in the production of connective tissue, at first in parts only, in other cases more widely distributed, and there will be the more of it the longer the disease has lasted.

I do not know that the distinction which is often made between the different forms of acute nephritis, according as it attacks the glomeruli or the convoluted tubes (for instance, acute diffuse nephritis and glomerular nephritis), is one which is borne out by observation. In most cases all parts of the kidney are affected, though one may be affected more than another. Whether the distinction be just or not, I do not think it bears in any important way upon the question as to the relation between acute nephritis and granular kidney.

The large red kidney of acute nephritis passes, as the disease lasts, gradually into the large white. In the large white kidney some interstitial change is often found, sometimes local, at other times more diffuse; and, admitting that pathological connective tissue contracts in the kidney as elsewhere, we should expect the large white kidney in time to become smaller, to undergo a certain degree of contraction in parts, if not as a whole, and of this we have frequent pathological proof. The kidney is then described as contracting white.

It is even conceivable, theoretically, that the contraction might go much further, so that in time we might have the large or contracting white kidney passing into what may be described as a small, or contracted, white kidney, or even possibly ending in a small contracted red kidney.

Now, admitting the pathological possibility that acute parenchymatous nephritis might end in a granular kidney, if this actually occurred frequently it ought to be capable of easy clinical proof, for the symptoms of acute nephritis are not such as are likely to be often overlooked, by the patient or by the friends. Such cases are recorded, but they are certainly rare, and many of them prove, on careful critical investigation, not to be so conclusive as they at first sight appear. I have been on the watch for them for years, and although I have seen many in which the lesion has gone so far as to produce a somewhat diminished white kidney, the majority of such kidneys are still much above normal size. I have never traced a single case beyond this—that is, as far as a small white kidney. I do not say that it never can be so traced; on the contrary, I believe it may. I merely say that, so far, I have failed to observe it. On this point the late Professor Kanthack told me that his experience was the same, and that pathologically he had not been able to satisfy himself that an acute parenchymatous nephritis did actually pass beyond the contracting white stage.

Appended to these lectures are two cases in which the disease was traced from the commencement of acute nephritis to death after some months in each case, and in which microscopical examination revealed more or less extensive fibrosis in the kidneys, though they were in neither case granular.

Macpherson's case (female, aged 29) seemed to be one of ordinary chronic parenchymatous nephritis, and so the kidneys appeared post-mortem. I had the kidneys carefully examined with the microscope, because shortly before death, which occurred after about nine months' illness, albuminuric retinitis had been found. The ordinary lesions of chronic parenchymatous nephritis were found, but with them also scattered patches of cortical fibrosis.

Blakeborough's case (female, aged 14) is a more remarkable one, for on the child's death, after about 12 months' illness, the kidneys, though of large size and not granular, and presenting the appearance of large white kidney, showed the most remarkable fibrosis, which did not involve the cortex alone, but the medulla too, and every part of the kidney uniformly. In this case, also, albuminuric retinitis was discovered about four months before death.

It might be urged that marked contraction in granular kidney would be more frequent if the patients lived long enough, but that they die too soon, perhaps after but a few months' illness, and before the interstitial changes have had time fully to develop. This is but to acknowledge that it does not necessarily or often occur.

But it does not necessarily follow, even when the symptoms of chronic parenchymatous nephritis have lasted for many years, that a contracted kidney will result.

I have had under my care a woman, who has had several attacks of parenchymatous nephritis in the course of 13 years, and who has never lost the albumen from the urine; yet now, at the end of 13 years, her arteries are thin, and her heart not hypertrophied; she appears in fair health, and her retinæ are normal; there are, in fact, in spite of the long duration of the case, no clinical signs whatever which would justify the diagnosis of granular kidney.

I know also of another case in a man who, 25 years ago, had parenchymatous nephritis of great severity, and who has continued to pass albumen in large amounts (one-third to one-half) ever since, and yet no signs of contracted kidney have so far shown themselves. Cases of

shorter duration than these are not uncommon.

Nor can any closer relation be proved by the clinical history to exist between granular kidney and antecedent acute nephritis. It is quite unusual in cases of granular kidney to obtain a history of symptoms which would in any way justify the diagnosis of acute nephritis. This fact has been always insisted on as long as granular kidney has been recognised as a disease, and is generally accepted.

Even when the history of antecedent acute nephritis is obtained, it does not necessarily follow that the granular kidney has been the result of it. The occurrence of acute nephritis is no proof in itself that prior to the acute nephritis the kidney was sound; or, in other words, that if after an attack of acute nephritis the kidneys are found granular, they became granular as the result of the acute attack. For, on the one hand, it is not uncommon, in the course of a case already recognised as one of granular kidney, to observe acute parenchymatous nephritis develop; and, on the other, to find in a patient, hitherto believed to be healthy, and presenting the symptoms of acute parenchymatous nephritis, thickened arteries and even eye-changes, which show that the disease really dated long before the commencement of the so-called acute attack-in other words, that the patient has got acute nephritis in both cases alike because the kidneys were already diseased. Indeed, I think we may almost go so far as to say that as in children acute parenchymatous nephritis raises a strong presumption in favour of a recent attack of scarlet fever, so in

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the adult it ought to suggest the suspicion that the kidneys were previously unsound—in other words, granular. Of this I am quite sure: that if, in cases of acute nephritis in the adult, the signs of granular kidney be looked for, they will very frequently be found.

Cases of this kind are pretty frequent, but I may mention the following as interesting instances:—

A young man, aged 27, came into hospital with what at first appeared to be acute nephritis. It was not a very severe attack, and he rapidly improved, but at the time when he was first observed his arteries were noticed to be thick and the tension high. He never recovered completely, never entirely lost his albumen, and he used frequently, without any apparent reason, to have attacks of hæmaturia. The blood was never in large amount, but sufficient to give a distinct bright red (not smoky) colour to the urine, and a well-marked reaction.

I ventured in this case, at the time of first seeing the patient, on the ground of a thickened artery and high tension, to say that he must have had some disease of the kidneys antecedent to his present attack, and to foretell that it would not run an ordinary course. This opinion was confirmed by the attacks of hæmaturia which recurred several times in

the hospital as well as after his discharge.

I have had the patient under observation since for a long time, and he has always had a little albumen in his urine, and has suffered from periodical attacks of hæmaturia. The disease has not otherwise affected his health, and, so far, no other symptoms have appeared. This case would at the present time be diagnosed as one of granular kidney, and, if it were not known that at the time of the first attack of nephritis there was already evidence of chronic kidney disease, would probably be regarded, from the history, as an instance of granular kidney following acute nephritis, and yet such a conclusion would be incorrect.

#### The following is another case of the same kind:-

A woman, aged 54, was admitted into the hospital with cedema of the feet and face, and a large amount (half or three-quarters) of albumen in the urine, which also contained casts and blood. The history was only of three weeks' duration when the attack came on somewhat suddenly, and it was diagnosed as acute nephritis. On examining the patient the arteries were found to be considerably thickened, and to be uniform and not patchy as one would expect in a case of atheroma. The heart was, perhaps, a little hypertrophied, but it was difficult to be certain of this. I stated at the time that this thickening of the artery was a very suggestive thing, and that if it was not due to atheroma the patient must have granular kidneys. The question was complicated somewhat by the patient's age, for at 54 atheroma would not be unlikely, although it would be not at all a common thing to see the arteries at that age as thick as they were in this patient. On ophthalmoscopic examination in the right eye a hæmorrhage was found in the right yellow spot and one or two small white patches between the yellow spot and the disc. Similar white patches were found in the left eye, but no hæmorrhages. The occurrence of retinal changes of this character rendered the diagnosis of granular kidney certain. In this patient, therefore, although she presented all the signs of acute nephritis, and had actually acute parenchymatous nephritis, still the kidneys were granular.

In cases of granular kidney it is clear, therefore, that the history may be misleading, for an acute nephritis, if there be the history of an attack, may be the consequence of a pre-existent granular kidney quite as likely as the cause of it.

If, then—in spite of the fact that in the majority of cases of granular kidney the history and symptoms of nephritis are lacking—granular kidney is still to be referred to some antecedent nephritis, it follows that the initial attack must either have been slight, and therefore overlooked, or else that it was of some peculiar and specially latent kind. Latent acute nephritis, diffuse or glomerular, in children, following diphtheria and other specific diseases, has been described and regarded by some writers as the germ of subsequent disease; but this is, of course, presumption and not evidence; it is opinion and not fact.

Acute nephritis certainly occurs sometimes without any obvious symptoms to suggest kidney disease.

As an illustration in point I may quote a case of a girl of about 10 years of age. I was asked to see her because she had been ailing in an indefinite way two or three weeks. The mother was alarmed when she noticed the urine to be dark in colour. The child showed nothing except an appearance of anæmia and debility, with a little dilatation of the heart in consequence, but on examining the urine it was found to contain blood and a large amount of albumen, and very numerous hyaline and epithelial casts. The child was treated in the usual way, and in two or three weeks recovered completely. The attack was ultimately traced to a sore throat, no doubt of a diphtheritic nature, which the child had suffered from some three weeks before, for one of the other children came under observation with paralysis of the muscles of accommodation in the eye about the same time.

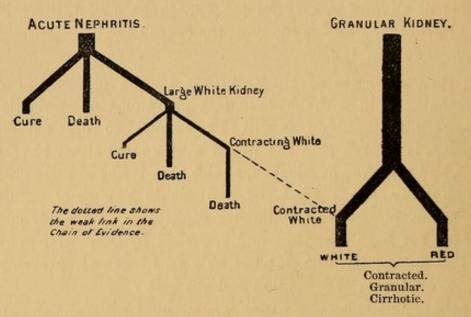
The interest of this case lies in the fact that it shows how easily a fairly intense nephritis could be overlooked—as, indeed, it was overlooked—for the time.

It is evident from what has been said that it is only in a very small number of cases of granular kidney that a history of antecedent acute nephritis can be obtained; that in still fewer instances can a case be traced from an acute initial acute nephritis to granular kidney.

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It follows, therefore, that most cases of granular kidney must be referred to some other origin.

The following diagram shows the relation which is assumed to exist between the acute nephritis and the white cirrhotic kidney—the dotted line shows the weak link in the chain:—



So far as the contracting white form the links are complete the weak link lies between the *contracting* white and the *contracted* white, *i.e.*, the pale granular kidney.

The increased tendency to refer granular kidney to acute nephritis which is obvious in many writers of the present time is due, to a great extent, to the question being regarded too much from an anatomical, that is, pathological, instead of a clinical point of view. Pathologically, of course, such a sequence of changes is quite possible, but the theories of pathology must be checked and corrected by the facts of clinical observation. The theory is one which ought to be capable of easy clinical proof, but the clinical proof, as far as I can judge, is lacking.

It would not have been necessary to discuss so fully the want of relation between granular kidney and acute nephritis had it not been for the frequent assumption of this connection at the present time by the sharp distinction so often drawn between the two forms of granular kidney, the white and the red.

# THE RELATION OF GRANULAR KIDNEY TO ARTERIAL DISEASE.

The changes in the arteries with granular kidney are general, widespread, in fact universal, throughout the whole body. They are found in all parts alike—in the kidney, for instance, as well as in the brain, eye, spinal cord, or even skin.

There are only two forms of general arterial change recognised in pathology, namely, atheroma and that connected with granular kidney.

Atheroma is a well-marked disease of the vessels. It is the degeneration which is usual as age advances, and though sometimes met with in earlier life, and even sometimes in quite young people, it is certainly a comparatively rare affection at the time when the changes of granular kidney are most common. Moreover, the thickening is characteristic; it is irregular and not uniform, and, when well-marked, can easily be diagnosed by the finger in superficial arteries like the radial and temporal.

Atheroma being a general disease will, of course, affect the renal arteries like any other, and will produce in the kidneys similar changes to those to which it leads in other cellular organs—for example, in the brain. Thus the obstruction to the circulation produced by the arterial changes will lead to malnutrition and fatty changes in the cells; these may ultimately atrophy, and as the result a certain amount of connective tissue may be formed in the interstitial tissue of the kidney. Thus it is not at all uncommon in the later periods of life to find the kidneys large and mottled, showing a good deal of interstitial tissue and of cellular degeneration; yet these atheromatous or senile changes do not as a rule, though they might conceivably, lead to the well-known granular contracted kidney.

The difficulty is further increased by the fact that the atheromatous changes in the arteries, if widespread, lead to secondary changes in the heart. Hypertrophy and subsequent affections of the heart follow, which so far resemble those met with in granular kidney.

Of course, old persons may suffer from granular kidney, and the two conditions may be associated. But for all that, if the question be regarded without bias, and in a general comprehensive way, it must be acknowledged that atheromatous disease of the arteries and the changes of granular kidney are different in kind as well as in history and clinical course.

In granular kidney the thickening of the vessels is fairly uniform, at any rate it does not occur in the irregular patches of atheroma, and is universal.

As to the nature of the vascular lesions dispute has long raged, the one side maintaining that it was of the nature of hypertrophy, the other of a degeneration. The facts are that both changes are found, the hypertrophic changes in the earlier stages and the degenerative in the later.

It is the changes in the arteries that are of prime importance in granular kidney, for in great measure, if not entirely, the hypertrophy of the heart is secondary to, and the consequence of, the changes in the vessels. Hypertrophy of the heart is met with, of course, where the vessels are atheromatous, as well as where they are the subject of the changes peculiar to granular kidney.

It is unfortunate that in many of the investigations as to the frequency of hypertrophy of the heart in renal diseases more accurate note has not been taken of the general condition of the vessels for the purposes of excluding atheroma, for this omission deprives the results of much of their value, and at the same time probably explains their divergence.

THE RELATION BETWEEN THE CARDIO-VASCULAR AND THE RENAL LESIONS.

So far as the cardio-vascular symptoms go I think we may assume that the cardiac lesion being of the nature of hypertrophy is, as in other cases, the response of the heart to some extra work thrown upon it of a permanent kind; it must therefore be secondary.

The hypertrophy of the arteries also is probably, like that of the heart, secondary; for we cannot suppose that there is any antagonism between the heart and the arteries, though this was once assumed to be the case—the heart hypertrophying, it was then supposed, in order to overcome the obstruction offered by the hypertrophy of the vessels. It certainly seems more probable that both the heart and the vessels hypertrophy together for the purpose of assisting the circulation to overcome some obstruction.

If this be so, the obstruction must be peripherally seated, and must be sought in the small peripheral arteries or capillaries. In these peripheral vessels the possible causes of obstruction are two: either there must be a structural change—that is to say, an anatomical lesion—or some functional disturbance which interferes with the passage of the blood through the vessels.

- (1) If the change were structural, and the lesions of the peripheral vessels of a degenerative character, being general throughout the whole of the body, the kidneys would be involved as well as other parts; in this way it is conceivable that the kidney disease might be a co-ordinate or subordinate part of the general vascular disease. This is a theory which is now indicated by the term arterial sclerosis, and such kidneys are described as arteriosclerotic kidneys.
- (2) If, on the other hand, the change were not of a structural kind, but a functional one, any structural change found being of a secondary and subsequent order, the obstruction would necessarily depend upon some impurity in the blood.

But this impurity of the blood, which rendered it more or less obnoxious to the tissues, might be either of renal or extrarenal origin. If of extrarenal origin then the result would be the same as in the former case—namely, a general vascular disease affecting the kidney as well as other parts. But it might also be of renal origin, in which case there must have been some renal mischief antecedent.

Thus, even from the point of view of the vessels, we are brought back again to the two original views about which so much discussion has raged, namely, whether the disease is primarily arterial or primarily renal.

If the changes in the vessels be regarded as primary, as they certainly are in atheroma and may be also in granular kidney, then it might be possible to find cases of marked changes in the vessels with little or no changes in the kidney. And the same would be true if the changes in the vessels and in the kidney both stood in relation to some common cause.

It is only by studying the beginnings of the disease, that is to say, granular kidney in its early stages, that we can hope to

arrive at a solution of these difficulties; for in the later stages all these changes are present together, and it is difficult, if not impossible, to form any sound opinion as to the precedence of the one or the other.

If the renal changes were primary (and that whether the explanation be mechanical or pathological) we might expect to have some evidence of similar changes in the vessels as the consequence of other affections of the kidney, which are not of the nature of granular kidney—for example, where both kidneys are diseased, as the result of obstruction to the ureters, or of tuberculous disease, &c.

Instances of the kind are recorded, and even instances in which the general changes have been associated with unilateral disease of the kidney.

Making all allowance for such exceptional cases, I think it must be admitted that, speaking generally, the vascular changes and the subsequent course of such cases are not those of granular kidney. Any given case which appears to break the rule requires to be carefully worked out, and it may then be found after all to prove it.

If the changes in the vessels were primary then we ought to have evidence of vascular disease before we get evidence of kidney disease, and there ought to be cases in which, at the time of death, the kidneys are found not in a condition of granular change.

Cases of this latter kind are described—that is to say, cases in which the clinical features of granular kidney have been present during life, but at death, though the vessels were diseased, the kidneys were not found granular. Of course, two questions at once arise:—(1) Whether these were really instances of what we should clinically call granular kidney? and (2) Whether the kidneys, though not granular in appearance, were not fibrotic, as in the case I have previously referred to (App., Case VIII).

From whatever point of view, then, we regard granular kidney, whether pathological or clinical, we come to the same conclusion—namely, that, whether primarily arterial or primarily renal, granular kidney is a disease, *sui generis*, and ought on that account to be treated in writing on the subject under a separate heading, and not split up, as it generally is, between diseases of the arteries on the one hand and diseases of the kidneys on the other.

#### ANALOGY TO CIRRHOSIS OF LIVER.

It is always dangerous to argue from analogy, but in many respects cirrhosis of the liver presents many analogies with cirrhosis of the kidneys. Thus the biliary form of cirrhosis (hypertrophic cirrhosis) of the liver would correspond with the ureteric cirrhosis of kidney obstruction, and the occurrence of malignant jaundice or acute yellow atrophy in the one case would correspond with the symptoms of acute uramia in the other. Portal cirrhosis of the liver would then correspond with arterial cirrhosis of the kidney. This analogy would suggest that cirrhosis of the kidney may be the result of some irritant in the blood, rather than of an anatomical change in the vessels. If this were the case, the question might fairly be asked, Why does the stress of the disease fall upon the kidney, and why do other organs escape? But we may ask the similar question in the case of cirrhosis of the liver. The analogy becomes still closer if it be remembered that there are widespread changes in chronic alcoholism-for example, in the heart, vessels, brain, nerves, &c., just as there are in granular kidney, and that cirrhotic liver is sometimes associated with cirrhotic kidneys; so that the same poison-for example, alcohol-does sometimes produce cirrhosis in both organs.

Yeld,\* at St. Bartholomew's Hospital, in 131 cases of cirrhosis of the liver, found the kidneys granular in 44 = 33.5 per cent., Hawkins + gives 15 per cent., Kelynack ‡ 18.5 per cent., Hamilton § 21 per cent.

Moreover, the last stages of cirrhosis of the liver are not very dissimilar from those of the last stages of granular kidney, namely, well-marked cachexia, ending occasionally in acute toxemia. As I shall show later, the resemblance between hepatic and renal toxemia in both the acute and chronic forms is very close. Though each has its individual characters there is a striking family likeness between them.

<sup>\* &#</sup>x27;St. Bartholomew's Hospital Reports' for 1898.

<sup>†</sup> Clifford Allbutt's 'System of Medicine,' iv, 173.

<sup>‡ &#</sup>x27;British Medical Journal Epitome,' May 15th, 1897.

<sup>§ &#</sup>x27;Pathological Society's Transactions,' ii, Part I, 283.

#### RELATION TO GOUT.

Gout may, of course, produce changes in the vessels. It is often associated with changes in the kidneys, and the association between gout and granular kidney is extremely close. The changes which long-standing gout is associated with in the vessels is usually of an atheromatous kind, and in elderly persons who have been the subject of gout for many years, interstitial nephritis is common, but the kidneys are not necessarily granular. In younger people, however, the conditions are different; there the changes in the vessels are not atheromatous, and the kidneys are granular; so that there appears to be justification for the view which is held by some authorities that in young people with gout the kidneys are, with few exceptions, granular.

It is stated that in almost every case of granular kidney, whether the patient has had gout or not, urate of soda is found in some of the joints. This may be, however, but an expression of the obvious fact that the elimination of nitrogenous waste products is defective when the kidneys are diseased. The association between gout and granular kidney is at any rate very common.

But the coexistence of the two conditions does not establish the relation between them; for in the one case an elderly person who has long suffered from gout may as a consequence develop atheromatous changes in his vessels, which may lead to interstitial changes in the kidneys; while a younger person with granular kidney may develop gout in consequence of the renal disease. In other words, as I have already stated, gouty kidneys and granular kidneys are not necessarily the same.

## PART II.

THE SIGNS OF GRANULAR KIDNEY.

#### THE SIGNS OF GRANULAR KIDNEY.

Granular kidney is a very insidious disease. For a long time it presents no symptoms at all, and can be recognised then by physical signs alone.

The only symptom perhaps in the early stage, and even this is not constant, is an increased frequency of micturition, especially at night; but as this has been of such gradual onset that the patient has become quite accustomed to it and does not regard it as peculiar, no complaint is made of it unless it be extreme, and the history of it is often only to be elicited on pointed questioning.

When definite symptoms arise the disease is already far advanced; in other words, the symptoms do not occur until late in the disease.

The symptoms fall, like the lesions, into two groups, namely, cardio-vascular and renal; and, speaking generally, the cardio-vascular are earlier than the renal.

The cardiac symptoms are those of heart failure, more or less pronounced.

The vascular symptoms are the more or less mechanical effects of the vascular lesion, and consist chiefly of hæmorrhage and its results.

The renal symptoms are the latest to develop, and fall into two groups according as they are of gradual development or sudden onset, and they are usually described as chronic and acute uramia respectively. I should prefer to call them acute and chronic renal toxamia. Both alike are to be connected with the wasting in the kidney and its consequent defective action.

Chronic Uremia.—The gradual and progressive wasting of the kidney is attended with the gradual and progressive development of the chronic forms of uremia. Renal cachexia is the name that I should prefer to give to chronic uremia.

It strongly resembles, both in character and course, the cachexia that is seen in a variety of other diseases, for example, in Addison's disease, in the later stages of cirrhosis hepatis, in diabetes, and malignant disease. It consists in a gradually increasing anæmia and asthenia, associated with various miscellaneous symptoms. The symptoms are similar in kind, differing only in the rate of development, to those that are seen after complete obstruction of the ureters or removal of the kidneys, and have been experimentally produced in animals or observed in man as the result of pathological causes or surgical operation.

Acute Uræmia.—Similar as all the symptoms are in chronic uræmia they differ from those which are usually described as acute uræmia, and the difference is not one of degree only but of kind, so that they ought to be distinguished by different names; for the first I would reserve the term renal cachexia, for the second I should use that term which is generally accepted, namely, uræmia, and both alike, both the cachexia and the uræmia, may be of slow or sudden development.

I shall deal with the signs and symptoms of the disease in this order:—

- 1. The physical signs.
- 2. The cardio-vascular symptoms.
- 3. The renal symptoms.

#### THE PHYSICAL SIGNS: THE EARLY STAGES.

It is the early signs of the disease rather than the late symptoms that are of importance. What is required is an early diagnosis before the disease is far advanced, and this is essential if light is to be thrown upon the causes and course of the disease, or if influence is to be successfully exerted upon it by treatment. In the early stage the diagnosis is to be made by physical signs and not by symptoms.

The physical signs are high tension and thickened arteries, hypertrophy of the heart, and albuminuria.

Where these are all present together the diagnosis is easy, even in the young, and the diagnosis thus made during life is verified post mortem.

But if one or other of these physical signs is absent, the question arises, Of what significance are those which remain? For instance, if albuminuria be absent, what do high tension and thickened arteries mean in the young? Or, if the arteries be not thick nor the tension high but albumen be present, what is the significance of this albuminuria? Each of these questions is of great clinical importance and difficulty.

We know that the vascular changes, namely, thickened arteries and high pulse tension, develop so early in the course of granular kidney that they seem to be—I do not say they are, but they almost seem to be—rather coincident, or, as some maintain, even antecedent, phenomena than effects consequent upon and produced by the kidney lesion.

If this were so, vascular changes might be found without the kidney lesion, and such cases are described. I have seen what I believe to have been one case of this kind, but as the kidney has been lost, and I have not had an opportunity of re-examining it, I do not like to lay much stress upon it. The late Professor Kanthack, in discussing this subject with me shortly before his illness, told me he had a case of this kind in his collection, and would lend it to me for demonstration, but this, alas! failing me, I have no fresh facts of my own to bring forward.

#### I.—HYPERTROPHY OF THE HEART.

Post-mortem evidence would point to hypertrophy of the heart as a most important sign of granular kidney, and so it is in the later stages, where the cardiac enlargement is such as to be easily made out.

The heart may reach an enormous size. There is a case in St. Bartholomew's Hospital Museum, in which the heart weighs 28 ounces.

In the early stages hypertrophy of the heart is of very little assistance in the diagnosis, because of the difficulty in recognising it then, especially if in slight degree only.

The frequency with which hypertrophy of the heart is found associated with granular kidney post mortem is great, but at the same time it should be noted that it is not constant.

Goodhart gives 89.6 per cent., Ewald 84 per cent., Galabin 80 per cent., Kanthack and Holmes 90 per cent.

The value of these results is unfortunately depreciated by the almost constant omission of any reference to atheroma in the vessels, for atheroma will equally lead to hypertrophy of the heart. If atheromatous degeneration in the vessels ought to be distinguished, as I maintain, from the changes met with in granular kidney, hypertrophy of the heart ceases to be so important and conclusive a diagnostic sign as it has often been regarded.

The only signs upon which reliance can be placed for the diagnosis of hypertrophy of the heart during life are the increased area of cardiac dulness and displacement of the apex beat downwards and outwards; but in the early stages—that is, with hypertrophy of slight degree—these signs are not marked; and even in the late stages, when the hypertrophy is considerable, they are easily masked by the condition of the lungs. Considerable hypertrophy of the heart may be present and yet be incapable of demonstration by physical signs if, as often happens in granular kidney, it is associated with pulmonary emphysema.

The accentuation of the aortic second sound, which is sometimes described as if pathognomonic of hypertrophy of the heart, is really valueless, for it is met with wherever the arterial tension is raised from any cause whatever, and will be absent even in granular kidney when the tension falls. The same is true of the prolonged first sound, though not quite to the same extent.

The hypertrophy of the heart is probably secondary to the vascular changes and the result of them, and therefore not of the same prime importance as they are, or so likely to be met with early.

## II.—THICKENING OF THE ARTERIES.

Thickening of the arteries is one of the cardinal signs of the disease, and is never absent in advanced cases.

On this point some observations of Holst are interesting, in which he showed in 14 out of 15 cases of granular kidney the vessels of the skin were thickened, though not atheromatous.

Brailey's microscopic, as do Gunn's ophthalmoscopic, observations on

the retinal arteries show the same thing.

#### ITS SIGNIFICANCE IN THE YOUNG.

Of course the arteries grow thicker as age advances, as the result of atheromatous changes, and in elderly persons due allowance must be made for this.

But thickening of the arteries is by no means uncommon in young people, and the question as to what its significance is becomes important in relation to the early stages of granular kidney.

As the thickening of the artery must be estimated by the finger it is necessary to have some sort of guide as to what may be considered real thickening of the artery.

In a young person the healthy artery cannot be distinctly felt with the finger, and when pressed upon flattens out like a piece of tape so as to be hardly felt; but if the artery be thick it can be rolled from side to side, and feels then like a piece of straw or rush, or even, when much thickened, like a pipe stem.

This thickening is real, and not apparent only as the result of increased tension, for the artery may be obliterated by one finger, and still felt by the other as thick as before, and when the tension is low, as it may be in the later stages, the thickening does not disappear.

There are, no doubt, physiological differences in the thickness of natural arteries, but, making allowance for this possibility, it is not uncommon to find the arteries so much thickened in young people as to be of necessity pathological, and it is thickening such as this that I say is by no means uncommon.

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Now, at this age the thickening cannot often be of an atheromatous nature, for although atheroma does occur in early life, it is very much rarer than is the thickening I am now speaking of. The change is no doubt muscular in great part, as it is in undoubted granular kidney, and the effect of nitrite of amyl upon the vessel is the same in each case.

We are thus driven to the conclusion, that if arterial thickening in the young is not an early indication of granular kidney, there must be some other form of arterial disease which we do not at present recognise.

Arterial thickening in young people always rouses my suspicion, and leads me to look carefully for other evidence of granular kidney. Sometimes nothing more is found, and its significance continues doubtful, but that the change is pathological there can be no question. Still, the frequency with which in these cases the signs of granular kidney are either discovered on more careful investigation, or found to develop subsequently, leads me to the conclusion that the probabilities are in favour of this being really the early stage of granular kidney.

I have no actual figures to give in proof of its frequency, but the 8 per cent. which Mahomed gives as the frequency with which the high-tension pulse occurs would represent, to my mind, at least the frequency of thickened arteries, and it may be that we are both dealing with the same thing, for he describes the hightension artery as rolling under the finger, but attributes this to high tension only. It is, however, really due to arterial thickening.

#### III.—HIGH TENSION.

In well-marked (that is, advanced) granular kidney the hightension pulse as well as the thickening of the arteries is well recognised. The sphygmographic tracing is characteristic; the curve has a round or square top, after which the line falls gradually. These peculiarities can be better felt with the finger; the slow, prolonged wave which the pulse makes under the finger is quite as evident as the high tension of the artery between the beats.

The contraction of the heart, which with healthy arteries causes a sudden rise—that is to say, produces a wave with a sharp and somewhat short crest—in granular kidney owing to the resistance which is offered to the circulation, instead of distending the artery greatly for a short time, spends itself in dilating the artery less for a longer time; in this way the long wave, with its square or rounded top, is produced.

The tension is measured between the pulse waves; the arteries, therefore, feel abnormally full as well as abnormally tense between the beats.

When the heart begins to fail, the diminished force of beat does not necessarily alter the character of the wave. The artery may be less distended, and therefore the wave not so high, but its rounded top will still persist. The cardiac weakness may also, by diminishing the amount of blood driven into the arteries at each beat, reduce the tension to some degree, but in spite of that the pulse long retains its peculiar character.

When the tension falls, the fall is due to a failure of the artery, and not necessarily of the heart at all, though both may fail together. The low tension then observed is a neuro-paralytic phenomenon, and a bad sign; it occurs only in the later stages of the disease, but may then continue for some time. Though the tension may be low, the thickening of the arteries can, of course, still be easily made out, and is as characteristic as ever.

A persistently high tension, to whatever cause it may be due, is of itself mischievous, but not so with granular kidney, paradoxical as this may seem. The patient would be best without granular kidneys, but, having granular kidneys, is better with a high

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tension rather than low; in other words, the patient is worse when the tension is low; hence the use of digitalis, which does so much good in these cases by raising the arterial tension.

Low arterial tension—or rather the fall in tension—in the later stages of granular kidney is of great clinical importance, the value of which Sir William Broadbent has lately emphasised.

One other phenomenon I may refer to, which, though implied in what has just been said, is not generally recognised, though it is easy to be observed if looked for. I refer to irregular fluctuations in tension which take place in the later stages of the disease, before the tension becomes persistently low. The tension may vary considerably even in very short spaces of time—for instance, while the finger is feeling the pulse. These fluctuations are analogous to the flushings, the irregular respirations, and other symptoms of irregular vasomotor action which arise under similar conditions. They are very interesting, and may give the earliest indications of the neuro-paralytic failure which is approaching.

In the early stages of granular kidney, go back as far as we may, as soon as the disease is diagnosible the pulse tension is high and the artery thickened. The question then arises, what is the value of a high-pulse tension in a person in whom there is not yet other evidence enough to diagnose granular kidney by?

The clinical importance of high tension has been insisted on in valuable papers written by Sir William Broadbent\* and Dr. Goodhart,† and if we go back 15 years we come to a series of papers written on this subject by the late Dr. Mahomed.‡ All alike directed attention to the clinical importance of the fact, though they do not altogether agree in their theories or conclusions.

Temporary or transient increase of tension may occur in a variety of affections, but it is not to these that I refer; I am dealing with those cases in which the tension is persistently raised.

Now, Mahomed's view was that these were the early initial stages of granular kidney, and this I take to be also Goodhart's opinion. I do not think Mahomed's work has been estimated at its

<sup>\* &#</sup>x27;British Medical Journal,' August, 1883.

<sup>+</sup> Bradshaw Lecture, 1885, 'British Medical Journal,' ii, 327.

<sup>1 &#</sup>x27;Lancet,' January 11th, 1879, &c.

true value. The term he introduced may have had something to do with this, for the expression, "the pre-albuminuric stage," of which he considered high tension to be the chief indication, seemed to assume entirely what he had to prove. His work was based on careful clinical observation, and I believe that he was in the main correct, though possibly he attributed too much to high tension and too little to the thickening of the arteries to which I have referred. Even his own descriptions show that high tension was not the only factor in the pulse, but that the arteries were also thickened.

Sir William Broadbent, differing as he does from Mahomed in theory, yet attaches quite as great significance to the increase of pulse tension. He describes as the ultimate results of this increased tension a variety of symptoms—for example, cardiac failure, general disturbance of health, a sort of cachexia, and even hæmorrhage, which, as he stated, could be truly predicted long before it occurred.

These are the same symptoms as those produced by advanced granular kidney. If the kidneys are not granular in these cases—and of this no proof is given—the arteries must become diseased if hæmorrhage is to occur, for it can hardly be maintained that mere increase of tension can lead to the rupture of healthy vessels. If the vascular change is not atheromatous, nor associated with granular kidney, what is it?

So far as the results to which high tension leads, the views of writers on the subject are agreed; they differ only as to the relation of high tension to granular kidney. These differences in theory would remain a matter of opinion still, if there were not some fresh facts by which to elucidate them. These have been obtained by the more exact and careful study of the early eye changes met with in granular kidney.

As I shall show shortly, our knowledge of the early stages of albuminuric retinitis has been greatly extended of recent years. If in many of these doubtful cases of high pulse-tension and thickened artery albuminuric retinitis or the early changes which lead to it are found, and that even in cases in which albumen may not be present in the urine, the diagnosis of granular kidney will be surely justified. Considering that albuminuric retinitis is not invariably found even in advanced granular kidney, the fact

that it can be discovered in these cases of doubtful nature is very significant and throws a light upon many of those other cases in which for the present the doubt must still remain more or less unsolved.

None of the writers referred to lay any stress upon eye-changes in their papers—at any rate, not as a means of diagnosis; but the importance of these early retinal changes was not then so fully recognised as now. Some, at any rate, of these doubtful cases must be referred to the group of granular kidney, and the probability that a much larger number of them may be fairly so referred is thereby increased.

It appears to me, therefore, that there is presumptive evidence in favour of regarding these cases of high pulse-tension, as well as those of thickened arteries in the young, as the initial stages of granular kidney which we are in search of.

I do not wish to go beyond my facts or to speak dogmatically upon points which may still be open to question, but this appears to me the conclusion to which the facts so far lead. At any rate, a larger number of these cases can now be proved to be granular kidney than has been hitherto supposed.

# ALBUMINURIA.

PHYSIOLOGICAL ALBUMINURIA.

### IV .-- ALBUMINURIA.

Of albuminuria in granular kidney it is not necessary to say much. We know that it is usually small in amount, and that it is not constantly present. It may be found at special times only or may be absent for irregular periods, and might therefore be described as cyclical or intermittent respectively. It may be absent for long periods—even, it is said, altogether, though this is hard to prove. Its amount may be large—as much as half or more—but this generally depends upon some accidental complication, intercurrent nephritis or failure of the heart.

Given a clear case of granular kidney, these variations in the albuminuria do not cause surprise; but clinically the question often presents itself in a somewhat different form. In a given case albuminuria may be the chief symptom; we have then to decide whether granular kidney is the cause or not. It often happens that the evidence is not conclusive, for the patient appears to be in ordinary conditions of health. We are thus introduced to a problem of very great difficulty—that of so-called physiological or functional albuminuria.

#### PHYSIOLOGICAL ALBUMINURIA.

For the present purpose we may regard the causes of albuminuria as falling into two groups, according as they lie in the kidney or outside it. In the latter case it may depend, on the one hand, upon some changes in the tissue or blood before the blood has reached the kidney, and may therefore be called prerenal; and, on the other, the urine may be normal when secreted, the albumen being added to it after secretion; these may be called postrenal. In each of these groups there may be some obvious cause or no cause obvious. Thus, the forms of albuminuria may be arranged into five groups:—

This table draws attention at once to the difficulties which have to be dealt with before the diagnosis of physiological albuminuria can be safely made.

The postrenal group is of great importance, for care must always be taken to exclude all accidental contamination, especially such as would result from the presence of cystitis, gonorrhœa, or from the admixture of discharges from the uterus and vagina, or from the prostate and vesiculæ seminales.

Experimentally, albuminuria has been produced in perfectly healthy persons by excessively albuminous diet, by violent muscular exercise, by cold bathing and exposure to cold; but even then it is probably not capable of being produced in every person, or at any rate not with equal ease, so that even in such cases some other factor is necessary.

Again, in an apparently healthy person albumen may be found occasionally present under certain circumstances, as, for instance, on rising in the morning or after food; and the albuminuria has then been called postural, dietetic, cyclical, or intermittent respectively.

Intermissions or variations in the occurrence of albuminuria are no evidence that there is no disease of the kidneys, for they are frequently observed in persons recovering from acute nephritis, in whom it is by no means uncommon to find albumen absent, it may be, for the greater part of the day, and present only at certain times; in other words, the kidneys may be affected, and yet albuminuria be only intermittent or cyclical. This is, of course, well known to be the case in granular kidney. Even acute nephritis in slight degree may be very easily overlooked, especially in children, and when cedema is absent the nephritis may not even be slight, as the presence of blood and epithelial casts shows.

Admitting all these exceptions, there remains a group of cases in which albuminuria is present, with apparently nothing whatever in the previous history or the actual condition of the patient to explain it. The choice of a term by which these cases can best be described is difficult. Latent albuminuria is, perhaps, that to which least objection can be raised, but it is often not so much latent as overlooked. Early albuminuria is open to the two objections, either that it might be thought to refer to albuminuria only in the young, which would be incorrect, or that it implied the opinion that it was an early stage of disease, and this again would be begging the question. Albuminuria in the apparently healthy, on the whole, seems to me to have least objection to its use, and to state the facts best.

## ALBUMINURIA IN THE APPARENTLY HEALTHY.

The statements made by different observers as to the frequency with which albuminuria occurs in the apparently healthy vary greatly.

Thus, Leube's \* observations upon presumably healthy young adults, which are so often quoted, yield 30 per cent. Fürbinger's † observations upon children yield 10 per cent. Goodhart's ‡ observations for all ages on the contrary only 2.6 per cent., while more recent observations upon boys yield more than 22 per cent. Finally, Possner states that by sufficiently delicate tests albumen may be shown to be present in the urine of everyone.

<sup>\* &#</sup>x27;Virchow's Archiv.,' 1878.

<sup>+ &#</sup>x27;Zeit. f. klin. Med.,' xiii, 1, 1887.

<sup>‡ &#</sup>x27;British Medical Journal,' May 17th, 1890.

Variations so considerable as these in observations made by equally competent observers show that there must be a fallacy somewhere, and it may lie in the fact that different sets of cases have been observed or different tests employed.

To consider Possner's statement first. There is no doubt a certain shedding of epithelium in the genito-urinary passages of everyone; if, then, a large quantity of urine be taken, and, after concentration, treated in elaborate ways, it is evident that the albumen will be detected which is derived from the normal epithelium, and which must be present to a greater or less extent in the urine of everyone. Whether this be the origin of the albumen or not, so far as Possner's observations go, they amount to no more than this, that by special methods a minute amount of albumen may be detected in everyone's urine. This, however, is not what is meant by the clinical term albuminuria.

Looking broadly at the figures given by the different authors, these facts are evident:—

- 1. Most of the observations upon which the statements are based have been made upon children and adolescents.
- 2. And those almost entirely of the male sex.
- That the higher percentages have been obtained by including cases in which very minute traces of albumen were found by the most delicate tests.

In respect of sex, the choice of males has probably been chiefly determined by convenience; at any rate I do not think sex has any influence upon the frequency of albuminuria, although the question has not, I believe, been worked out specifically from this point of view.

In respect of age, Heubner \* states that of the cases published, 77 per cent. were in persons under 20 years of age, and 39 per cent. in children, and to this I may add that hardly more than 10 per cent. at the most were in persons above 25.

Roughly speaking, the cases thus group themselves into two periods:—

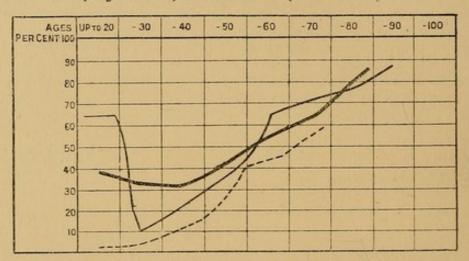
- 1. Those before the age of 25, and
- 2. Those after 25.

The difference between these two periods is indicated upon the diagram, which shows the remarkable frequency of albuminuria before the age of 25 years, the drop which occurs about that age,

<sup>\*</sup> Virchow's 'Jahrb.,' 1890, ii, 722

and the gradual rise with each age-period after that age. The diagram also indicates that the conclusions which apply to the one age-period cannot, without due allowance, be applied to the other.

Diagram Constructed from the Collated Statistics given by Stirling (Light Line) and Levison (Thick Line).



The dotted line shows the frequency of granular kidney in proportion to healthy kidneys, derived from Mahomed's figures.

#### FORMS OF ALBUMEN AND TESTS.

There are many forms of albumen, but we need only consider two forms:—

- 1. Serum-albumen, which for our purpose will also include serum-globulin; and
- 2. Nucleo-albumen, a mucin-like body, which was formerly confused with mucin.

It is by reckoning nucleo-albumen in with serum-albumen that the high percentages of albuminuria have been obtained.

Serum-albumen and nucleo-albumen both alike are precipitated by heat and acetic acid, by salicyl-sulphonic acid, and by picric acid.

The distinguishing tests are these:-

1. Nucleo-albumen gives with acetic acid and dilution a distinct cloud,

while serum-albumen gives at most a haze or nothing at all.

Acetic acid alone precipitates both albumen and nucleo-albumen, the former less rapidly; but on dilution the nucleo-albumen reaction is not diminished, or may be somewhat increased, while the haze with albumen becomes less distinct in proportion to the dilution.

- 2. Heller's test gives a distinct line with albumen at the junction of the two fluids. But with nucleo-albumen the ring forms  $\frac{1}{2}$  to 1 centimetre above the junction, or, if there is no ring, a haze is produced throughout the solution.
- 3. A saturated solution of sodium chloride with acetic acid; when heated, gives a faint reaction with nucleo-albumen but a distinct one with serum-albumen.

4. Ferrocyanide of potassium and acetic acid, which is very sensitive to serum-albumen, gives a reaction with nucleo-albumen only if it be present in considerably more than a trace.

5. A saturated syrupy solution of citric acid precipitates nucleo-albumen much more readily than serum-albumen. The ring method, as in Heller's

test, is the most satisfactory way of making this test.

Mucus also gives some of the above reactions—for example, with heat and acetic acid, salicyl-sulphonic acid, and picric acid, as well as acetic acid in the cold, but it is present only in very slight amount. It does not give the ferrocyanide of potassium test if performed in the right way—that is to say, if the urine be added to the ferrocyanide and acetic acid solution, and not, as the test is often made, by adding the ferrocyanide solution to the urine or by adding acetic acid first.

There is no single test upon which reliance can be placed to distinguish absolutely between nucleo-albumen and serum-albumen, but these tests systematically used in order will suffice to make the distinction quite clearly in most cases.

Desiring to form my own opinion upon this question, I asked Mr. Levison to undertake some observations for me. He has done the work with very great care, and his paper will shortly be published in extenso; for the present I shall only give the more important conclusions.

He examined 336 healthy persons, of whom 108 were young soldiers; the rest were hospital convalescents.

The cases were thus grouped:-

		Below 25.	Above 25.
Males	 254	155	99
Females	 82	31	51
Total	 336	186	150

A proteid reaction of some kind was obtained in 136, or 40.47 per cent., serum-albumen occurring in 22.02 per cent., and nucleo-albumen in 18.05 per cent.

The figures are set forth in the following table:-	The	figures	are se	t forth	in the	following	table :-
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	Below 25.	Above 25.
Proteid reaction of some kind in 136 cases = 40.47 per cent.	75 cases	61 cases
Serum-albumen in 74 cases = 22.02 per cent.	42 ,,	32 ,,
Nucleo-albumen in 62 cases = 18.44 per cent.	33 ,,	29 "
Negative in 200 cases	112 "	88 "

Making allowance for the different numbers in the two groups that is, above 25 and below 25, the percentage was almost exactly the same in each.

The amount of albumen in all cases was extremely small, and probably in quite half the cases would have been entirely overlooked in the ordinary methods of examination. The largest amount in these series was not more than would give a ring of 1 to 2 millimetres in thickness with nitric acid.

Nucleo-albumen was found alone in nearly one-half of the cases—18.44 per cent., and this was the same in both the groups—that is, before 25 as well as after 25. It is probable, therefore, that in Leube's results, as in these, one-half were due to nucleo-albumen.

Of the cases in which serum-albumen was present (22 per cent.), in 12 per cent. the amount was quite minute, and only in the remaining 10 per cent. would have been easily recognisable by the ordinary methods.

No clinical difference could be detected between the cases with serum-albumen and those with nucleo-albumen, nor should any be expected if it be true that nucleo-albumen is but a salt of ordinary albumen with chondroitic-sulphuric acid or nucleic acid, which are constituents of normal urine. The age distribution of the cases examined is shown in the following table:—

$_{ m Age-P}$	eriod.	Total Number of Cases Examined.	Albumen : Serum-A. Nucleo-A.	Percentage to Cases at each Age-Period	
1-5 years		 2	0	0.00	
5-12 ,,		 18	2	11.10	
12-18 ,,		 37	14	37.80	
18-25 ,,		 129	59	45.70	
25-35 ,,		 47	17	36 .10	
35-45 ,,		 32	11	34 · 40	
45-55 "		 37	15	40.50	
55-65 ,,		 22	11	50.00	
65-75 .,		 11	6	54.10	
Above 75 years		 1	1	100.00	
Total .		 336	136	40.37	

These observations show that the great frequency of albuminuria in apparently healthy persons is not overstated if all those cases be included in which there is the minutest possible trace evident only on careful examination, but inasmuch as in most of these cases, probably one-half, the trace is so small that it can only be detected with great care when specially looked for, the contrast between these results and the general impression obtained from ordinary clinical experience is not so great as at first sight it appears to be.

It is evident that the conclusions drawn as to the frequency of albuminuria in one age-period must not be applied without due allowance to any other age-period. Speaking generally, the significance of albuminuria is entirely different before 25 and after 25.

What is required is a systematic series of observations in which the same carefully-selected tests have been employed, and a sufficient number of cases of the one sex and of the other examined at the different age-periods:—

1. In infants	ip to th	e age of 5.
2. In young children		from 5 to 10.
3. In boys or girls—the school age		,, 10 ,, 18.
4. In young adolescents		,, 18 ,, 25.
5. In young adults		,, 25 ,, 30.
6. In the middle period of life		,, 30 ,, 50.
7. In the later periods of life		over 50.

- 1. Infancy and Early Childhood.—Of albuminuria in infancy and early childhood we have not much information. In new-born infants albuminuria is stated to be common, but that need not be a matter of surprise. In babies up to a few months old, Holt quotes Cruse as having found albuminuria in 28 out of 90 cases (31.1 per cent.).
- 2. From Infancy up to the Age of 10.—Albuminuria is said to be less frequent up to the age of 10. Ward \* examined 120 cases between the ages of 5 and 12 years, but his results bear this statement out fairly well, for he obtained a reaction with heat and acetic acid in 29 (24·16 per cent.), but the amount was always minute and sometimes the merest trace. In only nine cases (that is, 7·5 per cent.) was the amount appreciable.
- 3. From 10 to 18 years—that is, Children during School Age.—At this period statistics abound and show the extraordinary frequency of albuminuria.

The following are some of the figures:-

```
.... 369 boys
                                                   .... 20.8 per cent.
Stirling ....
                                            ....
                                                       22.0
Ribbert ....
                    240
                              summer (104 cases) ....
                                                       29.8
                             winter (136 cases)
                                                       16.0
                                                                   at least
                             many years' experience
                                                      22.0
Grainger Stewart
                    100 boys
                                                      17.0
```

<sup>\*</sup> These observations were made in Dr. Garrod's out-patient department in the Hospital for Sick Children, Great Ormond Street.

Stirling's table shows a gradual increase in frequency from the age of 12 to 16.

Age	 12 years.	13 years.	14 years.	15 years.	16 years.
Number of cases	 20	59	88	147	55
Percentage	 5.0	10.2	16.0	29.4	23.6

Although the amount of albumen is usually small it may be considerable.

Thus in a specimen which was kindly sent me recently for examination by Dr. Clement Dukes the amount of albumen was as much as 2 per cent. —that is, 20 grammes in the litre. This was in the morning urine. In the evening, after a day's rest in bed, the albumen was not more than a trace, and this chiefly nucleo-albumen. In a third sample, after the boy had got up again, the amount of albumen was nearly as large as before —namely, 1'4 per cent., and about  $\frac{1}{8} = 0.18$ , was serum-globulin and nucleo-albumen. This specimen was centrifugalised, and showed a few granular and epithelial casts and some epithelial cells.

It has been suggested that the presence of albuminuria at these ages is due to the active development of the sexual organs, and probably also to the presence in the urine of discharges derived from these organs, and that the form of albumen is generally nucleo-albumen. The albumen is, however, generally serumalbumen and not nucleo-albumen, and there is no proof that nucleo-albumen is derived from the urinary passages and not from the kidney. Nor is there any proof that masturbation is a predisposing cause; indeed, what evidence there is, is against it.

4. From 18 to 25 years, Adolescents.—It is upon cases of this period that most of the statements as to physiological albuminuria in adults are based.

Most of the observations have been made upon young soldiers:

Leube			119 3	oung	soldiers	 20.4 pe	r cent.
Grainger 8	Stewa	art	205	"	"	 27.6	,,
Tieman			186	,,	,,	 27.4	,,
Zeehuisen			144	"	,,	 14.6	,,
Levison			108	"	17	 47.25	. ,,
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The 108 young soldiers that Levison examined ranged from 17 to 27 years of age, but of these only eight were above 25.

A proteid reaction of some kind was found in 51 cases = 47:25 per cent-

This was due to serum-albumen in 30 cases = 27.75 per cent. to nucleo-albumen in 21 cases = 19.50 per cent.

In all the nucleo-albumen group and half the serum-albumen group the quantity present was very minute = 33.4 per cent., that is, in only 14 per cent. was the quantity certain to have been detected by ordinary testing.

In three of the latter cases in which a moderate amount of albumen was found, careful microscopical examination was made after centrifugalising, and nothing discovered except a few epithelial cells.

The effect of exercise is well shown-

In 29 Cases after Drill.	In 79 Cases without Drill.	24 New Recruits who had not been Drilled.
Proteid of some kind in 18 cases	In 33 cases	5 cases
=62 · 3 per cent.	=41.7 per cent.	= 20 .75
Serum-albumen in 10 cases	In 20 cases	3 cases
= 34 '48 per cent.	=25.31 per cent.	=12.54
Nucleo-albumen in 8 cases	In 13 cases	2 cases
= 27 ·82 per cent.	=16:45 per cent.	=8 ·25

Thus morning drill considerably increased the total frequency of albuminuria, but made no difference in the relative frequency of the two kinds of albumen.

5. From 25 to 30 Years.—For this period there are very few published statistics. By the kindness of friends I have been enabled to obtain the experience of some life offices relative to the occurrence of albuminuria in applicants for insurance presumably healthy below the age of 30 years.

At the Provident Clerks' Life Assurance Association I find that in the course of the five years 1893 to 1898, 7,950 policies came before the office, and 4,488, that is to say, a good deal more than half, were persons under 30 years of age; out of this number, 25 cases were found to have albumen in the urine. This was a

percentage well under 1, actually of 0.55; of this number no fewer than 18, that is, two-thirds, were under the age of 25.

At another office, for the period of 10 years, the number of applicants below 30 years of age was, roughly speaking, about 750, and out of these seven only were deferred or rejected on the ground of albuminuria; this gives a percentage of nearly 1.

No doubt more precise examination would have raised this percentage somewhat; still, I think the facts are sufficient to show that at this age-period albuminuria is much less common than in any precedent period, and that it probably stands at its lowest point in life.

6. Above 30 Years.—There are a great many figures to show the general frequency of albuminuria for all ages during the insurance period, but they tell us little of what we really want to know—namely, the relative prevalence of albuminuria at the different age-periods throughout adult life.

Thus Washburn, for 1,000 cases, found 3.5 per cent.

", Munn ", 1,000 ", 11·0 ", Tieman ", 2,000 ", 9·0 ", Anonymous ", 6,400 ", 7·1 ",

To these we may add as derived from general sources :-

Grainger Stewart 100 adults .... 10.0 per cent. Goodhart .... 1,600 out-patients 2.6 ,,

With these we may compare Levison's figures, which yield a much higher average percentage, equal to 40 per cent.

Petersen's results give the key to the difference in the percentages obtained.

He examined 1,000 soldiers and recruits by Heller's test only, and found albumen present in the morning urine, on rising, in 3.79 per cent.; at 11 a.m., after three hours' drill, 15.11 per cent.; at 6 p.m., after two hours' drill, 9.02 per cent.

The difference in results is evidently due to the different tests employed, and possibly also to the different times at which the urine examined was passed.

It would greatly simplify matters if we could agree upon a standard test, and the best, in my opinion, would be Heller's, *i.e.*, the cold-nitric-acid-ring-test. It is sufficiently delicate, for it will

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show one part in 10,000 at once, and one part in 35,000 in four minutes.

An amount of albumen which cannot be shown by Heller's test may,  $qu\hat{a}$  albumen, be disregarded clinically.

THE SIGNIFICANCE OF ALBUMINURIA IN THE APPARENTLY HEALTHY.

Albuminuria in the apparently healthy, apart from its scientific interest, has a practical bearing—in boyhood as affecting the school career, in young men as affecting the chance of appointments, and in adult life as affecting insurance.

In considering the significance of albuminuria, it will be well to retain the division into two groups, before and after 25, as we have hitherto done.

## SIGNIFICANCE IN BOYS AND ADOLESCENTS.

Albuminuria is common during the period of growth and immaturity, and becomes less frequent when development is approaching completion.

The question arises whether we can connect these two facts together. Assuming that during the period of growth all the tissues of the body are in a condition of instability and immaturity, it is easy to suppose that very slight causes might disturb their balance, and thus in the case of the kidneys albumen might appear in the urine as the result of causes which would have no effect upon the fully-developed or adult organism or organ.

The clinical significance of this albuminuria in childhood and adolescence can only be determined by clinical observation, by carefully investigating the cases at the time, and watching them over a long period.

The boys in whom albuminuria is found appear to fall into at least two groups. In the one the lad appears to be robust and healthy, has a rigid artery and high tension. These are the cases which Clement Dukes has recorded as met with so frequently in schoolboys. In the other the lad is not robust and healthy, but feeble and pale; the tension is low and the artery not thickened. These two groups probably indicate not only different conditions but a different prognosis.

In no case is the albuminuria strictly speaking physiological; it is always pathological, though not necessarily renal. What we require to know is the course which these cases run in after-life.

If albuminuria is so common in youth and adolescence, and becomes so much less frequent in early adult life, it follows that many of the cases have no very serious significance—in other words, that they get well. This, indeed, we also know from direct observation. Yet with those who have most experience there is evidently still some lurking doubt about the ultimate result in not a few instances.

Granting that many, perhaps the majority, ultimately recover, there remains another group in which the patients continue to pass albumen for many years and yet remain in good health, and a third in which signs of renal disease ultimately develop.

Johnson\* described a case in which recovery took place after seven years of persistent albuminuria, and other cases are recorded in which the albuminuria persisted for 10, 15, or even 20 years, without other evidence of disease appearing. Saundby+ gives the case of a man rejected for insurance on account of albuminuria who was in good health 18 years afterwards.

Yet, as will be shown later, maintenance of health for many years is not incompatible with damaged kidneys and premature death.

Making all allowance for exceptional cases such as these, the significance of albuminuria in early life must for the present still remain doubtful.

Clement Dukes says in one of his last writings on the subject:—
"Familiarity with the disease has not bred the proverbial contempt,
for I am convinced that a number of these cases never recover. In many,
indeed the majority, the albuminuria is transient and never recurs; in
others it becomes persistent from a frequent repetition of transient attacks,
from neglect or imprudence, or from failure of accurate diagnosis, and
eventually results in chronic disease of the kidney."

All these cases must be carefully watched for a long time before nephritis can be positively excluded; the more constant and persistent the albuminuria is the greater the probability of renal disease, and the longer it continues the more serious the outlook.‡

<sup>\* &#</sup>x27;British Medical Journal,' ii, 1879.

<sup>+</sup> Ibid., May 10th, 1879.

<sup>#</sup> Cf. Holt, 'Diseases of Children.'

#### SIGNIFICANCE IN ADULT LIFE.

This is important in relation to life insurance.

Before 25 many cases may be curable; after 25 the chances of renal disease increase rapidly. Conclusions drawn from cases under 25 cannot be applied without consideration to cases over 25.

The diagram already given (p. 44) shows, first, the frequency of albuminuria at the different age-periods after 25, and, secondly, the relative frequency of granular kidney after 25.

There is a great difference of opinion professionally as to the significance and importance of the traces of albuminuria met with in otherwise apparently healthy persons applying for insurance, and I think there is also much difference in practice.

It would be important, therefore, to trace these cases in order to ascertain what became of them in after-life. In some instances this has been done.

Thus, in Washburn's series, out of 1,072 cases, 38 had albuminuria—that is to say, 3.55 per cent. Of these 38 cases, 18 were traced; 14 more of these cases were known to be living, but the condition of the urine was unknown, and six were lost sight of. Of the 18 cases traced, six were stated to have recovered; six died of renal disease; five others had albumen still some years after; and one died of phthisis.

Thus, out of 18 cases, six had renal disease for certain and five more probably, giving a percentage of not less than 33, and possibly of 60. Washburn calculated that the mortality rate among these cases for the age was 17.54 per cent.—that is to say, was nearly double the normal average.

Munn found that, out of 25 cases, one died within the year following the examination, and four more died during the subsequent three years, while in all the rest the health had obviously deteriorated.

Rabagliati's results bear, perhaps, only indirectly upon the question we are discussing. He showed in connection with the Scottish Widows' Fund that, of 3,246 deaths, 255 were referred to urinary diseases—that is, 7.8 per cent., and of these, 4.3 per cent. were due to diseases of the kidneys and nephritis. During the same period in Bradford the general mortality from urinary diseases of males above 15 yielded the rate of 3.4 per cent. Thus, the insured lives had a mortality rate for kidney disease much above the normal. He further states that the average age of albuminuria at death was 57.

We may thus conclude that, in spite of all ordinary care and consideration, a considerable number of renal cases slip through the medical examination; and hence the importance of not minimising the evidence, even when it is slight, if any early renal mischief is apparent.

From another office I have a very valuable report, to the author of which I should like to acknowledge my indebtedness, but I am prevented by the condition upon which the information is furnished me, so that, while I can vouch for the figures, the report must remain anonymous.

In a series of 6,400 adults examined between the years 1877 and 1893, 454 cases of albuminuria were found. Of 137 cases among these in which the urine was examined microscopically, casts were found in 31—that is, in about 23 per cent. Thus, in round numbers, albumen occurred in about 7 per cent. of all apparently healthy adults; the probability of finding casts in the urine associated with albumen was about 1 in 4.

Some of these cases have been traced in after-life, and the following figures have been furnished me:—

## Albuminuria in Adults Apparently Healthy.

Very few were examined microscopically. The specific gravity ranged from 1,034 down. Personal and family history and build were good as a rule, but some cases have been admitted in which one or more of these factors have been under the average.

TABLE I.

		Ages bet and	ween 20	B. Ages 40 and over.			
		Living at end of	Died during	Living at end of	Died during		
1st year	 	 194	2	120	4		
2nd ,,	 	 193	1 5	115	5		
3rd ,,	 	 188	5	113	2		
4th ,,	 	 187	1	109	4		
5th ,,	 	 181	5 7 5	106	3 5		
6th ,,	 	 174	7	101			
7th ,,	 	 166	5	89	12		
8th ,,	 	 147	6 2	78	2 3		
9th ,,	 	 99	2	53	3		
10th ,,	 	 44	-	27	2 2		
11th "	 	 22	1	13	2		
12th "	 	 16	1/	10	-		
13th ,,	 	 11	_	5			
14th ,,	 	 8	_	3	-		
15th "	 	 .5	-	1	-		
16th ,,	 	 2	-	-	-		

Among these cases 49 were stated to have had casts, and the following table gives the results in these:—

TABLE II.

	_		Ages bet	ween 20	Ages 40 a	
			Living at end of	Died during	Living at end of	Died during
1st year		 	25	_	22	2
2nd ,,		 	25	_	20	2 2
3rd ,,		 	24	1	18	2
4th ,,		 	24	_	18	_
5th ,,		 	22	2	18	-
6th ,,		 	21	2 1 1	16	2
7th ,,		 	20	1	13	3
8th ,,		 	20	_	12	1 1 1
9th ,,		 	17	1	10	1
10th ,,		 	12	-	5	1
11th ,,		 	5 2 2 2	1	4	-
12th "		 	2	1	3 3	-
13th ,,		 	2	-	3	-
14th ,,		 	2	-	-	-
15th "		 	1	-	-	-
16th ,,		 	1	_	-	-
17th "		 	1	-	-	-

Table I.—For the first eight years or so nearly all the cases were traced, and the record is remarkably complete; after this many apparently were lost sight of. During those eight years the total mortality in Group A, that is, in cases under 40, was 17 per cent., and in Group B 30 per cent., a very considerable death-rate for presumably healthy lives. Evidently, therefore, the albuminuria largely increased the risk.

But the table also shows that some of the cases lived a long time. Thus, in Group A, at least 44 persons, that is, 22 per cent., were known to have lived 10 years, and probably several others were alive who had been lost sight of. Sixteen were known to be alive after 12 years, eight after 14, and two at least lived more than 16 years. Similar facts are shown in Group B.

TABLE II.—In this class, taking eight years also, the mortality was still higher—namely, 20 per cent. in Group A, and 50 per cent.

in Group B. Still, here again some individuals were known to have survived for many years.

The following table has been calculated for me by an actuary friend, to show approximately, as far as the figures permit, the difference in mortality compared with healthy males, and to make the results more obvious they have been taken for differences of two years in age:—

	Rate of Yes			Rate of following Year.		
Ages Attained.*	Rate from Figures Given.	ures Healthy	Rate from Figures Given.	Rate for Healthy Males.		
30	_	_	50½	3.70	1 .97	
32	1.56	1.06	$52\frac{1}{2}$	2.64	2.20	
34	3 .27	1.11	54½	3.74	2.43	
36	3.33	1.16	561	7 .13	2 .69	

<sup>\*</sup> Starting with average of those given, and assuming uniform increase for eight years.

Without laying any stress upon the actual figures these calculations show how largely the presence of albuminuria raises the mortality, as well in those below 40 as in those above.

We must conclude, therefore, that for the ages at which life insurances are generally effected, that is, from 25 years upwards, the presence of even a trace of albumen in the urine is of considerable significance. It is more and more likely to mean disease as age advances, and therefore the risk to the office continually increases. Even at the earlier periods—from 25 to 35—it is a question whether these lives should be accepted even with a considerable addition, owing to the difficulty of excluding the commencement of granular kidney.

Rabagliati threw his conclusions into the following form:—
(1) over 40, reject; (2) under 40, load heavily; (3) in youn adults, rate up moderately.

With the first recommendation I entirely concur. The second

is necessary, but the loading might be prohibitive and tantamount to rejection for any age over 30. In respect of the third, between 25 and 30 there would have to be a fairly heavy loading, but between 18 and 25 many cases could be safely accepted without any great risk.

Each case of this kind, however, must be considered on its merits. Albuminuria is not the only fact to be considered, suspicious as it may be. At each age there may be innocent and harmful albuminuria, and it is the business of the physician to distinguish, if possible, between them.

I do not know any class of case which presents greater difficulties to the medical adviser to the life office, or affords greater scope for good judgment and skill; so that while rightly appraising the risk to the office on the one hand, he should at the same time advise what is fair and just to the proposer.

#### Conclusions.

The general conclusions to which these considerations lead are these:—

- 1. That the so-called physiological albuminuria is always pathological, even if not always renal, when the amount of albumen is more than the merest trace.
- 2. It is probably pathological, even in those cases in which the amount of albumen is but a trace, and no cause obvious.

In this respect it is interesting to recall the experience of Eales, who, out of 14 cases sent him as instances of physiological albuminuria, found no fewer than five with marked albuminuric retinitis, showing that what he had to deal with was not even physiological albuminuria at all, but well advanced kidney disease.

It is clear, therefore, that in every case the patient must be carefully examined, every possible cause of albuminuria searched for, and every other condition in the patient noted.

If nothing else be found and the albuminuria exist alone, it may possibly be harmless or accidental, and of no serious significance.

If renal derivatives are found as well as albumen the chances of renal disease are greatly increased. Even if no renal derivatives are found, the kidneys are in all probability granular if the arteries are thickened and the pulsetension high.

The two following cases are of interest as illustrating the questions that arise in connection with life assurance. There is the further interest in them both that my suspicion was aroused by their "facies"; in the lad on account of the pink and white somewhat pallid delicate appearance; in the man on account of the earthy, sallow, tanned colour. The former was without doubt a case of granular kidney, and the latter in all probability, in spite of the fact that the urine on the three occasions on which it was examined (once by the local doctor and twice by myself) presented no abnormality other than a slight lightness of colour and a somewhat reduced specific gravity:—

Eustace H., aged 33, was referred to me for report by the local advisers of the insurance company, as being a case of aortic disease, and therefore

ineligible for insurance.

He was a muscular and well-developed man of 5 feet 8 inches in height and 10 st. 4 lbs. in weight. He said he was in excellent health, and had never been ill in his life. He had, however, a sallow, earthy complexion, and looked more like 50 than 33 years of age. His appearance was that of a man who had spent many years in the tropics and had only recently come home, but as a matter of fact he had never been out of England.

The heart's apex was in the sixth space just inside the nipple line, and the cardiac dulness a little increased upwards but not to the right. The second aortic sound was much accentuated, the first sound over the ventricle prolonged and booming, but no murmur was audible. The murmur which had been heard by the local doctor was probably systolic and the result of the excitement of examination. At any rate, though there were no signs of valvular disease, there was obviously considerable hypertrophy of the left ventricle.

The arteries at the wrist were remarkably thick—thicker, indeed, than they often are at 70; the tension could not be estimated because of the

extreme change in the walls of the vessels.

The urine was light in colour, but contained no albumen, though I

tested it carefully on two separate occasions.

The hypertrophy of the heart, the extreme change in the vessels in so young a man, suggested the existence of granular kidney in an advanced stage, though the urine yielded no trace of albumen.

I examined the eyes, but could discover no white spots or hæmorrhages, but some of the arteries had a broad white streak, which, though not quite bright enough to deserve the name "silver wire," was certainly abnormal.

It was evident that the man had extensive arterial disease, in all probability associated with granular kidney, but whether so or not the condition of the arteries rendered his acceptance for insurance impossible, and the life was declined.

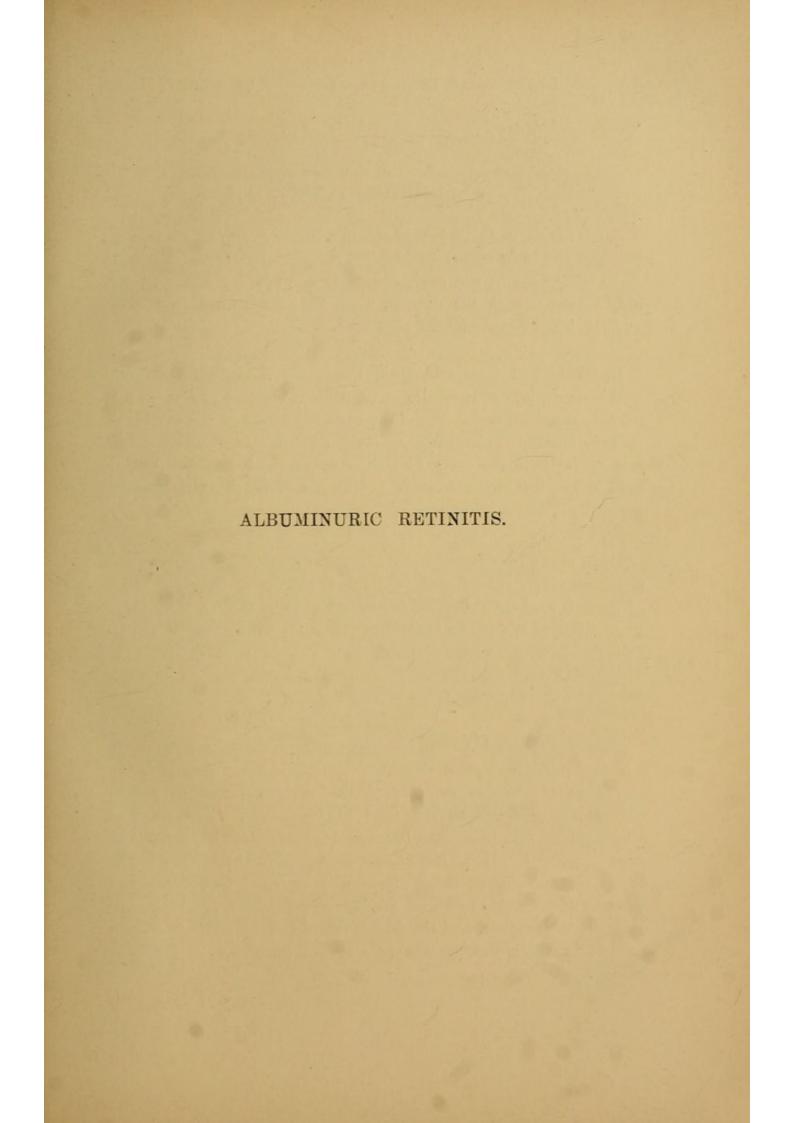
The second case was that of a lad, 19 years of age, who gave a perfectly good history of health both as regarded himself and his family. I was struck by his florid, pink and white complexion, which gave him a delicate wax-doll appearance.

The arteries were somewhat thickened, and the tension Ligh; a small

but very distinct trace of albumen was found in the urine.

The only conclusion under the circumstances to be drawn was that the albuminuria could not be physiological, but that, being associated with thickened arteries and high tension, it was due to granular kidney.

I was therefore compelled to advise that the application should be declined, with the result, I fear, that the lad lost his appointment, for it was contingent on his being accepted for insurance at ordinary rates.



#### V.—ALBUMINURIC RETINITIS.

Albuminuric retinitis brings me to another group of signs, viz., those of the later stage; for, typical as albuminuric retinitis is, it gives little help in the early diagnosis of granular kidney, for it only occurs late in the disease, when the arteries are degenerate and the kidney-mischief far advanced.

In its typical form albuminuric retinitis is characteristic and pathognomonic, i.e., it occurs in no other condition except that of chronic renal disease. In some stages, especially in the exudative or inflammatory form, it may closely resemble the optic neuritis met with in intracranial disease, e.g., cerebral tumour, but in such cases its importance is not so great, for the diagnosis is generally clear on other grounds.

Upon many important points the statements of different authorities are very conflicting and difficult to reconcile. This difference of opinion could, I think, be explained if it were true that there were different forms of albuminuric retinitis with different pathological histories. No attempt, however, is usually made to distinguish the different forms from one another or to connect them with the different forms of renal disease.

Kidney diseases fall into two great groups, according as dropsy is a prominent symptom or not. Granular kidney may be taken as a type of the one group and the various forms of parenchymatous nephritis as the type of the other. The kind of albuminuric retinitis most frequently met with in these two groups will, I think, be found to be different. Thus, the exudative and inflammatory form will be most frequently met with in those cases in which dropsy predominates, *i.e.*, in parenchymatous nephritis, and the degenerative and hæmorrhagic form in that in which dropsy is absent or accidental, *i.e.*, in granular kidney.

#### FORMS OF ALBUMINURIC RETINITIS.

The lesions of albuminuric retinitis consist of (1) white patches, (2) hæmorrhages, and (3) exudation variously combined with each other, and, lastly (4), quasi-inflammatory conditions.

It would seem from some of the statements on the subject as if these were but different stages of an affection culminating in the last, or as it is often called the most extreme, form. Yet this is by no means the case; for the last form is often independent of the others, is frequently of very rapid onset and acute development, and, extreme as it is, may disappear without a trace.

## 1. THE EXUDATIVE (INFLAMMATORY—EXTREME) FORM.

In this form the changes are wide-spread and extreme. Thus, the disc may be greatly swollen, the edge indistinct and frayed out, and the whole retina hazy, as the result, no doubt, of cedema. White patches, more or less bright, of varying size and irregular shape, are scattered over the whole central part of the retina, especially round the disc and yellow spot. They are due to exudation in the deeper parts of the retina. The vessels are often visible as they run over the white patches, and are generally not so much covered with effusion as is the case in other forms of neuro-retinitis. The veins are greatly distended and the arteries small, while hæmorrhages are common, both flame-shaped and irregular. In fact, this form closely resembles what is seen in other forms of acute neuro-retinitis, and may in some cases introduce difficulties of diagnosis.

Thus I have recorded two cases in which the resemblance to cerebral tumour was so close that the diagnosis was not certain until the patient had been under close observation, the symptoms in both cases being violent headache, vomiting, giddiness, loss of sight, and well marked neuro-retinitis.

Yet in most cases there is something in the condition of the eye to suggest the true nature of the disease.

Speaking generally, so far as I can judge at present, this form of albuminuric retinitis is rare except in the parenchymatous group of renal disease, *i.e.*, in the acute and chronic tubal forms.

It may be connected, I think, with renal dropsy, and as renal dropsy is not very common in granular kidney, so this form of albuminuric retinitis but rarely occurs in granular kidney.

We do not know why it occurs in these cases, for it is not simply associated with dropsy, i.e., it does not seem to be the direct result of the dropsy, for, speaking generally, it is not common even in parenchymatous nephritis when the dropsy is extreme, and it is met with, too, when the dropsy is only moderate. Again, it is rare in acute cases, or in the early stages, of parenchymatous nephritis, though it is in these cases that the dropsy is usually most marked, while it is not so rare in the later stages, i.e., in the chronic cases. This form is, I believe, always bilateral; and taking this fact into consideration I think it is most probably a subacute toxic inflammation.

One thing is remarkable considering the amount and extent of the exudation, viz., that detachment of the retina in these cases is comparatively rare. Most of the instances recorded, and the only ones I have myself seen, have occurred not in the acute cases at all, but in granular kidney, where there was but little or no general dropsy.

It is sometimes seen in quite early cases of parenchymatous nephritis, *i.e.*, during the acute stage, as in the following instance:—

Emily R., aged 23, was in good health until the beginning of May, when, after a severe cold, the eyelids were found swelled in the morning, and the legs became swollen towards the end of the day. She passed a small quantity of water, but had to rise once or twice in the night for that purpose. She gave up work after a few days, and remained at home, though not in bed. At the end of May her sight became dim. She was a good deal troubled with headache, but had no vomiting.

When she came under observation, at the end of June, she was very pale, with much cedema of the legs and body walls, and some puffiness of the face. The urine contained a great deal of albumen (two-thirds), with hyaline and granular casts. Urea, 1.15 per cent.

The pulse was of low tension, and the artery normal. The heart was somewhat dilated, and the sounds feeble. The pupils were widely dilated, and reacted with little energy.

Ophthalmoscopic examination revealed very extreme albuminuric retinitis; both discs were hazy, and the edges indistinct; the whole background was occupied by irregular white areas, over which some of the fine retinal vessels could be seen running. There were, besides, a few irregular hæmorrhages, the veins were much distended, and the arteries

small. The sight was greatly impaired (about  $\frac{1}{36}$ ) in both eyes, and there

was some general reduction in the field of vision.

On October 20th the retinitis had greatly improved, the large patches of effusion had almost gone, and in their place were left small, many of them minute, glistening white patches very like those of the degenerate form. The disc swelling had almost completely disappeared. Vision had improved, and was still much impaired.

It is more common in the later stages of chronic parenchymatous nephritis.

Mary B., aged 58, had rheumatic fever at the age of 16, and was left with heart disease. She had married young, and had had four children. She had been in good health all her life, but for the last eight years had suffered from shortness of breath and attacks of bronchitis. Otherwise she had been fairly well until December, 1897, when she had a severe attack of bronchitis, and had been invalided since.

In October, 1898, the legs and abdomen began to swell; she had much headache; double optic neuritis was discovered; and she was sent to the

hospital with a diagnosis of cerebral tumour.

She was found to be very dropsical, to have mitral incompetence and general bronchitis, and to be passing a considerable amount of albumen in the urine. Extreme albuminuric retinitis was present in both eyes, with large white areas and small hæmorrhages, and with well-marked radiating patches round each yellow spot, the discs being swollen and indistinct.

The chief symptoms were dyspnœa, occasional vomiting and diarrhœa, cramp, severe headache, and pain in the upper part of the cervical and dorsal region.

The urine was 1024, small in quantity, free from blood and sugar,

but contained much albumen.

Shortly after admission she became very noisy, restless, and delirious. Ultimately she grew almost maniacal, so that she had to be isolated. Gradually the delirium subsided, and she returned to the ward; the dropsy diminished somewhat, but the weakness increased, and she finally died of exhaustion two months after her admission.

I inclined to the opinion that she had granular kidney, the amount of albumen in the urine and the dropsy being greatly dependent, I thought, upon the mitral disease and the failure of the heart. The tension was low throughout, but this was thought to depend upon her general asthenic condition; but, on the other hand, the arteries were not thickened.

Post mortem.—Mitral disease, with its concomitants, was found; the liver was nutmeg, and weighed 75 ounces; the kidneys were large, weighing 7 and  $6\frac{1}{2}$  ounces respectively; the capsule was adherent, and there were a few small cysts beneath it, but the surface was not

granular.

The kidneys presented the usual lesions of chronic parenchymatous nephritis. The vessels were greatly congested, consequent, no doubt, upon the morbus cordis. There was a good deal of imperfectly developed fibrous tissue in places, both in the cortex and in the medulla. In patches the fibrous tissue was fully formed, but the kidney did not present the microscopic characters of the granular contracted kidney. It was described as "contracting-white" by the pathologist.

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Though in many of these cases of chronic parenchymatous nephritis the fibrosis is patchy and not extensive, in others it may be widespread or general throughout the kidney, both in the cortex and medulla, and the capsules of the malpighian bodies may be considerably thickened.

Edward B., aged 23, was admitted into St. Bartholomew's Hospital with general cedema, headache, vomiting, and occasional fits. His face was much swollen, and he had the typical aspect of chronic parenchy-

matous nephritis.

The history which he gave was this:—He was well until February, 1898, when he began to get out of health. In the middle of March, without any warning, he had a fit, the first in his life; a succession of fits followed during the next few hours. After this his face and body began to get a little puffy, and his strength failed; the swelling continued, and gradually increased.

At the end of October, six months later, he suddenly lost his sight, and in a few days became blind, except that he still retained a general sense of sight. In the middle of November he began to be sick after food, and had some epigastric pain. He then had another series of fits, and since that time had found himself a little deaf. He was admitted a fortnight

later.

The patient was a tall man, extremely anæmic, with a great deal of cedema of the legs and subcutaneous tissue generally, some cedema of the face and eyelids; the cardiac dulness was much increased, and the heart appeared dilated and hypertrophied; there was some general bronchitis, slight enlargement of the liver, and a little ascites.

The urine, of 1010 specific gravity, contained about one-sixth of albumen with a little blood and some blood- and epithelial-casts. The arteries were somewhat thickened, but not by any means markedly so,

and the tension was low.

The ophthalmoscope showed the most extreme double albuminuric retinitis that could well be seen; the discs could hardly be defined on account of the swelling which surrounded them, the whole fundus was involved, and there was scattered over it numerous large white patches, especially about the yellow spot; there were a few hæmorrhages irregularly distributed.

On December 3rd he had another group of fits, and similarly on December 19th, 20th, and 27th. The strength rapidly failed, and the

man died of asthenia on January 1st.

The autopsy showed, beside general anæmia, some ascites and pericardial effusion, great ædema of the lungs, considerable hypertrophy of the heart, especially the left ventricle, and a large hard liver weighing 80 ounces. The kidneys weighed 19 ounces together; they were large and tough, reddish-brown in colour, the capsules stripping off readily. The cortex was not much reddened, and the surface was not granular. The diagnosis by the pathologist was: "Large red kidney, apparently with fibroid change commencing." The microscopical examination showed besides the chronic cellular degeneration (parenchymatous) changes, a large amount of immature connective tissue, especially in the cortex and round the malpighian bodies. Some of the capsules were greatly infiltrated with cells, and their tuft of vessels compressed and degenerate; others presented well developed fibrous tissue. Similar interstitial

changes were present in the medulla, but not to the same degree. The changes were those of parenchymatous degeneration with early diffuse

interstitial nephritis.

It is difficult to know exactly how to classify this case, but it is probably an instance of subacute parenchymatous inflammation with subsequent fibrosis. The kidneys in many respects resemble those of Blakeborough (App. Case IX), in which the sequence of the changes is better traced clinically.

Yet we are not justified in connecting this form of albuminuric retinitis simply with interstitial fibrosis in the kidney; for it may be seen in chronic parenchymatous nephritis with but little interstitial change as well as in acute cases where there has been too little time for fibrous tissue to develop and where post-mortem examination has proved its absence.

Although if albuminuric retinitis occur at all in chronic parenchymatous nephritis, it is, I believe, generally of the more extreme exudative form, still it may be restricted to a few small white patches near to the yellow spot closely resembling those of granular kidney, yet generally rather woolly grey in appearance than pearly white. Usually these are but the early stage of exudation and run on into the more extreme forms, but the converse is sometimes observed (as in the case of Emily R., p. 64), where, as the large patches resolved, nothing was left at last but a few minute patches, which also in time disappeared.

Complicated as the question is, we seem to be justified in drawing these conclusions: that this form of albuminuric retinitis is of an exudative, inflammatory, type; and that it is probably of toxic origin, and related rather to the cellular degeneration than to the interstitial fibrosis.

Albuminuric retinitis may occur in the course of lardaceous disease, but there are few instances of it recorded. It is probably to be connected with the parenchymatous inflammation or with the dropsy rather than with amyloid disease as such.

Amyloid disease is, however, a rare affection now, and with the improvement in surgery is becoming rarer every year, so that individual experience is necessarily small.

As to the general frequency of albuminuric retinitis in parenchymatous nephritis, statements vary widely. I should have (9772)

thought, judging from my own experience, that it was rare in the acute stage, and far from common in the later or chronic stage, and that altogether the frequency was much less than in granular kidney.

\*\*Tred'k\*\*\* C. Shattuck.\*\*

Fagge, however, stated that it was far from rare in parenchymatous nephritis; and of Sutton's 50 cases 15 occurred in parenchymatous nephritis, the remainder being in granular kidney. This gives a relative frequency of 15 to 35, or 3 to 7. The actual frequency in relation to the total number of cases observed was 14 per cent. for tubal nephritis and 9 per cent. only for chronic interstitial nephritis.

I have no actual figures to oppose to these, but my impression certainly

does not accord with them.

It is to this acute exudative group that some of the cases of albuminuric retinitis of pregnancy belong. The onset is acute, its progress rapid, the impairment of sight early and considerable, and yet in spite of all this the prognosis is by no means so bad either in respect of life or sight.

On the other hand, many more of these cases in pregnancy belong to the degenerative group, and are evidence of granular kidney. In these there is often no complaint of impairment of sight, even when the lesions in the eye are well developed; the course is insidious and chronic; and the prognosis bad both in respect of life and of sight.

Puerperal eclampsia occurs in either form; in the former rarely without dropsy, but in the latter not infrequently without.

If the view I am expressing prove to be correct, it follows not only that the kind of albuminuric retinitis which prevails in the two forms of renal disease is different, but that it has a different diagnostic value in the two cases. In parenchymatous nephritis the diagnosis of the disease is obvious, and the albuminuric retinitis is an interesting by-phenomenon only. In granular kidney the diagnosis may be uncertain until all doubt is dispelled by the discovery of the characteristic eye-changes. Anyway, in future investigations on the subject it will be well to keep the acute exudative or inflammatory forms (the so-called "extreme" degrees) separate from the more chronic and less obvious forms which are frequently discovered by the ophthalmoscope without any special symptoms suggesting eye-lesions.

## 2. THE DEGENERATIVE FORM.

The degenerative form of albuminuric retinitis consists in white patches and hæmorrhages. Of these the most characteristic are the white patches.

#### White Patches.

The white patches are bright spots usually seated in the neighbourhood of the yellow spot, or between the yellow spot and disc. In their typical and favourite form they are arranged round the yellow spot in a radiating form, like the spokes in a wheel. They are usually found in both eyes, and are often remarkably symmetrical. In very early stages they may be so minute as to be easily overlooked, and may be found here and there only, generally between the disc and the yellow spot. Even then it is remarkable that they are usually present in both eyes, and often symmetrical, though of course in this early stage they are more likely to be unilateral and unsymmetrical.

The white patches may for a long time be the only lesions visible, if we disregard for the present certain changes in the vessels which are possibly still earlier, and will be referred to later.

There are, I believe, two kinds of white patches, the one forming bright points glistening like fish scales, the other not so glistening or so sharply defined, but woolly in appearance. The former are the result of degenerative changes, and their brilliancy depends upon the presence of minutely refractive oil drops, or even cholesterine crystals; the latter are often small patches of exudation only. The former are of slow development and unlikely to disappear at all, or only slowly and after a long time; the latter, however, may come and go rapidly.

If there be two kinds of white spots, as I think there are, then the conflicting statements made about them may be reconciled. Thus it is asserted by some authorities that the white patches readily come and go; while others hold that once present they never disappear. The patches of exudation might appear rapidly and also quickly disappear, but the patches of degeneration would persist for long, and possibly till the end of life. Most authorities hold that the brilliant patches are almost pathognomonic of granular kidney, while others state that they are frequently seen in parenchymatous nephritis. If in granular kidney the patches are degenerative and in parenchymatous nephritis due to exudation, this difference of opinion also would be explained.

Of course it may not be always possible to distinguish by the eye alone between these two forms of white spots, yet I think it can generally be done. From a practical point of view the distinction is not so important as it might seem, for in parenchymatous nephritis the diagnosis of renal disease is usually obvious, whether there be white spots or not. In granular kidney, however, the diagnosis may be uncertain until the eye-changes are discovered. The white spots, whether they be really exudative or degenerative, have, therefore, in granular kidney a diagnostic value which they do not possess in the other forms of nephritis.

## Hæmorrhages.

These usually occur at a later period; they are minute and flame-shaped if seated in the upper layer of the retina, but if seated in the deeper layers are larger and less regular. Sometimes they are numerous round about the yellow spot, but at other times are scattered widely over the fundus.

Similar hæmorrhages may occur in both the exudative and the degenerative forms, though they are probably produced in different ways in each case. In the latter they are the consequences of the vascular degeneration, and due to the rupture of the diseased arteries, in the retina as in other parts of the body; in the former they are probably due to the rupture of over-distended veins, the over-distension being the result of the pinching to which they are subjected as they pass through the swollen disc.

When of considerable size the hæmorrhages naturally interfere seriously with vision, and so may even a small hæmorrhage if seated in the macula. On the other hand, it is surprising how numerous the hæmorrhages may be without any defect of vision at ali. If the hæmorrhage is very profuse, it may burst the retina and fill the eye.

This happened, I believe, unless it was due to rupture of one of the ciliary arteries in the case of the woman, now aged 58, who was under my observation with well-marked albuminuric retinitis for five years. The right eye was found completely filled with blood right up to the posterior surface of the lens. The sight had been entirely lost for some time previously, but the hæmorrhage had apparently occurred a month prior to her last visit, when she was seized suddenly with severe pain in the eye (App. Case VI).

The hæmorrhages are sometimes absorbed completely and leave no trace behind. They rarely lead to choroidal atrophy and pigmentation, as other forms do. Indeed these lesions may follow effusion in parts where there has been no previous hæmorrhage.

There is nothing characteristic about the hæmorrhages in renal disease for exactly similar hæmorrhages may be seen in grave anæmia, as well as in optic neuritis of other origin. Indeed in renal disease some of the smaller hæmorrhages may be connected with the anæmia, and be due to simple extravasation; but the larger ones must be the result of rupture of the vessels from disease.

## ARTERIAL CHANGES .- SILVER-WIRE ARTERIES.

Early as the white patches or degenerative changes are, they are preceded by, and result from, still earlier changes in the vessels.

The lesions in the vessels have been well described by Brailey and Edmunds, and are briefly summed up by them as obliterative arteritis leading to inflammatory degeneration of the structures supplied.

The small arteries and even the capillaries are thickened, degenerate, and rigid. In the arteries the earliest pathological change appears to be a general thickening and hypernucleation of all the coats of the artery without any diminution of their calibre. Gradually the arteries become still more thickened and structureless, and the capillaries hyaline and rigid. Later still the arteries show very great thickening of all the coats, especially the subendothelial part of the intima; this leads to an increased total diameter of the vessel, though the lumen is greatly diminished

or may even be completely obliterated. In the most advanced stages some of the arteries may be found in a state of fibroid or structureless degeneration, and similar change may affect many of the capillaries. The changes are exactly the same as those found in the renal vessels.

All the vessels in the retina are affected, but not every vessel, nor even all parts of the same vessel, to the same extent.

The ophthalmoscopic appearances connected with these changes have been admirably described by Marcus Gunn.

The arteries look narrower than usual; they are somewhat irregular in breadth in different parts, sometimes presenting fusiform enlargements, and in others a long tubular enlargement followed by a constriction; they may be pouched, and thus form small aneurysms; they are often tortuous.

They frequently present a brilliant central streak of metallic lustre (the silver-wire arteries of Gunn). This streak sometimes runs uniformly for some distance along it, at other times it is broken, patchy, or dotty. It does not involve all the arteries, nor even all the branches of the affected artery. It is especially seen in the secondary branches of the central artery, that is to say, at some little distance from the discs.

The whole vessel shows a broader reflex than normal, and gives the impression of unusual fulness and roundness of contour.

The vessel loses its translucency, so that the veins below are not visible through it, or, on the other hand, if the vein lie above, the artery may show through the vein with unusual distinctness.

Where a vein lies below an artery it loses its central streak, showing that it is somewhat pressed upon, and may be distended peripherally.

The whole retina is usually grey and hazy, which Gunn explains on the assumption of there being a small amount of cedema, especially near the macula and in the area of distribution of the most diseased vessels.

The hæmorrhages are frequently due to rupture of the distended veins, but the arteries of course often rupture, too, in the eye as in other parts of the body.

The ophthalmoscopic appearances are connected with the changes in the vessels thus; the narrowness and irregular size of the vessels are explained by the thickening and by the diminished lumen; the tortuosity by the increased rigidity and loss of elasticity the increased light reflex and the bright central streak by the fibro-hyaline change; the distension of the veins by the great thickening and resistance of the artery as it lies upon them.

The difficulty of circulation leads to the general œdema; the progressive disease of the vessel to hæmorrhage; the defective nutrition of the nerve-cells and fibres to the degenerative white patches. The radiating arrangement of the white patches round the yellow spot Gunn refers to the radiating folds into which the retina in that region is thrown when œdema occurs there.

The silver-wire arteries are not to be confused with the streaks often seen at the side of the vessels, which are either produced by exudations, as occurs in cases of optic neuritis or in leucocythemia, &c., or by periarterial change, as in the case described by Mules.\*

Although the silver-wire arteries are no doubt ophthalmoscopic evidence of the vascular degeneration, as are also the hæmorrhages and white spots, it does not follow that the vessels necessarily show the white silver-wire streaks before the other lesions are visible. On the contrary, I have observed the white streaks develop in the arteries after other lesions had been conspicuous for months (App. Case V).

The changes in the vessels described, Gunn states, begin to be seen usually between the ages of 40 and 50, but they are not due to old age, i.e., to atheroma, for this does not produce them. They may be seen, however, much earlier in life than this—indeed, at any age, provided the vascular degeneration is far enough advanced.

The changes, of which Gunn gives so good a description, are really those of granular kidney. This his cases prove, for of the 14 cases upon which the paper is based, nine were certainly cases of granular kidney, and three more probably, while in the remaining two only is the diagnosis indefinite.

The dependence of these changes on granular kidney is confirmed by a collateral series of observations which he made. He chose 17 cases of

<sup>\* &#</sup>x27;Ophthalm, Soc. Trans.,' 1881-82.

hemiplegia, presumably due to vascular disease, for the purpose of comparing with those in his paper; seven showed characteristic retinal changes such as he had described, and four of these had albumen in the urine; three more had slight vascular changes in the eye, and one of these had albumen; seven had no changes in the eye at all, but one of these also had albumen.

Of these last seven, four died, and *post-mortem* examinations were made. In three of them well-marked granular kidneys were found, and in the other the kidneys were not granular, but as there is no record of any microscopical examination, the absence of interstitial nephritis is not proved.

The papers of Brailey and Edmunds, on the one hand, and of Gunn on the other, are complementary, and together establish the fact that the changes in the eye which we know as albuminuric retinitis certainly depend upon the disease of the vessels, and that at the time these changes become evident, the kidneys are already granular.

They give us no help, however, in determining whether the vascular changes or the renal changes are the primary. On the whole they seem to show that the vascular changes are late, considering how delicate the retina is and how early the changes in the vessels could be detected by the ophthalmoscope if they were present.

Gunn's paper will fix attention upon the changes in the vessels which precede albuminuric retinitis, and possibly these ophthalmoscopic changes in the vessels will be found at a much earlier period in the disease than is now supposed.

# SYMMETRY OF ALBUMINURIC RETINITIS.

It is a remarkable fact that albuminuric retinitis is almost always bilateral. In the extreme exudative form this is, I believe, always so; but it is also the case usually even when the changes are slight. The changes are not only bilateral, but frequently also remarkably symmetrical, and differ but little on the two sides. In the acute inflammatory form this is not a matter of surprise, for it is probably of toxic origin, and, like other forms of toxic neuritis, is symmetrical. It is more remarkable in the degenerative forms—i.e., in the less acute and chronic—where the changes are more or less mechanical, and consequent on the vascular degeneration.

There are exceptions to this general rule, and the lesions

may be well marked in one eye, and absent, either entirely or almost, in the other. Several instances of well-marked unilateral albuminuric retinitis have been recorded, and I have recently published two instances myself; but cases of the kind are really rare.

In one of my cases, a male in middle life, the right eye presented the usual features of well-marked albuminuric retinitis of the degenerative kind, with numerous white patches and hæmorrhages; while the left showed nothing except two very tiny white spots, which were so small as to be at first overlooked.

In another case repeated examination of the other eye failed to

discover any abnormality at all.

Anderson\* records a case in which no change in the opposite eye occurred for four years.

## FREQUENCY OF ALBUMINURIC RETINITIS.

It would be interesting to know in what proportion of the cases of granular kidney albuminuric retinitis occurs, but that we cannot yet tell, for we have not the figures upon which any safe conclusion could be based. The figures given vary from 6 to 30 per cent. I should say that in most cases of granular kidney if the patient live long enough albuminuric retinitis does ultimately develop, but many die from other causes, e.g., from hæmorrhage in the brain, and so do not reach the later stage in which albuminuric retinitis is found.

#### DETACHED RETINA.

Detached retina is an interesting, but not altogether rare, phenomenon in granular kidney. It is in most cases due to an effusion of serum beneath the retina, and not, as might be expected, of blood. I have seen hæmorrhagic detachment of the retina, but it is a rare affection. The detachment is usually peripheric—that is to say, occurs at the outer part of the retina, and in very many cases affects both eyes, and is remarkably symmetrical.

Granular kidney; rapid loss of sight; purpura; retro-bulbar hæmorrhage; detachment of the retina (not hæmorrhagic).—Lydia B., aged 22, was admitted into St. Bartholomew's Hospital under my care on March 2nd, 1893, suffering from headache, vomiting, and failure of sight. She

<sup>\* &#</sup>x27;Ophthalm. Soc. Trans.,' viii, 130.

stated that she had been in her usual health until nine months ago, when the present symptoms began. Since then she had been getting gradually worse, the sight failing more and more, until 10 days ago she

became quite blind.

It was ascertained that she was an in-patient in Faith Ward seven years before, and that her case was then diagnosed as "chronic nephritis of four months' duration." The following account is given of her case at that time:—She had considerable dropsy of the face and body, and passed but little water, with about 6 per cent. of albumen. A few days after her admission she had several fits, 16 in one day, and they were followed by noisy delirium, ending in complete coma. At that time she lost her sight temporarily, but there were no eye lesions discovered by the ophthalmoscope, so that the attack was thought to be one of uræmia with uræmic amblyopia. For some days she seemed likely to die, but she rallied and then rapidly improved, so that she left the hospital after a stay of nine weeks "wonderfully better." The albumen on leaving was reduced to 1.6 per cent.

Soon after leaving, the dropsy reappeared and disappeared again, but since then she has had several slight attacks of the same kind, so that she had been always more or less ailing until nine months ago, when the sickness, vomiting, and failure of sight set in for which she sought

admission now.

Nocturnal micturition had been constant with her, at any rate since the illness first described, but it is not clear that it did not precede it also; but she had only recently noticed any marked increase in the amount of urine and in the frequency of micturition by day. No history of scarlet fever could be obtained. The family history was negative, her father, mother, her two brothers, and one sister being all alive

and well, and one sister only having died as an infant.

Condition on admission:—A fairly nourished woman, very pallid, with a little cedema of the eyelids, feet, and lumbar region. The breath seemed ammoniacal; respirations quiet and lungs normal; the tongue clean and moist; appetite good and bowels regular; the pulse was 80, of increased tension; the artery thickened; the heart's dulness increased slightly upwards and a little towards the right side; the impulse forcible; the first sound prolonged at the apex and reduplicated; the second sound at the base accentuated; no murmur. The urine contained much albumen (one-third); no casts were found. The headache was almost constant and at times very severe all over the head. The vomiting did not bear any relation to the taking of food, and was very irregular in occurrence. She was very restless and slept badly.

Ophthalmoscopic examination revealed extreme double albuminuric retinitis, with numerous white patches, especially round the yellow spot, and hæmorrhages. The discs were considerably swollen; vision was limited to perception of light only; the conjunctivæ were a little glassy

and swollen from slight cedema.

Six days after admission (March 15th) several small purpuric spots were observed on the body, legs, and arms, and over the buttocks a few large purple patches of extravasation developed. These gradually faded and disappeared, the headache and vomiting became less, the breath less ammoniacal, the ædema almost disappeared, and altogether the patient seemed better.

On March 19th detachment was discovered in both retine. This could not have developed more than two or perhaps three days before it was detected, for frequent examination of the eye were made by myself and

by my house physician. The detachment was peripheral, and at first was limited to the south or lowest part of the retina. It rapidly spread, and in a few days involved the whole periphery except the middle upper segment. No change had occurred in the patient's symptoms to indicate any fresh complication in the eye, and the only new symptom was the occurrence of moderate and repeated epistaxis for a day or two before the detachment was discovered. The colour of the detached portion of the retina was dull grey, and no sign of hæmorrhage was found then or afterwards. No change took place in the detachment after it had once fully developed, either by way of extension or diminution, nor did it ever spread to within a fair distance of the disc.

In other respects the patient seemed to be improving; the pallor was extreme, the œdema had disappeared altogether, the albumen had diminished to little more than a cloud, the headache was better, and the vomiting had almost ceased. She was taking her food and slept soundly. The urine varied in amount a good deal day by day, but

averaged about 50 ounces.

The patient seemed to be going on fairly well until April 9th, when she was suddenly seized with severe pain in the left eye attended with flashes of light. The eye became protruded somewhat, and the conjunctiva as well as the eyelids and adjacent part of the face became swollen. She also vomited several times. There was no rise of temperature or

other change.

The question arose whether she had hamorrhage into the eye (hamorrhagic glaucoma) or behind the orbit. On account of the swelling of the external parts it appeared to me to be retro-bulbar, and this it ultimately proved certainly to be; for the next day the conjunctiva became ecchymosed, and when the eye could be again examined the retinal condition was found unchanged, and there was no trace of hamorrhage within the bulb. The pain rapidly subsided under treatment, and the general condition of the patient seemed to be in no wise changed.

On April 19th, during the night, the patient became suddenly quite delirious and unable to recognise anyone about her; she complained of pins and needles all over the body, and had some general twitchings. Under Cannabis Indica and pilocarpine, she was quieted, and the next

day she seemed to have recovered.

May 15th.—There is little more to record; she remained in statu quo. Perhaps there was a little general improvement in health, but none in the condition of her eye. Finally she became tired of the hospital and

went home, where she died shortly afterwards.

The treatment consisted of perchloride of iron three times daily, and nitrate of pilocarpine one-twelfth grain, subsequently increased to one-sixth grain night and morning, with an occasional dose of extract of Cannabis Indica to secure sleep.

Granular kidney; sudden loss of sight; detachment of the retina; epistaxis; diarrhæa; death; granular kidneys.—Frederick F. S. was admitted into John Ward in St. Bartholomew's Hospital on March 2nd, 1893, under my care, complaining also of vomiting, headache, and loss of sight. He stated that he was in good health and at work until two months before his admission, when he began to suffer from morning vomiting, and to be much troubled with headache. It was not until February 24th, or six days before admission, that he first noticed that his eyes ached, and that things looked misty. Up to that time his eyesight

had been good. He gave absolutely no history of illness prior to two months ago, except that he had a slight attack of congestion of the lungs nine years before, from which he quite recovered. He had never had scarlet fever so far as he knew. His mother and two brothers were alive and well, but his father was dead. On cross-examination he admitted that he had to get up at night for some years past to make water, and he had lately passed more urine than usual, and had been thirsty, but with this exception he seemed to have been free from symptoms of any kind till two months ago.

He was a pale, anæmic man, with a somewhat sallow, earthy complexion. The tongue was flabby and moist; the appetite fair; the bowels regular. The breathing good and lungs natural. The pulse 84, regular, of high tension; artery much thickened and tortuous. The heart-dulness was a little enlarged; the first sound at the apex prolonged and booming, and the second sound at the base accentuated. A systolic murmur (hæmic) was heard at both bases, but it varied greatly, and

was sometimes absent.

The urine was acid, 1010, contained a fair amount of albumen (one-fourth), and gave a slight blood reaction. Some finely granular casts were stated to be present, but I did not see them myself, and they were not found again. There was no ædema of any part of the body, but the

eyelids looked a little puffy.

Ophthalmoscopic examination revealed well-marked albuminuric retinitis. The discs were hazy and somewhat ill-defined, but there was no swelling or effusion. There were numerous white patches, and a few recent and small hæmorrhages. Vision was almost completely lost; all that could be seen were large objects placed near to the eyes against the light.

The urine was much increased in quantity, and was on several days

more than 100 ounces, and only rarely less than 60 ounces.

On account of the condition of the eyes and the headache three leeches were applied to each mastoid, and a small blister to each temple, with some relief to the headache. No other improvement occurred, and on the

18th the retinal hæmorrhages had greatly increased.

On the 19th detachment of the retina was discovered on the right eye, the left being unchanged. The detachment was on the nasal side, and involved about one-third of the periphery. By the 21st it had extended so as to involve the whole periphery except the "N.W." segment. Nothing had occurred in the condition of the patient to suggest any fresh complication on the side of the eye, and the only fresh symptom was an attack of troublesome but not copious epistaxis at the same time that the hæmorrhages were found to be increased in both eyes (i.e., on the 18th), the day before the detachment occurred.

From this time the patient gradually lost ground, becoming weaker and weaker every day. On the 28th troublesome diarrhæa set in, which still further reduced him, and on the 30th epistaxis recurred, which had

to be treated by injection of perchloride of iron.

On April 1st he died, having during the last three days of life been greatly troubled with vomiting, which caused him to reject and finally to refuse all food, and having passed but little water—about 25 ounces daily. He died quietly of asthenia, and was conscious to the last.

The patient was treated throughout with nitrate of pilocarpine, one-

eighth grain, three times daily by the mouth.

The post mortem showed no lesions save well-marked contracted granular kidneys and hypertrophy of the heart, which weighed 14 ounces.

It might have been expected that the detachment was, under the circumstances, due to hæmorrhage, but, on the contrary, the colour of the affected parts was always pale and the effusion was clearly serous, as I have more than once satisfied myself by postmortem examination (cf. Case, p. 102).

In both cases it commenced in the southern or lower segment of the eye, but rapidly extended until it involved the whole periphery except the top or upper segment. Both patients being blind at the time, the detachment manifested itself by no fresh symptoms, and was discovered only on ophthalmoscopic examination. It is further to be noted that in the second case the detachment occurred in one eye only, viz., the right, but in the first case it affected both eyes equally.

### OTHER EYE AFFECTIONS.

The vascular changes of granular kidney are of great importance in relation to various hæmorrhagic affections of the eye. Thus Gunn connects Hæmorrhagic Retinitis with granular kidney. Brailey and Edmunds found the retinal arteries extensively diseased in 16 out of 17 eyes excised for Hæmorrhagic Glaucoma. Gunn suggests that many cases of so-called Embolism of the Central Artery of the retina are really due to thrombosis in an artery so diseased, and that thrombosis here may give rise to retinal change similar to that met with in Retro-bulbar Neuritis, which some of the extreme forms of albuminuric retinitis so closely resemble. Similar conditions might be produced by hæmorrhage into the sheath of the optic nerve, of which some instances are recorded.

Cataract is rare in granular kidney, but Gunn suggests that it might be the result of sclerotic change in the ciliary vessels.

Knies records two instances of iritis.

I cannot remember to have myself seen any instance of either cataract or iritis which I felt justified in referring to granular kidney, and I should regard their association as accidental.

#### EXTRA OCULAR HEMORRHAGE.

Hæmorrhage occasionally occurs behind the eyeball in the orbital chamber (cf. Case, p. 78). Then sudden pain is felt behind the eye, which is thrust considerably forward. The hæmorrhage may soon extend forwards and become visible beneath the conjunctiva, or, if not, in the course of a day or two the characteristic staining appears in the eyelids or beneath the conjunctiva. In most cases there is no defect of vision and recovery is complete.

Spontaneous hæmorrhage under the conjunctiva, just as occurs in aged people as the result of atheroma, is not at all uncommon. In young and middle-aged persons such hæmorrhage is very significant. Similar hæmorrhage into the eyelids, especially the upper, is also sometimes met with.

Knies describes one result of hæmorrhage which I mention, but cannot endorse from my own observation, viz., paralysis of the ocular muscles, the consequence of hæmorrhage either into the nerve-trunks or into their nuclei. The cases, he states, recover with or without treatment, but are subject to relapses.

Thus he describes abducens paralysis in a case of albuminuria of 15

years' standing; this relapsed twice and the patient died.

In another case diagnosed as granular kidney, paralysis of the left troclear nerve occurred, and when, six months later, the patient died,

hæmorrhage was also found in the optic nerve.

In a third case there was complete right ophthalmoplegia externa with albuminuria. At first the troclearis was affected, then the internal rectus, finally the other branches of the third, and later there was unilateral and subsequently bilateral ptosis. All these symptoms ultimately disappeared and the patient recovered.

The obvious objection to all these cases is that third-nerve paralysis generally develops more or less gradually, whereas if it were due to hæmorrhage its onset ought to be abrupt. I cannot recall a case of the kind in which the onset of ocular paralysis was as sudden as the theory of hæmorrhage would require, and I do not think that such unusual cases could well have been overlooked.

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## AFFECTIONS OF SIGHT.—AMBLYOPIA.

The early lesions of albuminuric retinitis produce little or no defects of vision, and even in the later stages it is very remarkable how extreme the eye-changes may be without a complaint being made of impairment of sight.

I have recently seen a case with extreme albuminuric retinitis of the exudative form, in which not only could the finest type be read and the finest needle threaded, but the perimeter showed no diminution in the field of vision. I mention this because it has recently been controverted, but of course it is only what we are quite familiar with in other forms of extreme optic neuritis.

Routine examination with the ophthalmoscope will often discover albuminuric retinitis when there has been nothing to suggest its presence, and will make a diagnosis clear which may till then have been obscure. Indeed the recent progress in our knowledge of granular kidney has been largely coincident with the systematic use of the ophthalmoscope in medicine.

As a rule, we may say that when patients complain of defect of vision, the albuminuric retinitis is already far advanced. When the vision once begins to fail it may fail very rapidly, so that within a week or two it may be completely lost.

# AMBLYOPIA.

In albuminuric retinitis, as in optic neuritis, transient attacks of great impairment of sight, or even of complete blindness, occasionally occur, lasting it may be but a few minutes at a time, the sight in the intervals being good and equal to the finest work—they would be called attacks of amblyopia. They may recur during weeks or even months, but, as a rule, vision soon begins to fail, and then is quickly lost.

Amblyopia is often said to be a common symptom of uræmia, and is usually regarded as either of peripheral origin in the retina or of central origin in the brain or special ganglia. Most of these statements date from a time when the ophthalmoscope was not systematically used.

Of toxic retinal amblyopia we know little or nothing, for most of the cases are associated with very definite lesions in the retina visible with the ophthalmoscope.

The amblyopia of central origin, i.e., non-retinal, is often associated with other symptoms, e.g., hemiplegia. In such cases the amblyopia is also in all probability due to lesions of an organic kind. It is not rare when a patient dies of uramia to find the symptoms which appeared to be merely toxic or functional explained by an organic lesion in the brain, viz., small hamorrhages, and in cases of so-called uramic amblyopia in which the defect of sight persists after the uramic attack is past we must presume that there has been an organic lesion.

In cases of toxic amblyopia recovery ought to take place in the course of a few hours or less, though instances are recorded in which recovery has been sudden and complete even after four days.

Some clue as to place of origin of the amblyopia may be given by the condition of the pupil. If the pupil-reaction be retained and normal, the lesion, if there be one, must be high up or cortical.

If the reaction to light be lost there is probably some affection of the optic nerve or optic ganglia. In some cases described by Lytton, in which absence of the pupil-reaction to light occurred, each attack was associated with pronounced swelling of the discs, so that there was probably some hæmorrhage or lesion in the optic nerve.

Toxic amblyopia no doubt occurs, and may even be ununilateral, as uræmic fits may be; yet lesions are now found much more frequently than used to be thought likely.

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# THE DIAGNOSTIC VALUE OF ALBUMINURIC RETINITIS.

In parenchymatous nephritis, albuminuric retinitis has no great diagnostic value, for the signs of renal disease are usually obvious enough. There is only one question which it may then raise, viz., whether the kidneys were or were not granular prior to the acute attack.

In this condition the retinitis is usually of the exudative type, and may resemble closely that met with in other forms of acute neuro-retinitis, e.g., that occurring in cerebral tumour, of which instances have been given. It is in granular kidney that albuminuric retinitis has its chief diagnostic value—that is to say, in cases where albuminuric retinitis has been found without any very obvious renal symptoms, but where the high tension and thickened arteries have suggested renal disease. In such cases, whether there be albuminuria also or not, the presence of albuminuric retinitis is conclusive, and settles the diagnosis. In granular kidney it is the degenerative type of albuminuric retinitis which is most frequent and most important. It is, indeed, pathognomonic; for, though there is described a form of retinitis in diabetes which some authorities profess to be able to distinguish from that of granular kidney, I must confess my inability to distinguish it myself. Indeed, I am inclined to hold the opinion that they are the same thing; in other words, that the kidneys in these cases are granular, for granular kidney is by no means a rare association of long-standing diabetes.

## PROGNOSTIC VALUE OF ALBUMINURIC RETINITIS.

The significance of albuminuric retinitis is grave in respect of life even more than in respect of sight.

So far as the eye-changes are concerned, something will depend upon their nature and upon their cause. Thus hæmorrhage may be absorbed and disappear whether due to granular kidney or not. White patches which are due to exudation may also disappear, but the white patches which are due to degeneration, such as are usually met with in granular kidney, I have not myself ever observed to disappear. Again, where the albuminuric retinitis occurs in the course of chronic parenchymatous nephritis it is possible that if the primary disease gets well the eye-changes may also disappear and recovery of health and sight be complete.

1. The Exudative Form.—Paradoxical as it may seem, it is in the so-called extreme forms of albuminuric retinitis or, as I should call them, the exudative forms that the prognosis is, both in respect of life and in respect of sight, not nearly so grave as it might appear to be, for if the kidney mischief recover the eye lesion may resolve and the sight be completely restored.

In respect of sight, indeed, the prognosis is better with albuminuric retinitis of this type than it is with similar forms of neuroretinitis due to other causes. Possibly this is due to the fact that in albuminuric retinitis the exudation may be more of the nature of cedema or dropsy than of inflammation, so that its effects are rather mechanical than degenerative. Anyway many of the cases recover without any defect of sight.

If, as in pregnancy, the cause return, the retinitis may also return, and with each succeeding pregnancy the prognosis in respect of sight of course becomes worse, but the significance of the eye-lesions is usually dwarfed by the importance of the renal disease of which they are the accompaniment, for the danger of renal disease during pregnancy is well recognised.

In respect of life the prognosis is that of the renal disease, and all that I think the albuminuric retinitis in these cases does is to

show that we have a form of parenchymatous nephritis to deal with of a somewhat unusual severity.

Thus Sutton's figures show that while in cases of chronic parenchymatous nephritis without retinal change 22 per cent. only were fatal, in those in which retinal changes were present no less than 60 per cent. died. In 10 fatal cases the average duration after the retinitis was first noticed was four months, and from the time of the beginning of renal symptoms only 11 months.

2. The Degenerative Form.—The degenerative forms of albuminuric retinitis have great importance in granular kidney both in respect of sight and in respect of life.

In respect of sight.—The white patches of granular kidney rarely disappear; I have not myself seen any instance of their disappearance, but they are very often present without much defect of sight. The longer they persist the greater the chance of impairment of sight developing, either as the result of progressive degeneration of hæmorrhage or of other changes in the eye already referred to. When once such impairment of sight has commenced it steadily progresses. Sight is, however, rarely seriously impaired, still less completely lost, until the case is near its end, unless of course there has been detachment of the retina or severe hæmorrhage.

The ophthalmoscopic changes in the vessels are important as evidence of an arterial degeneration which is not limited to the eye, and it is a visual evidence of the risks to which the patients are subject from the disease of the vessels elsewhere, e.g., in the brain. But, as I have stated in most of these cases, the eye-changes are but rarely seen until the other signs of granular kidney are obvious enough.

In respect of life.—The duration of albuminuric retinitis, or of life after its appearance, it is not possible to determine accurately, for albuminuric retinitis is not as a rule discovered in its early stages, either because the patients do not come under observation early enough, or because the eye is not examined with the ophthalmoscope until defects of vision are complained of.

In granular kidney, speaking generally, the duration of life after albuminuric retinitis has been discovered is short.

Thus, Miley traced 45 cases, and found the average duration of life to be under four months from the time when the eye-changes were first observed, and though one of the patients lived 18 months and two 14 months, all the rest died within the year. In nine cases in which the first appearance of eye-changes was noticed the duration averaged less than six months, and in two cases it took a month for white patches to

develop after the appearance of hæmorrhages.

Bull, in 100 cases of albuminuric retinitis, found that 86 of 103 died, 57 in the first year, 12 during the second, and 17 after a longer period. Of the 17 remaining cases that were still living at the time his paper was published, 14 had been seen only during the six months immediately before the paper was written, but one had been diagnosed seven years previously.

Where the patients are in a condition to take the best care of themselves life may be prolonged for some time.

Thus, the Baroness Possauer found that within two years of the time of observation, among hospital patients, all the men died and 68 per cent. of the women; among private patients, of the men 59 per cent. only, and of the women 53 per cent.

Instances, however, are recorded of considerable duration.

Thus, I have a patient of my own who was under my observation for more than five years, and for four years remained in much the same general condition as when first seen; and I have already referred to a case of Miley's in which the patient was known to have lived for more than seven years.

Anderson records some remarkable cases. One died 12 years after the albuminuric retinitis had been detected, and two others were living four

and seven years afterwards respectively.

Cases such as these are quite exceptional, and speaking generally, when patients with granular kidney are found to have albuminuric retinitis they have not many months to live.

#### CONCLUSIONS.

I may bring this part of my subject to a conclusion by summing up the facts which, I think, justify the drawing of a sharp distinction between the two forms of albuminuric retinitis, the degenerative and the exudative.

They stand in strong contrast with each other in the following respects:—

- (1) Of the form of disease with which they are associated—the degenerative with granular kidney, the exudative especially with parenchymatous nephritis.
- (2) Of their nature and cause—the exudative being inflammatory and probably toxic in origin, the degenerative consequent on the vascular changes, and more or less mechanical in origin.

- (3) Of sight—for with the exudative, even in the extreme forms, recovery may take place with little or no defect of sight, but with the degenerative the impairment of sight, if there be any, is usually progressive.
- (4) Of diagnostic value—the exudative being an interesting byephenomenon of chronic parenchymatous nephritis, the existence of which is obvious enough, while in granular kidney the degenerative often makes the diagnosis certain in cases which have been hitherto obscure.
- (5) Of life—for while in both cases it indicates a grave form of renal disease which may of itself prove fatal, in granular kidney it indicates in addition all those dangers to which arterial disease exposes the patient.

I think, therefore, that the distinction is not only justified by the facts but explains many of the apparent contradictions which are made by different writers. PART III.

SYMPTOMS.

#### 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 always 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; so that they are very misleading, and the true nature of the case is often overlooked.

The symptoms fall into two groups, the cardio-vascular and the toxemic.

The latter are better called toxemic rather than renal, because, though no doubt of renal origin, they are not such as are commonly understood by the name renal and do not of themselves point to the kidney as their cause.

Speaking generally, the cardio-vascular symptoms occur first and the toxemic subsequently, though they may both be present together.

The cardio-vascular are important, because they often cause death earlier than might otherwise occur.

The toxemic always develop if the patient live long enough. They depend upon the wasting of the kidney, and become manifest when it has reached a certain degree and progress with it, pari passu.

# A .- Cardio-Vascular Symptoms.

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 vessels.

#### I. CARDIAC.

Heart-failure is very often the first symptom which causes anxiety. Thus a little shortness of breath and palpitation on exertion are complained of, with, it may be, slight cardiac pain and swelling of the feet. The heart is found hypertrophied or dilated, without obvious cause for such changes in the heart itself.

Cardiac failure, due to granular kidney; sudden onset of uramia; death in convulsions; kidneys large, not granular on surface; microscopical lesions characteristic of granular kidney.—J. D., aged 47, presented himself with signs of cardiac failure. He had been in his usual health until Christmas, 1897, when he had some pain in the left side, with a little cough. In June, 1898, he had a similar attack. In October, 1898, the feet and legs began to swell, and the breathing became very short.

The patient presented the signs of cardiac failure, had a little bronchitis and general cedema. The heart-sounds were weak, but there was no murmur; the cardiac dulness could not be made out on account of emphysema. The patient looked somewhat ill, and had a sallow, earthy complexion. The artery was considerably thickened, and the pulsetension high. The urine had a specific gravity of 1010, and contained a

small quantity of albumen.

It seemed clear that the cardiac failure was connected with granular kidney, and, on examining the eyes, well-marked albuminuric retinitis was found in both eyes. There were the characteristic white spots in the region of the macula, though they were not quite as bright and glistening as usual. The disc was normal. This was confirmed by

subsequent examination.

One afternoon, a few days later, the patient was attacked suddenly, and without warning, with a fit. He drew himself backward, twitched, and gave a cry; after that he became still, but never regained consciousness. His pupils were widely dilated, fixed, and the conjunctival reflex present. He had several of these fits one after the other. The fits began by movements of the eyes and twitching of the eyelids, then followed violent twitchings of the left side of the face, associated with conjugate deviations of the head and eyes to the left. Then twitchings spread to the left arm, and were soon followed by general convulsions, with much

frothing at the mouth and deep cyanosis. Altogether, six or seven fits occurred in the course of about two hours, and between them there was no evidence whatever of any local paralysis. The patient seemed to be somewhat relieved for the time by venæsection, but he sank and died in the course of the night.

On post-mortem examination, the lungs were slightly emphysematous, with a little bronchitis; the right pleura had old adhesions all over its surface, especially over the diaphragm; the left pleura none; the pericardium had a small adhesion at the posterior part about the size of

a shilling.

The heart itself was much enlarged, and weighed 19 ounces; the right ventricle and auricle dilated, the left ventricle greatly hypertrophied; no valvular disease beyond a small atheromatous patch on one of the flaps of the mitral valve, and a little atheromatous thickening round the orifices of the coronary arteries.

The liver weighed 62 ounces, and was not cirrhotic; spleen normal;

brain and brain-vessels normal.

The kidneys were both above normal size, weighing 12 ounces. On microscopical examination, extensive fibrosis of the characteristic kind was shown. A good many glomeruli were atrophied and destroyed. The cells were very degenerate. The arteries were remarkably thickened.

Cardiac failure; dilated heart; extremely rapid action; artery thick and tortuous; small amount of albumen; albuminuric retinitis (white spots) in both eyes.—Charles B., aged 50, was admitted into the hospital as a case of tachycardia. The action of the heart was very rapid; the pulse-beats feeble. The heart much dilated, but without any murmurs. The artery was thick and tortuous, but the tension moderate. There was a small amount of albumen in the urine, and characteristic white spots of albuminuric retinitis in both eyes. Rest and the appropriate treatment of the cardiac weakness and irritability quickly restored him to his usual health.

Cardiac failure; ædema of feet; headache; silver-streak arteries.— A man, aged 41, had been told he had Bright's disease (albuminuria) two years previously, but he had been in his usual health till 10 days before he was seen, when the ankles began to swell and he had severe headache. The cardiac dulness was increased, due to hypertrophy and dilatation of the left ventricle. The aortic second sound was much accentuated; there were no murmurs. The arteries were thick and tortuous, and the tension raised. The urine was dark in colour, and contained 0.5 per cent. of albumen. Some of the vessels in the retina had the silver-wire streak. The patient evidently had granular kidney. His symptoms were due to weakness of the heart; they rapidly passed off with treatment, and the patient returned to work as well as usual.

Cardiac failure; ædema of feet and ascites; dilated heart and general bronchitis; granular kidney; recovery.—The patient, a woman, aged 33, was confined in October, 1897, and lost much blood. Since then she had been weak, and at Christmas time found her legs swelling and her breath short. On admission she had much ædema and some ascites; a good deal of bronchitis. The heart was dilated, especially the right side. There was much shortness of breath, some cyanosis, and orthopnæa The arteries were thickened, but the tension was not obviously raised.

The urine contained a small amount of albumen. Ophthalmoscopic examination showed no lesion.

It was at first thought that there might be mitral disease, but the systolic apex murmur disappeared as the patient improved and the bronchitis subsided. It became clear that the cause of the dilatation did not lie in the heart itself, but was the result of granular kidney.

After a few weeks the patient left the hospital well, except for the

signs of granular kidney.

As in cardiac-failure of other origin, the symptoms are usually gradual in onset, but they may come on suddenly after violent effort, or may follow a serious illness.

Influenza; cardiac pain; blood in urine; granular kidney.—A man, aged 41, was attacked with influenza, and had much pain in limbs, back, and head; two weeks later he was seized with attacks of violent præcoriald pain, which were easily brought on by exertion, for which he was admitted. The heart was found hypertrophied; apex in the sixth space in the nipple line; the second aortic sound greatly accentuated; no murmurs. The arteries much thickened, but the tension not high. The urine contained a trace of albumen and some blood. The retinal arteries showed bright streaks (silver-wire), but there were no other ophthalmoscopic lesions. The albumen varied much from day to day, and the hæmaturia was also irregular, recurring several times for a day or two at a time. He was discharged in the course of a month in his usual health.

The pain is usually slight, but may be severe enough to be called angina.

\*\*Cardiac pain; weak heart; unilateral white spots.—Henry M., aged 49, suffered from cardiac pain and shortness of breath. He stated that he had been told he had "kidney disease" eight years previously—apparently this must have been albuminuria. There was evidence of hypertrophy of the heart, but none of valvular disease. The arteries were thickened and the tension raised. The urine contained a little albumen. In the left eye, half-way between the disc and yellow spot, were a few minute glistening white spots; none could be found in the other eye. Rest and iron, with some digitalis, quickly relieved his symptoms, but he returned subsequently with a similar attack.

In App. Case II, which is interesting in so many other respects, the first symptom complained of was cardiac pain of sufficient severity to be called angina.

The cardiac symptoms may take the form of repeated attacks of severe dyspnœa.

Paroxysms of cardiac dyspnæa; albuminuric retinitis.—James B., aged 39, was admitted into the hospital on account of an attack of severe dyspnæa. This was evidently of cardiac origin, for his heart was dilated, though there was no evidence of valvular disease. The artery was tortuous, the walls much thickened. The urine contained a good deal of

albumen (one-fourth) and there was well-marked albuminuric retinitis in both eyes. Many of the knuckle joints were gouty. He gave a history of repeated attacks of gout for many years, and confessed to being a heavy drinker.

He was an in-patient in January, March, and May of the same year for similar attacks, each time making a good recovery on appropriate treatment and rest.

Œdema may be extreme. This is in most cases in great part of cardiac origin, but where ascites predominates it may suggest the combination of cirrhosis of the liver with granular kidney.

This association was thought to be present in App. Case I, but was shown by the autopsy not to be so. In App. Case VII the two conditions were associated, but in the latter the diagnosis was clear enough, owing to the great dilatation of the superficial abdominal veins, a sign which in the former case was absent.

Where the heart is affected with valvular disease as well, symptoms of cardiac failure are of course more likely to occur.

Granular kidney and mitral disease.—Alex. W., aged 26; one month previously, while in good health, was seized with frequency of micturition, especially at night, pain across the loins, cough, and thirst. The urine was dark in colour and contained blood. He looked ill, had slight ædema of the feet; thick arteries and high tension. The urine was 1010 specific gravity, contained a small amount of albumen and blood, and a few granular casts. The ophthalmoscope showed well-marked silver-wire arteries.

The heart was dilated, especially on the right side, and the mitral valve incompetent. Improvement was rapid, but the urine continued to contain albumen, and blood recurred irregularly.

In elderly persons the cardiac symptoms might be the result of atheroma, but in middle life and in the young granular kidney is the most likely cause, and, attention being thus directed to the kidney, the signs of granular kidney are often discovered. Yet even in the elderly there may be but little atheroma, and the cardiac failure be, as in younger persons, the result of granular kidney.

A man of 74 came under my care with the history of the feet having begun to swell about three months previously. He gradually died of failure of the heart, and at the autopsy the heart was found to weigh 16 ounces, and to be fatty. This might have been explained by atheromatous change in the vessels, but from this they were unusually free; the kidneys were markedly granular, yet the patient had only passed a little albumen during the last few days of his life.

I have recently seen a similar case in a woman of 72.

Cardiac symptoms are, however, not constant, even where the heart is greatly hypertrophied or actually diseased. On p. 123 I give an account of a young man who was under my observation for some years with aortic regurgitation. He developed granular kidney and subsequently died of uræmia, yet his heart gave him no trouble throughout, and his symptoms were of another kind entirely.

In this connection I may mention Cheyne Stokes breathing, which in granular kidney is almost without exception of cardiac origin. Although described as occurring in uramia it is hardly ever seen except in those cases in which there is heart failure, to which it is really due. It is, as in many other forms of heart affection, of grave omen, and may usher in the end, which is rarely long deferred.

I have described a case of a man of 55 who had Cheyne Stokes breathing almost continuously for three months before his death. Except for gout, to which he had been subject for 34 years, he had had good health till his breath began to get short 18 months before admission. Ten months later he began to have attacks of severe dyspnæa of cardiac origin without pain. The last occurred three weeks ago, after which his breath was so short that he sought admittance to the hospital. Cheyne Stokes was found on his admission, although he made no complaint of it.

Acute pericarditis belongs to a somewhat different category of symptoms, but this is perhaps the most convenient place to refer to it. It is always a very severe complication, and even where it does not itself cause death it is a warning that the end is near.

I was asked to see a gentleman in consultation because he had suddenly developed pericarditis without any obvious cause. I found the patient in bed, well nourished and muscular, with a somewhat sallow, unhealthy complexion, looking not seriously ill. There was well-marked pericarditis, friction being unusually loud. His breath was slightly short, and his pulse a little hurried, but except for feeling generally ill he seemed to have nothing special to complain of. The urine contained a small amount of albumen, the arteries were thickened, and the tension raised.

The patient had been in perfect health until three weeks before I saw him. He had been hunting two or three times a week, and it was because he found he could not see the wire fences that he began to be uneasy about his eyesight, which on one occasion caused him to get a fall. The eyesight gradually got worse, and it was this only which took him to the doctor. A week or so before I saw him his vision had become so considerably affected that he could not read at all; the pericarditis was discovered by accident, and he was then sent to bed, much against his will. Ophthalmoscopic examination showed the most extensive albuminuric retinitis, with numerous white patches in both eyes, and a few hæmorrhages; the discs were greatly swollen, so that the condition fully explained the loss of sight. The breath was somewhat urinous; the quantity of urine passed was sufficient in amount, but the specific

gravity was low. A very grave prognosis was given, and in the course of a few days the patient died.

Now this patient had thought himself to be in perfect health, and was

out hunting a month only before his death.

In the course of a case already recognised as granular kidney it may produce no symptoms, and be detected only by physical signs. It is then liable to be overlooked or discovered only accidentally.

## II. THE VASCULAR.

The vascular lesions produce three sets of symptoms :-

(a) Those due to rupture and consequent hæmorrhage.

- (b) 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.
- (c) Besides these it is necessary to refer to aneurysm, and that not only of the small vessels, e.g., one of the arteries of the base of the brain, but of the main trunks, such as the thoracic aorta.

# (1) Aneurysm.

The connection of granular kidney and aneurysm of large vessels is, I believe, 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, i.e., in 6 per cent.

In the same series there were, moreover, two cases of death from the rupture of small aneurysms at the base of the brain.

There is no reason why, if a vessel is diseased enough to rupture, it should not first lead to an aneurysm.

To the possible causes of aneurysm, viz., laborious work, drink, and syphilis, must now be added granular kidney.

# (2) Degenerative Changes.

The next group of cases is an important one, viz., 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 the connection between granular kidney and some chronic affections of the nervous system Gull and Sutton long ago drew attention, but this subject has not of recent years received the attention it deserves, perhaps because Gull and Sutton made their theory of a primary arterio-capillary fibrosis depend too much upon it.

The changes in the eye are the most striking and most familiar, but these have been already dealt with.

Bond has drawn attention to the remarkable frequency of granular kidney in *post-mortem* examinations of the insane, and has shown that it is nearly double that of a general hospital like St. Bartholomew's. He rightly concludes that the two diseases stand in more than an accidental relation to one another.

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.

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## (3) HÆMORRHAGE.

The affection of the vessels being general, the hæmorrhage may take place in almost any part of the body.

Cerebral Hæmorrhage.—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 cases of granular kidney death is brought about by cerebral hæmorrhage. On the other hand the statistics of St. Bartholomew's Hospital 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 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 among Woodbridge's cases of granular kidney cerebral hæmorrhage was met with in one case at the age of 19, in one at 27, in one at 30, and in two at 37 years of age.

Of course many patients with cerebral hæmorrhage do not die of it, but are left with paralysis, as in the following case:—

Reginald H., 28 years of age, presented himself with the signs of partially recovered right hemiplegia. It appeared that eight months ago he was suddenly attacked with loss of power on the right side of the body and aphasia. He soon recovered his speech completely, but only partially regained the use of arm and leg. He walked with the usual halt of an old hemiplegic, and there were besides some jerky movements of the right arm which were worse when the arm was used. The knee jerks and elbow jerks were increased on the affected side. The cause of the hemiplegia was difficult to ascertain. The patient stated he had been perfectly healthy until the time of his attack. There were no signs or history of syphilis or other venereal disease, and the heart was healthy. The history of the attack suggested that it was due to cerebral hæmorrhage. The artery was thick and the tension high, so that the pulse was of a typical renal character. The heart presented no obvious signs of hypertrophy. The urine, when it was first examined, contained no albumen. In spite of this I ventured to make the diagnosis of granular

kidney on the ground that such thickening of the artery could hardly occur in a young person apart from this disease. Fourteen days later the urine was examined again, and was then found to contain a trace of albumen. The eyes also were examined at this time and no change detected, but the next week, when the pupils were widely dilated with homatropine, some lesions were discovered. The discs in both eyes were normal. The left yellow spot and its neighbourhood were quite normal; the right yellow spot presented the appearance as if there had been an old hæmorrhage which had partially disappeared; it was three or four times as large as the other and presented a somewhat granular, pigmented appearance. In both eyes, almost in a line with and about half way between the disc and the yellow spot, were found two or three minute white patches of degeneration. They were extremely small and difficult to see except after careful search and might very easily have been overlooked, as I have no doubt they were on the first occasion. If there had been any doubt previously about the diagnosis of granular kidney this discovery removed it, and justified the opinion expressed that the cause of the hæmorrhage was the arterial degeneration associated with that disease.

Right hemiplegia and aphasia of two years' duration; urine contained albumen (one-half); arteries thick and tortuous; eyes nil; death with cerebral hæmorrhage; post mortem, granular kidney.—Sophia S., aged 44, was admitted into the hospital on February 4th. She had had an attack of right hemiplegia two years previously from which she recovered almost completely. A second attack followed a year later from which again she partially recovered, but was left with some thickness of speech. Since then she had been subject to attacks of giddiness. She was admitted for a third attack with complete paralysis of the right side and aphasia. The arteries were tortuous and much thickened; the tension was high, and the urine contained nearly one-half albumen; the eyes showed no change; cerebral hæmorrhage consequent on granular kidney was diagnosed. The patient died shortly afterwards, and the diagnosis was confirmed by autopsy. The recurrent attacks of paralysis were explained by repeated hæmorrhages.

The difficulties of diagnosis are sometimes considerable. In the following case the symptoms at first seemed to suggest fracture of the skull:—

A man of about 40 was brought into the hospital unconscious and bleeding from a cut on the head. The question was raised as to whether he had a fractured skull, but the symptoms seemed to fit in best with uræmic coma, and that diagnosis was made. The patient died within 24 hours, and on the autopsy no lesion was discovered except granular kidney. The brain was free from hæmorrhage.

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 (9772)

hæmorrhages are found of that peculiar kind known as miliary aneurysms.

Where the small hæmorrhages are not numerous they may produce no pressure signs, but only localised symptoms of peculiar character depending on their position. They probably explain some of the cases of unilateral fits occasionally observed in uræmia. Even when death follows uræmic fits of apparently the ordinary kind, multiple minute hæmorrhages are not unfrequently found, so that the distinction between the hæmorrhagic and the toxic form of uræmia is not always possible.

Bulbar Hæmorrhage.—In the medulla a very small hæmorrhage of this kind may lead to death, or to localised nuclear paralyses of special nerves. Pontine hæmorrhage is, of course, rare, but in some instances granular kidney is the cause of it.

Spinal Hæmorrhage.—Of hæmorrhage into the spinal cord below the medulla I have met with no example myself in granular kidney, nor do I know of any conclusive case recorded.

Ophthalmic Hæmorrhage.—The various forms of hæmorrhage in connection with the eye are of great importance, but have been already dealt with.

Of other hæmorrhages which are not of such immediately serious character as the preceding, epistaxis and hæmaturia are the most interesting and important.

# Epistaxis.

Epistaxis is common and may be the first symptom of disease, so that its significance may be missed.

Patient known to have had albuminuria for two years, but well till one month before admission, and seven weeks before death; first symptom failing sight, then epistaxis; extreme albuminuric retinitis with detachment of retina; Cheyne Stokes breathing; death from asthenia; post mortem, kidneys granular, but above ordinary size.

E. J., aged 44, a clerk, was admitted into St. Bartholomew's Hospital for severe epistaxis. His previous history appeared to be fairly good, and he had during his life suffered from nothing in particular, except attacks of quinsy from time to time. He had syphilis at the age of 22, but with

that exception had had no special illness, except two years before, when on consulting a doctor he was found to have albuminuria; but he had at that time no swelling of the legs or ordinary signs of acute nephritis. One month before admission his sight began to fail him somewhat, and about this time he began to be subject to morning sickness. Otherwise he was in his usual health until the morning of August 7th, when he woke and found his nose bleeding. This stopped of itself in the course of the day, but on August 10th recurred, and became so severe that the left nostril had to be plugged. This stopped the bleeding until he coughed out the plug, and then it began again, when he was sent to the hospital and admitted, after several attempts had been made in the surgery to control the bleeding without success. In the wards the bleeding lasted on and off for nearly a week, and was very severe, so that it was necessary to plug both nostrils behind and in front. He must have lost on the

whole several pints of blood, and became very weak and pale.

The patient was a stout man, but very anæmic and feeble, and spoke in a weak, whispering voice. The pulse was 100; the tension raised; its volume good; the artery thickened, but not tortuous. The heart seemed natural, and no signs of hypertrophy were obtained. The skin was somewhat dry and harsh; the odour of the breath and skin somewhat urinous. The urine was of low specific gravity, containing about one-tenth of albumen and a certain number of granular and blood casts with some epithelial detritus. The sight was greatly affected. With the left eye the patient could only count fingers, and with the right he could hardly read. On examination with the ophthalmoscope well-marked albuminuric retinitis was found in both eyes, with abundant hæmorrhages irregularly scattered over the fundus, and considerable swelling of the discs. In the left eye there was also a small peripheral detachment of the retina in the south-west segment. The quantity of urine was about normal, and varied from 40 to 60 ounces daily.

After the hæmorrhage had stopped there is little to record, except that

the patient became progressively weaker.

A few days later the urine was examined again, was found to be 1012 in specific gravity, to contain about one-twelfth of albumen with a great many casts, some large and hyaline, some cellular with many granular epithelial cells. Micturition was frequent, and the patient had to rise about three times during the night to pass water.

The patient was placed upon a sixth of a grain of nitrate of pilocarpine three times daily. This produced a fairly good action of the skin. He also had vapour baths from time to time for about half an hour, but

these seemed to make him faint.

The urinous odour from the breath and body became more marked.

He vomited occasionally without obvious cause.

The temperature, which for a few days after the epistaxis had risen to about 100° for a short time each day, after about 10 days became markedly subnormal, and got lower day by day. With this depression of temperature the patient's strength also flagged, and he became somewhat wandering in his mind.

On the 26th he grew very much weaker, and began to have some difficulty in his breathing, which became of a "Cheyne Stokes" character, and there was a good deal of rhonchus in the chest. He was very restless at night and faint, but some bromide and chloral gave him sleep. He complained from time to time of numbness in both his legs.

The breathing became gradually more and more laboured, and the weakness greater, and finally the patient died on the 26th, just six weeks

from the time he dated the commencement of his illness, and three weeks from the onset of the epistaxis.

His first symptoms were not those of illness in any way, but simply

failure of sight.

Post-mortem examination.—A well-nourished, powerfully-built man. Both lungs ædematous and markedly emphysematous, only a normal area of heart wall being exposed, though the heart was so large. A moderate amount of fluid in both pleural cavities. The heart, with the pericardium, which was everywhere closely adherent to the heart, weighed 23 ounces. Very great hypertrophy of the left ventricle, the wall of which had in places a thickness of over an inch. Right ventricle not markedly hypertrophied, but the cavity dilated and full of post-mortem clot. Slight atheroma of the coronary arteries, and some calcareous patches in the aortic valves, which were, however, competent. All the vessels of the body atheromatous to a slight degree, especially the arteries of the circle of Willis. The brain decidedly anæmic, but with no subarachnoid cedema. The liver large, weighing 80 ounces, smooth on the surface, but unduly hard, with a considerable increase of fibrous tissue in the organ, and some local perihepatitis. The kidneys weighed 11 ounces, were grey and firm, the capsules adherent, and the surface granular. On section there was obviously much connective-tissue increase, but both on the surface and on the sections there were extensive pale areas of fatty change. There were no urates in either great toe joints, or other sign of gout. In both eyes well-marked optic neuritis with swelling of the optic disc, and round the discs numerous flame-shaped hæmorrhages; no white patches were obvious on the retinæ In the left eye, that in which the attachment of the retina had been observed during life, there was no sign of hemorrhage behind the retina, so that the effusion must have been serous.

Even in the young granular kidney must not be disregarded as a cause of repeated epistaxis. A good example of this is recorded by my friend and former house physician, Dr. Rawlings, of Dorking.

A lad,  $17\frac{1}{2}$  years of age, was subject to frequent epistaxis, and he also suffered from frequent headache, had thickened arteries, an hypertrophied heart, and a trace of albumen in the urine. In this case also, although in so young a patient, the epistaxis was the result of granular kidney.

#### 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 first case I recorded of the kind occurred in a girl of 21, in whom the symptoms, viz., fits, giddiness, vomiting, and optic neuritis, at first suggested intracranial disease. It proved to be a case of granular kidney. The day after admission the urine was of a bright red colour, and contained much recent blood. It continued to contain much blood for 16 days. When the blood disappeared the urine contained one-third of albumen. When the patient died no lesion except granular kidneys was found.

The case is fully reported on p. 115.

The blood is intimately mixed with the urine, and is usually bright in colour, and may look almost like pure blood, but even then there are no clots. I suggested, in my original paper, that the hæmorrhage was probably vesical in origin, as, in the absence of acute nephritis, the urine was rarely smoky or dark in colour. This may be correct in some cases, but two of Bowlby's cases show that the blood may also come from the kidneys themselves, and it has been seen with the cystoscope (App. Case III) passing out of the ureters.

This form of hæmaturia has led to many mistakes, chiefly to the diagnosis of calculus in the bladder—or in the kidney if there has been lumbar pain or attacks of renal colic. Operation has even been suggested and performed, and in fatal cases the absence of any lesion except granular kidney has been proved by autopsy.

Mr. Bowlby's cases are the following :-

Male, aged 73, was admitted for retention of urine. This commenced without obvious cause on October 13th; the urine, which dribbled away, was found to be bloody. When drawn off the catheter contained

<sup>\*</sup> Mr. Bowlby published shortly afterwards a valuable paper on the same subject.

a considerable amount of blood, but no clots, and the hæmaturia continued till the patient's death on October 21st. On post-mortem examination the bladder was found filled with a pint of what looked almost like pure blood. The prostate was somewhat enlarged, but well-marked contracted granular kidneys were the only other lesion found.

The whole of the kidneys were infiltrated with blood, both the renal tubes and the fibrous stroma being alike affected. The hæmorrhage was

most profuse in the cortex, but not limited to it.

Male, aged 49; was in good health till three months before admission, when he had pain in the loins and passed blood. From this time the urine contained blood continuously. The arteries were rigid, the pulse strong and jerky; the cardiac dulness increased and the heart's action heaving. The urine was bright red, 1015 specific gravity, alkaline, containing much blood and one-third albumen, and smelling very offensively. On standing it separated into three layers, the upper smoky, the middle bright red, the lower gritty and whitish in colour. Blood cells and triple phosphate crystals were found but no casts.

For a week the man continued to pass two pints or more of bright-red

bloody urine, when he became unconscious and died.

Post mortem.—The heart was found greatly hypertrophied, weighing 18 ounces. The kidneys, weighing only 3½ ounces each, were contracted and granular. The pelvis and ureter of each contained a little blood. There was also a stricture of the urethra.

Male, aged 64; was in good health till 16 months before admission, when he had an attack of pain in the loins with slight shivering, and passed bloody urine. This attack lasted five or six days. He then remained free till five weeks before admission, when he had a similar but rather more severe attack. The pain diminished but did not entirely go away, and the urine continued to contain much blood. For 16 days after admission he continued to pass about three pints of urine containing large quantities of blood, probably at least a fourth part. The arteries were hard and tortuous.

The patient was pallid and looked as if he had lost flesh lately. On leaving the hospital the urine averaged 40-50 ounces daily, was acid, of 1008-1013 specific gravity, and contained a little albumen.

In the first case the blood was thought to be of vesical origin.

In my original paper I refer to a case communicated to me by Dr. Sharkey, in which the patient, a young girl, passed so much blood with the urine that the bladder was sounded and, failing to find a stone, dilatation of the urethra and digital exploration of the bladder was suggested. To this Dr. Sharkey did not consent, and, the patient dying shortly after, no stone was found post mortem, but only markedly granular kidneys.

Mr. Mansel Moullin records a case\* in which the diagnosis of renal calculus was made, and the kidney was explored without anything being found:—

<sup>\* &#</sup>x27;Clin. Soc. Trans.,' vol. xxv.

The patient was a woman 34 years of age, who was admitted for renal colic, from which she had suffered at frequent intervals for two years. Between the attacks she suffered much from almost constant aching in the loins. She passed urine frequently, and it contained blood—sometimes in considerable amount—evenly mixed with it and without any clots. The urine averaged 40 ounces, was of 1012–1014 specific gravity, and contained when free from blood a small quantity of albumen. The arteries were hard, and the heart slightly hypertrophied. There was some bronchitis and emphysema, but no ophthalmoscopic change.

The woman died of exhaustion three days after the operation, having had several attacks of colic after the operation of even greater severity

than before, for which no cause could be assigned.

Post mortem.—Nothing was found but well-marked granular kidneys.

Copious hæmorrhage, as in the cases described, is not common, but hæmaturia in slight amounts is frequent enough, and it is often long continued or recurrent. To this recurrent slight hæmaturia experience has led me to attach considerable diagnostic value.

Hæmorrhage from bowels five weeks previously; sore throat; blood in urine; granular kidney; recurrent hæmorrhage.—A young man, aged 19, a warehouseman, believed himself to be in good health until three months before admission, when he suffered from hæmorrhage from the bowels, and was confined to bed for five weeks. He seemed to get well, and remained in his usual health until two days before admission (January 14th). He then had a sore throat and felt sore all over, and in the evening he noticed that his urine was very dark coloured. He had a little pain in the back, and during the night felt hot, then shivered and perspired. There was no

history of chill or of any cause for the attack.

The patient was pale and of a pasty complexion, with slight herpes on the lips. The right tonsil was slightly ulcerated. There was no cedema anywhere. The urine was porter-coloured, acid, specific gravity1014, and contained one-quarter of albumen. The arteries were thickened and the tension raised. The microscopical examination of the urine showed the presence of numerous red blood-cells, with triple phosphate crystals and a few fragmentary granular casts. The quantity of urine passed was on the average above normal. The temperature on admission was 101°, but it fell the next day to normal and remained normal afterwards. The throat affection rapidly disappeared, so that the rise of temperature depended probably upon this condition. Œdema was completely absent.

The urine contained blood for a week after admission, and continued to contain albumen, though only a very faint trace, until his discharge nearly three months later. The history of recent sore-throat with albumen and blood in the urine led me to think at first that the case was probably one of diphtheria associated with nephritis, but the condition of the arteries, the long persistence of albumen, and the absence of cedema, convinced me later that the case was one of granular kidney. This conclusion was confirmed by the subsequent course of the case, for the urine for the last two months of his stay was characteristic, being large in quantity (80–100 ounces), of low specific gravity, and with but a trace of albumen.

Recurrent hamaturia under observation 11 years.—The patient was a man, aged 23. Hæmaturia was first observed in 1881 for 10 days. Two attacks (ten days and seven days) followed in 1883; one in 1884; two in 1885; one in 1886; one in 1888. These attacks occurred under my observation. The blood was on all occasions bright in colour, and enough to colour the urine well. The urine was of 1010 specific gravity, and contained albumen (about one-twelfth), but varied much on different occasions. The arteries were thick. There were no retinal changes observed. Frontal headache was the chief symptom.

The patient was last seen in January, 1894, being then aged 30. No new symptoms had developed and no retinal changes were present; no distinct cardiac hypertrophy could be made out, but the arteries were thick and tension high. The specimen of urine then brought contained

no albumen.

I formed the opinion in 1883 that the man probably had granular kidneys, and I saw no reason subsequently to change my opinion. I do not know the result of the case, which has not been seen since 1894.

Admitted as acute nephritis; recurrent hæmaturia; kidneys probably granular.—Edward P., aged 34, was admitted into the Royal Free Hospital as a case of acute nephritis. He had been a free liver and had drunk much beer, but was in good health until one month before admission. Then his legs swelled, and a fortnight later his toes also. On admission there was slight general ædema. The urine was reduced in quantity, and contained one-half albumen with granular casts, and was smoky. The eyes were normal on ophthalmoscopic examination. The arteries were slightly thicker than normal for his age. The case ran the ordinary course of acute nephritis, ending in convalescence. On several occasions while the ædema persisted the urine contained blood, being sometimes bright red in colour, at other times only smoky. These alterations could not be traced to any cause, for they occurred during the time that the patient was kept entirely in bed. After about two months the ædema completely disappeared, and continued absent till the patient's discharge from the hospital. The albumen was at times completely absent, and at most times there was only a trace.

On several occasions after the cedema had gone the blood returned in the urine, generally to the extent of giving it a smoky tint, but occasionally the colour was bright red. Generally at these times there was an increase also in the amount of albumen over and above what the blood would account for. The duration of these attacks was about two or three days, but during them there was no other change in the patient's condition. The arteries, however, were distinctly thicker and harder on leaving the hospital than they were on admission. I was led to regard the case as one probably of old granular change, with an intercurrent attack of acute nephritis. At any rate, at the time of leaving the case

presented the characteristic features of granular kidney.

Admitted as acute nephritis, but arteries very thick; recurrent hamaturia.—
The patient, a man, aged 48, was well till four weeks ago, when the face and legs swelled and the urine became scanty. On admission the signs of acute nephritis were present. The albumen was abundant (one-half). The arteries were very thick and the tension high. A month after admission, during convalescence, the patient began to pass bright blood in the urine. This continued for a few days, and recurred at intervals of two or three weeks, lasting a few days each time. The patient also had two attacks of

gout in the hospital, which, however, stood in no close relation with the hæmaturia. Great variations occurred in the albuminuria, and on leaving the patient had lost all ædema, but continued to pass blood at times. The diagnosis made was granular kidney with intercurrent acute nephritis.

Granular kidney; great variations in albuminuria; recurrent hæmaturia.—Male, aged 32, was admitted for severe headache, ædema of feet, and hæmaturia. The urine contained about one-third of albumen and a good deal of bright blood, and numerous granular casts. The radial artery was thick and the tension high. The diagnosis of granular kidney was made 10 days later, the urine contained hardly a trace of albumen or blood, and there were no casts. Specific gravity 1014. 82 ounces were passed in 24 hours. There were no ophthalmoscopic changes. A week later the urine again contained blood. After leaving the hospital the patient returned a few days later with a recurrence of hæmaturia, which again quickly passed off. He was seen subsequently with similar attacks.

#### OTHER FORMS OF HEMORRHAGE.

Hæmatemesis.—Hæmatemesis is very rare, but I have seen one instance of it.

The patient was a man of 45 years of age, fairly well nourished, but a little pale; a cab-driver, but a total abstainer for the last 13 years. The arteries were greatly thickened, the tension high, and the heart slightly hypertrophied. At times there was a small amount of albumen in the urine, but it was often absent. Four years ago the patient had an attack of profuse hæmatemesis, and brought up one or two pints of blood. He had no definite gastric symptoms of any kind, and nothing whatever pointing to the presence of ulcer then or subsequently. This attack left him for a time very weak, but he recovered and went on well till a few weeks ago, when he had another attack of hæmatemesis, bringing up also a considerable amount of blood. A fortnight ago he had another attack, bringing up about a pint of blood, and it was this which brought him to the hospital. The case was obviously one of granular kidney, though there was no albuminuric retinitis to make the diagnosis incontrovertible. The only other question was whether anything of the nature of gastric ulceration existed. All that I can say is that there was no sign and no history of it. This, of course, is not quite conclusive, for the signs of gastric ulcer may be latent. There was, at any rate, no evidence whatever of cirrhosis of the liver, and the history of total abstinence for so many years was against it.

Hæmorrhage from the Bowels.—Hæmorrhage from the bowels is very rare, and in this connection it is interesting to remember that in a small number of cases ulcers of the intestine have been discovered in granular kidney, of which no signs had been given during life to suggest their presence. In other cases, however, the autopsy has shown no gross lesion to explain the hæmorrhage (App. Cases III and IV).

Hæmoptysis.—Hæmoptysis in the course of granular kidney, though I can have no doubt it occurs, is an event I have not personally met with. Hæmoptysis of this kind probably stands in the same relation to granular kidney as the hæmoptysis of old people does to atheroma. Sir Andrew Clarke described these cases as Arthritic Hæmoptysis. The name, though striking, is really one to which much objection can be taken, though it expresses an important clinical fact, viz., that old people may suffer from

hæmoptysis, even to a considerable amount, as the result of atheromatous disease of their vessels, this change being in Sir Andrew Clarke's opinion the consequences of gout. The condition is, at any rate, a rare one, for Sir Andrew Clarke had only met with 15 instances of it in the course of 20 years' experience.

Metrorrhagia.—I have recently had to deal with a case in which very troublesome and persistent hæmorrhage occurred from the uterus, which was ultimately, after some difficulty, checked by full doses of ergot. There was no diagnostic difficulty in this case, for the signs of granular kidney were already obvious enough.

Oozing.—Hemophilia.—In the last stages of granular kidney the patient may pass into an almost hemophilic condition, in which slight, though continuous and almost uncontrollable, oozing takes place from various parts of the body, from the gums, nose, tongue, lips, pharynx, vagina, or from any wound or scratch in the skin. A considerable amount of blood may be thus lost, and the anemia from which the patient is already suffering be very greatly aggravated (App. Case VII).

Purpura.—Although almost any part of the body may be the seat of hæmorrhage, it is remarkable that while acute and severe affections of the skin are not rare in granular kidney, they show no special hæmorrhagic tendency, and it is quite rare for any of these eruptions to be of such a character as to be fairly called purpuric (cf. Skin Affections, p. 133).

## B.—Toxæmic Symptoms.

ACUTE AND CHRONIC UREMIA.

The toxemic 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, of longer duration, of less apparent severity, and of a very indefinite character. They are respectively called acute and chronic uramia; 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 uramia in its ordinary acceptation might be retained. For the chronic group on account of its varied and indefinite symptoms chronic renal toxemia would be the better term.

There are three main theories of uramia, 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 definite proof so far of an internal secretion in the kidney

The retention theory, which maintains 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, &c., is now discredited.

The third theory only remains, viz., that which refers the symptoms only to perverted metabolism. According to this theory the products of metabolism—extractives as they are usually called—are either produced in abnormal amount, or not properly elaborated and 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."

Various poisons are normally produced in the tissues which ought to be eliminated by one organ or another, and especially by the kidneys. If their elimination be suspended or inadequate, toxemia results. A healthy man, it is said, manufactures in little more than two days enough poison to kill himself.

There are many different extractives and they have different physiological actions; thus the symptoms produced might vary according as one or other of the extractives predominated.

Bouchard has separated from the urine no less than six different toxic substances, which fall into two groups, of which the one produces somnolence, coma, and salivation, and the other myosis, fall of temperature, and convulsions.

This is Bouchard's theory of multiple intoxication. According to this theory the poisons are produced in the body, and by processes not differing essentially from those which take place in health. The kidney plays its part only so far as it makes the elimination of the poisons defective; and Uræmia would thus be brought into close relation with other conditions in which the normal metabolism of the body is perverted.

Clinically the symptoms of uramia 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 uramia, and Murchison did not hesitate to call it uramic. 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 uramic; so, again, in the later stages of cirrhosis hepatis, diabetes mellitus, the last stage of Addison's disease, of myxædema, and indeed in almost all slowly-dying persons.

We might thus place all these conditions together under the one heading of Toxemia, adding some prefix, as renal, hepatic, supra-renal, thyroid, diabetic, febrile, or others to indicate what is believed to be the cause in the particular case.

Symptoms resembling uramia may thus arise under conditions with which the kidneys may have nothing to do. When, as in uramia, the kidneys play the chief part, it is very tempting to refer the symptoms to defective internal secretion, for it is certainly not due simply to defective elimination.

It is for this reason that I prefer to call Uræmia Acute and Chronic Renal Toxamia, so as to bring it into its proper relation with other allied clinical conditions.

Uræmia may thus arise in two ways:-

- (1) The metabolism may be normal and the elimination defective.
- (2) The metabolism may be increased or perverted, while the elimination is not deficient and may be, on the contrary, much increased.

In uramia the tissues are enormously rich in extractives, and that even when elimination by the kidney is active; when elimination by the kidney is impaired the extractives are still further increased. This is not inconsistent with the view that the increased metabolism of the tissue itself may be the result of a defective internal secretion by the kidney.

If, then, we are thus led to associate the symptoms of chronic uramia with chronic extractive poisoning, *i.e.*, 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 uramia with the condition of the kidney-cells in granular kidney just as we do in parenchymatous nephritis.

### CHRONIC RENAL TOXÆMIA.—CHRONIC URÆMIA.

It is to the chronic toxemic group that many of the symptoms belong which bring the patient suffering with granular kidney under medical observation. They may be of such a kind as to indicate almost any part of the body as the seat of disease rather than the kidney, and may thus lead to frequent errors in diagnosis. This is especially the case in connection with the digestive and nervous systems. As the disease advances the general nutrition becomes profoundly affected, and a cachexia may develop which may be as extreme as that of malignant disease, or of Addison's disease.

# (1) Gastro-Intestinal Symptoms.

Dyspepsia.—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.—Vomiting is often a source of difficulty, for it is very obstinate and does not stand in relation to the taking of food. The two cases which follow are of great interest because of the

difficulties they presented in diagnosis:-

Periodical vomiting; thought to be due to pyloric obstruction; signs of granular kidney.—Austen S., aged 32, a groom, was placed under the care of Mr. Bruce-Clarke by his doctor on account of his having gastric symptoms which seemed to point to some lesion there, and perhaps to require operation. It appeared that he had been well till October, 1896, when he had an attack of vomiting which lasted four days; this was associated with some abdominal pain and constipation. From that time he had several attacks occurring at intervals of a few weeks at first, but the intervals becoming progressively shorter while the attacks themselves lasted somewhat longer. The last attack before coming up to the hospital lasted for eight days, and the interval between it and the previous one was only 14 days.

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The patient was a fairly healthy looking man, but he stated that he had been losing flesh rapidly, about 2 stones since the beginning of the year, i.e., during the last six months. He complained of feeling frequently sick and vomited three or four times on the morning of admission. His temperature was sub-normal; pulse, 76; the organs of the chest healthy; the abdomen showed nothing whatever abnormal; he complained of a small tender spot in the epigastric region, but nothing could be felt there, and the pain that he occasionally complained of only came on at the time of his vomiting. During the attacks of vomiting he vomited five or six times during the day, did not necessarily bring up his food, but generally only a small amount of watery fluid, at other times it

might be the contents of the stomach.

I was asked to see the case, and made a very careful examination also, but failed entirely to discover anything abnormal in the abdomen. What attracted my attention first was the thickness of his artery; the pulse was also of a high tension. Finding nothing whatever to account for the abdominal symptoms I cast about for some other cause of the vomiting which was not abdominal, but could obtain no cerebral symptoms of any kind, and examination of the eye showed the retina and discs to be quite normal. The possibility of the attacks of vomiting being due to locomotor ataxia had been previously considered, but the knee jerks were found to be normal, and, as the pupils were equal and reacted to light and the patient had none of the other characteristic symptoms, that diagnosis was excluded. thickness of the artery and the condition of the pulse led me then to have the urine carefully examined. It had been examined once or twice before soon after admission and no albumen detected, but when the examination was made at my suggestion an eighth of albumen was found. After the patient's admission the attack of vomiting lasted for seven days and then gradually ceased, though he still, for a day or two longer, complained of some nausea. For the next month he had no attack at all, but the albumen was continually found in the urine, the amount of urine not being much increased, but the specific gravity remaining low, 1016; it contained 2.8 per cent. of urea.

Taking into consideration the condition of the artery and the albuminuria I concluded that the symptoms, therefore, were uræmic and dependent upon granular kidney. So far as the case has progressed at present no fresh symptoms have developed; the condition of the urine persists, and no signs of abdominal disease have appeared. As granular kidney will explain the symptoms, and as no other disease has been discovered, I cannot help thinking it is granular kidney that the disease

will prove to be, but the case is still under observation.

I have heard subsequently from the doctor, who states that the attacks still continue unaltered, and but little influenced by treatment. He endorses the opinion that they are renal in origin.

I am indebted to Dr. Horder for the notes of another case of the same kind in which the diagnosis was confirmed by autopsy:—

Recurrent vomiting with emaciation; thought to be due to malignant disease of stomach; nothing found post mortem but granular kidney.—Thomas J., aged 62 years, previously a healthy man, and accustomed to a

life of hard manual work, began to suffer from "indigestion" about March, 1896, the symptoms being loss of appetite, nausea, and vomiting. The vomiting continued and increased in frequency, but was unaccompanied by pain, was always slight in amount, and seemed independent of food. Emaciation followed, until about August the patient was extremely wasted. Though no abdominal tumour was at any time discovered, the continued vomiting and the great loss of flesh led to the diagnosis of malignant disease of the stomach. At this time the urine was being passed more frequently than normal, but showed the presence of no albumen when carefully examined on several occasions. There was constipation throughout. In the beginning of October the patient became too weak to get out of bed, and suddenly developed a tendency to bleed-at first from gums and mouth, then from the navel. This bleeding continued for some three days, when the patient died of exhaustion. A post-mortem examination (of abdomen only) revealed the presence of an extreme degree of granular kidney—the left organ being the size of a large walnut and practically destitute of cortex, the right being smaller than natural, cystic, bright red, and having its cortex diminished to some 4 inch in depth. The pelves and ureters were dilated. The prostate was much enlarged and the bladder-wall hypertrophied. The stomach and the rest of the abdominal viscera were quite natural.

When to the vomiting optic neuritis is added, confusion with intracranial disease, such as cerebral tumour, abscess, or meningitis, is only to be expected. The vomiting may occur only or chiefly in the morning, and might then suggest pregnancy, or potus. I have seen cases of granular kidney confused with all these conditions.

Agonising headache; vomiting; fits; albuminuric retinitis; chronic ear disease; variations in pulse tension; epistaxis; severe præcordial pain; post-mortem, kidneys granular.—Josephine W., aged 21, single, came to the hospital complaining of severe headache and occasional fits, from which she had suffered more or less for two years, and which she attributed to grief for the loss of her father, who died shortly before this time. The fits were of frequent occurrence, sometimes even two or three a day, and lasted each some minutes, and occasionally half an hour; they were generally, but not always, attended by loss of consciousness, and usually preceded by a "bilious attack," i.e., by sickness and vomiting, sometimes for 24 hours before the attack began. For two years she had had a chronic discharge from the left ear, though she had been slightly deaf from childhood. During the last six weeks she had been troubled with frequent micturition, and had been altogether worse. During the week preceding her admission had suffered intense agony from headache, and had had several fits. There was no history of any illness beyond those mentioned.

She was a small but fairly developed young woman, extremely pale and anæmic. Her face bore an expression of pain. She suffered from very severe headache across the brows and vertex. Beyond slight increase of the cardiac dulness and of the heart's action there were no physical signs in her chest. The arteries were unduly hard for a girl of her age. The pupils were slightly dilated but were equal, and reacted readily to light. There was well-marked double optic neuritis with

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numerous white patches and copious hæmorrhages, and this although

she did not complain of any defect of vision.

On the evening of admission she had a fit, during which she threw herself violently from side to side, clenched her hands, and had severe retching but no actual vomiting. She did not lose consciousness, but complained of palpitation and pain in the cardiac region and of a choking sensation in her throat. She was in an extremely hyperæsthetic, almost hysterical, condition, so that the slightest interference distressed her. The urine was now found to contain albumen, as well as some blood, and to be of low specific gravity, but no casts could be discovered.

The severe persistent headache, with fits and double optic neuritis, associated with discharge from the ears and deafness of long standing, suggested the diagnosis of some intracranial mischief, either chronic meningitis or abscess in connection with disease of the middle ear; but the hypertrophy of the heart, the thickened arteries, and the characters of the urine, with the peculiar condition of the retina and the disc, made

it clear that granular kidney was the cause of the disease.

The course of the case was shortly this:—For some time after admission she remained in statu quo, the headache and retching being severe, and the fits occurring at irregular intervals. As the headache prevented sleep, cannabis indica was administered in Mxx doses three times a day, with a double dose at night. This had an excellent effect for a few nights, and, coupled with hot baths daily and iron as a tonic, she improved for about three weeks. The urine, however, still remained scanty and albuminous, and from time to time was bright red from the presence of blood. The symptoms then returned, and the urine diminished. Vapour baths were then administered with a diuretic mixture. This also relieved for a time. The optic neuritis remained all the time in statu quo. The hæmorrhages, which were exceedingly numerous, were slowly absorbed, and but few fresh ones appeared; but otherwise the retina and the disc were but little changed.

The patient gradually grew more anæmic, and with the change began to complain of greater præcordial pain. The heart dulness was found further increased, and a blowing systolic murmur was audible over the whole præcordial region, though loudest at the left base and at the apex, faint in the intermediate parts, and not audible at all in the axilla or behind or away from the præcordial region. The murmur was therefore a dilatation and not an organic murmur. At the same time the legs and arms began to be slightly ædematous, but the ædema never became considerable. Fourteen days after admission she had a severe attack of epistaxis, which was repeated the next day, the patient losing on each occasion about half a pint of blood. This recurred, though not so severely, on several subsequent occasions, and though it temporarily relieved the headache, of course increased the anæmia. With the increasing anæmia the præcordial pain increased, until it became the chief symptom of which she complained.

The condition of the arteries remains to be noticed. The slight thickening has been already referred to, but what was chiefly remarkable was the rapid and apparently causeless variations in the tension of the vessels. No tracings could unfortunately be obtained, but the artery could be felt at one time quite hard and rigid, the pulse being small, with a long low wave, as is characteristic of granular kidney, and shortly after becoming large and soft with a full and short wave. The patient became rapidly exhausted, though at last she became so noisy and almost

maniacal that she had to be isolated.

On post-mortem examination the heart was found greatly hypertrophied, weighing 15\(^3\) ounces, the left ventricle measuring nearly an inch in thickness, though the patient herself could hardly have weighed more than 6 st. The left kidney weighed 3 ounces, it was small, granular, very fibrous, the capsule adherent, and the cortex much reduced in thickness. The right kidney measured only one and a half inches long by three-quarters of an inch broad, and was very little more than a fibrous capsule of about one-sixteenth of an inch in thickness. The pelvis and ureter of this side were of normal size, or perhaps even a little larger than normal. There was no obstruction in the course of the ureter, and no cause for this condition of the kidney could be found, though from the smallness of the arteries and veins it was clearly of old date. There was a little serum in the ventricles of the brain, but beyond slight thickening of the vessels the brain and meninges were absolutely healthy. The pleural, peritoneal, and pericardial sacs contained a little clear serum, and the spleen, lungs, and liver were congested.

Headache; fainting fits; chronic discharge from ear; albuminuric retinitis.—A woman, aged 50, came as an out-patient to Victoria Park Hospital, complaining of debility and frequent morning sickness, which, in a temperate woman of her age, in whom the catamenia had been absent for five years, was peculiar. On inquiry I found that she had been losing power for about 12 months, during which time she had occasionally "fainting" fits, and for the last eight months had been troubled with frequent micturition. She had had a chronic discharge from the ear since scarlet fever in childhood, and had suffered from periodical headaches all her lifetime. Albuminuric retinitis was found with numerous white patches in both eyes. The urine contained a moderate quantity of albumen. The arteries were a little thickened, but not remarkably for her age. There was no edema of the feet. Her sight, it appeared, had been slowly failing for 12 months. There was no history of any previous renal disease.

She was under observation for about four weeks, during which time the albuminuric retinitis increased considerably, but the other symptoms remained unchanged. She then absented herself from attendance, and

has since been lost sight of.

Diarrhæa.—The symptoms in connection with the bowels are not, as a rule, so puzzling. Diarrhæa is common with any form of kidney disease, but there are cases in which diarrhæa, extremely obstinate or almost uncontrollable, is practically the only symptom.

Uncontrollable diarrhæa; erythematous rash; death from exhaustion; post mortem, granular kidneys only.—The patient was a man of 42, who had lived in Singapore for many years, and had had there various illnesses and some attacks of fever. He was a heavy drinker, but did not seem materially to have suffered from it. He came to England on leave; and while away on a short holiday from London he was seized with very troublesome diarrhæa, and came back. From that time till his death he was afflicted with the most profuse, uncontrollable diarrhæa, passing on some days 12 or 15 copious motions in the 24 hours.

The patient was a spare man with a somewhat earthy complexion, and looked as though he might have been a fairly hard drinker, as in fact he had been.

He lay throughout in a listless, apathetic condition, not actually delirious, but taking little notice of what was going on around him. His pulse was 102, the tension a little above normal, but the artery not markedly thickened. There was a good deal of tremulousness about his movements, especially in the face, hands, and tongue. The urine contained a little albumen, and for the first day or two a few granular casts, which, however, were not found subsequently. The liver was slightly enlarged, extending about three-quarters of an inch below the costal arch in front.

Having an obscure illness to deal with in a patient returned from the tropics, the blood and fæces were carefully examined to see if any information could be obtained from them, but none was forthcoming.

The temperature, though raised to 101.4° at the commencement of his illness, soon fell, and for the latter part of the time was below normal.

In the fourth week of his illness an erythematous rash appeared on his trunk, and rapidly spread over the whole of his body. It itched a great deal, and subsequently peeled. The diarrhea continued, and treatment had little or no effect upon it. The patient became weaker and weaker, and ultimately died, after about six weeks' illness.

On the post-mortem examination nothing was found except granular kidneys, and that not to a very advanced degree. The liver was a little enlarged, and weighed 54 ounces. The kidneys weighed 14 ounces together; they were red on section, the surface slightly granular, and the

capsule a little adherent. The eyes showed no lesion.

In another case the patient was under treatment for general pityriasis (cf. p. 129); obstinate diarrhœa developed, though not so profuse as in the previous case. The patient sank and finally died in uræmic convulsions. Here again granular kidney was the only lesion found post mortem.

Cramps.—The dyspeptic symptoms are often associated with cramps. I have seen several cases in which cramps were the chief complaint.

Cramps; lead colic and gout many times; retinal hamorrhage. -James C., aged 41, a coach painter, came to the hospital complaining of attacks of cramp in his calves from time to time, and of occasional morning sickness. His sight had been misty during the last six weeks, and during this period he had suffered with severe frontal headache. He had had lead colic several times, for which he had twice been an in-patient in the hospital, and had also had several attacks of gout. The urine was increased in quantity, and he had to rise once or twice each night. The specific gravity was 1010, and it contained about one-sixth of albumen. The artery was thick, but the tension low; the heart presented no definite physical signs of hypertrophy. On examination of the eye, the condition of the left disc was a little indefinite; it was thought to be possibly an imperfect development of the optic nerve. The disc on the right side was also not quite normal, but it might have been a similar condition less developed. However, three weeks later, on examining the eye again, a few recent hæmorrhages were found in the right retina, with some minute and somewhat indistinct white patches in the neighbourhood of the yellow spot. The left disc was somewhat obscure and difficult to see, but there did not appear to be any white patches in that eye.

## (2) Gout.

Cramp naturally leads to the consideration of gout.

The occurrence of chronic kidney mischief as the result of longstanding gout is well recognised; but in many cases it is quite possible that the opposite relation exists, viz., that the patients are gouty because their kidneys are granular.

Indeed it has been stated that no young person has gout unless the kidneys are granular. This I believe to be an over-statement, but it represents a part of the truth.

I do not know how far the uratic deposit in the joints can be taken as proof conclusive of gout, because it may be found in patients who have never presented during life any gouty symptoms. It is, however, certainly true that a very large number of cases of granular kidney have such deposit in their joints, though this may really not be more than an evidence of the renal inadequacy.

The two affections may certainly coexist side by side for years, but it is not easy to determine the true relation in which they stand to each other.

Gout for 22 years, the kidneys being found granular.—Walter W., aged 46, had been subject to gout for 22 years, the worst attack being at the age of 41, which left him with tophacious bursæ over both elbows. The arteries were greatly thickened and the tension high. A slight amount of albumen was present in the urine. The eyes showed characteristic changes; in the left was a large hæmorrhage on the macula lutea, and in both many of the arteries presented the characteristic silver-wire streaks.

Per contra, gout is not a necessary consequence of granular kidney; in other words, patients may have granular kidney for years and die of it without ever having suffered from gout at all, or the gout may develop quite late in the course of the disease (App. Case II).

# (3) Lead Poisoning.

Gout in the course of granular kidney naturally suggests the consideration of lead poisoning, for the three affections—gout, granular kidney, and lead poisoning—stand in close relation to one another.

Gout for 30 years; frequent lead colic; violent headache; granular kidney.—The patient was a man, aged 52, a glass-cutter. His work was to cut glass which was backed with a preparation of lead, and was used for the common looking-glasses and Chappuis reflectors. This had been his occupation all his life. He had had gout since the age of 22; had had many attacks of lead colic, and came under treatment for an attack of this kind. He had had many attacks of gout, and had large gouty

deposits in the bursæ of his elbows and fingers.

He was anæmic, sallow, with a well-marked blue line on the gums. He presented the signs of granular kidney, viz., thickened arteries, hypertrophied heart, a good deal of albumen in the urine, and, in addition to that, well-marked albuminuric retinitis of the most typical kind, with numerous white patches round the yellow spot. What brought the patient to the hospital, besides the cramp, was the recent gradual failure of vision and severe frontal headache. The frontal headache ultimately became the most prominent symptom. It apparently was agonising and of a violent neuralgic character, and though relieved temporarily by phenacetine and similar drugs, was most benefited by persistent adminis-

tration of small doses of nitrate of pilocarpine.

Wrist-drop due to lead poisoning; slight gout; granular kidney.—A man, aged 47, came to the hospital complaining of weakness in the right wrist. He had some loss of extension, and the two middle fingers dropped entirely, the index and little finger, however, being still partially extended. It was evidently a case of slight lead poisoning, and there was a faint lead line over some of the teeth. The man was a carpenter in some lead

works, and had occasionally had attacks of colic.

He looked pale, thin, and had been complaining lately of some swelling over the right wrist, and also the right great toe, not of a very painful character, but evidently of the nature of gout. On examining his pulse his artery was found very much thickened and the tension high; the heart somewhat hypertrophied; the first apex sound prolonged, and the second aortic sound accentuated. The urine was of low specific gravity, with about a quarter albumen; the eyes were examined, but no albuminuric retinitis found. In this case it was clear the patient had lead poisoning and gout; but it was also evident directly the finger was placed upon the pulse that he was suffering from something more serious than either, viz., granular kidney.

Gout for years; worker in lead factory, but never lead poisoning; granular kidney; death from asthenia.—William O'B., aged 49, a worker in a lead factory, had suffered occasionally from gout for years, but had never had colic or wrist drop. Eight months before coming under observation he had become too weak to work, his breath became short, and his feet swelled slightly.

On admission he had orthopnea, chronic bronchitis, edema of the feet, and a weak heart; the artery was much thickened, but the tension low. There was a small amount of albumen in the urine, and well-marked albuminuric retinitis, i.e., white spots and hæmorrhages in both eyes. He

died of asthenia gradually, and was delirious at the last.

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, 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, viz., that they suffer so much from lead symptoms, just as others do from gout, because their kidneys are granular already.

## (4) 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. The complexion loses the transparency of health, and becomes thick, muddy, earthy. The patients become feeble and anæmic, lose health and strength, and often flesh.

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 malignant disease.

It is often out of all proportion to the other symptoms, or may even exist alone. In some cases the anæmia predominates, and in others the asthenia.

I have seen instances in young people in which chlorosis has been diagnosed.

In those cases in which extreme anæmia is the chief symptom I do not know that the blood has been systematically examined. In the few instances in which I have had such an examination made the changes have been those of simple but extreme anæmia.

In the following cases the patients were suffering from mitral incompetence, but their anæmia was out of all proportion to their other symptoms, and suggested some other cause beyond the morbus cordis. Advanced granular kidney was discovered:—

Mitral incompetence; extreme anamia; granular kidney; albuminuric retinitis.—Mary E., aged 38, a housewife, came to the hospital complaining of shortness of breath and some swelling of the feet.

For two years she had suffered from pain in the loins and lumbar region, with occasional cedema of the feet and puffiness of the eyes; this had been getting worse lately. She had had three attacks of rheumatic fever, at the ages of 15, 27, and 34. She had four children alive, and the

five last pregnancies had ended in miscarriages.

She was extremely anæmic and ill, had considerable ædema of the feet, and much albumen in the urine. The apex was in the nipple line, and the cardiac dulness somewhat increased upwards and to the left; there was a systolic apex murmur, but both sounds at the apex were audible. The arteries were very thick, although the tension was not high. There was some visible pulsation in the neck. The anæmia was in excess of what could be accounted for by the amount of morbus cordis that she had, and the thickening of the arteries was such as is not met with in simple mitral disease.

When the eyes were examined, well-marked albuminuric retinitis was found in both eyes; it was most marked in the left eye and in the neighbourhood of the yellow spot, there being a good deal of pigmentary change there, with numerous white patches. The changes in the right eye were in an earlier stage. No defect of the sight had been complained

of or existed.

Mitral incompetence; extreme anamia; granular kidney; albuminuric retinitis.—Thomas B., aged 28, a potman, came to the hospital with ædema of the feet and shortness of breath. He had mitral regurgitation and considerable dilatation of the heart. The history which he gave was that he was well till three years ago, when his face and legs swelled; this continued more or less to the present time. Two years ago he found his sight dim, but in a month this recovered, and he had no trouble with it since.

He was extremely anæmic, and altogether his condition did not seem entirely explained by his mitral disease. The arteries were greatly thickened, though the tension was low. The urine contained about one-eighth of albumen. The condition of the arteries and the general appearance of debility and anæmia led to the examination of the eyes, when colonies of white bright spots were found round the yellow spot in both eyes, and well-marked silver-wire arteries.

The patient, therefore, had granular kidney as well as morbus cordis.

The next case is also interesting, as occurring in a young man with a rtic regurgitation :—

Aortic disease for 12 years, producing no symptoms; gradual asthenia; frequent hæmaturia; uræmic attacks on and off for two years; death in one.—R. L., aged 33, a medical man, consulted me for gradual loss of strength and energy, which had been coming on for a period of 12 months. I had seen him previously as a student about 12 years before, in consequence of his having accidentally discovered a diastolic aortic murmur in himself. This he certainly had, but it had produced no symptoms, and he remained well until 1892, the year before I saw him again.

In November, 1892, he had an attack of some indefinite kind, of which I could not get a complete account, in which the temperature was raised to 104° for several days; he was very ill, and passed black urine. After a few weeks he got well enough to go abroad, and spent the next three

months in Italy and Egypt. On his way home, in March, 1893, he had an attack of collapse and fainting in Rome. A little later he had another attack. He felt extremely weak and fit for nothing; had tingling in the arms and legs, and some difficulty in speaking distinctly. He felt extremely unwell and unfit for any fatigue, and remained in bed for three weeks. The urine at that time contained a considerable amount of blood, varying in quantity from time to time. He shortly after became very drowsy, almost bordering on coma, and had twitchings in the arms and legs. It was nearly a month before it was safe to move him home. The urine was examined frequently, and was found to contain blood in varying quantities on several occasions. Granular casts and a few hyaline casts, as well as blood-casts, were also seen at first, but these soon disappeared. There was a certain amount of albumen, not a large amount; the reaction acid, specific gravity 1015, and the quantity about 50 ounces in the 24 hours.

Four months later I saw him again. He had been gradually getting better, but was still feeling extremely weak and unfit for any work. He looked very pale, somewhat sallow and feeble, but not thin. The heart had hardly changed from the time when I saw him first; the apex was just in the nipple line, the murmur was still distinct, but the pulse was not characteristic of aortic disease. The arteries were somewhat thickened, and the tension slightly raised. The urine varied from 80 to 100 ounces

daily, and contained a trace of albumen.

The history he gave of the frequent passing of blood—the urine on many occasions being black in colour—suggested the diagnosis of paroxysmal hæmoglobinuria, but there is no doubt that it was one of those instances of hæmorrhage in granular kidney to which I have already referred; but it was peculiar in this respect, that the blood was dark, and not, as it usually is, bright in colour. There was no reason to associate his symptoms with the affection of his heart, which seemed an accidental complication, and one which had little to do with his present illness.

He went to Egypt, where he spent six months of the later period of each year. About two years later he came home, and shortly after his return was seized with an attack of a somewhat similar kind to that from which he suffered in November, 1892, passed into a condition of unconsciousness with twitchings, and finally died with uræmia.

The asthenia is often extreme, so that the patient can hardly stand or walk without assistance.

Of this extreme asthenia I have seen two remarkable 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 for a time, but recurred a few months later. In both cases the asthenia was ultimately fatal.

Extreme asthenia; general pityriasis; disappearance of rash; death from asthenia; granular kidney.—Clara S., aged 41, was admitted into the Royal Free Hospital on October 5th, 1897, for debility and a general eruption of the skin. For six or seven years she had been losing health,

and had suffered from palpitation on exertion or excitement. Five years ago she had influenza, but it was especially during the last six weeks that she had been losing flesh and strength. Three weeks ago she observed the eruption; her ankles began to swell at the same time. She was up each afternoon, but was quite unable to work. For the last 12 months she had been subject to headache coming on in paroxysms. Her father and mother lived to a fair age. Of her seven brothers and sisters, one sister died at 54 of Bright's disease, and one at 50 of morbus cordis; two brothers died as infants; the two remaining brothers and one sister were well.

The chief symptoms the patient exhibited were those of extreme debility and the rash; the rash covered the whole body, and consisted of a red, scaling eruption, which could only be called pityriasis. It affected all parts of the body, including the face and head, and the eyelids were in a condition of extreme blepharitis. The heart was slightly dilated, the apex being just in the nipple line; the feet were slightly swollen; the pulse 96; artery somewhat hard, but tension low; the first sound at the apex was prolonged, and there was a blowing, systolic murmur at the pulmonary base; the urine was pale in colour, specific gravity 1015, contained a thick cloud of albumen, a few pus-cells, but no casts; a trace of blood-colouring matter was present, as shown by the guaiacum test. Although the weather was warm the patient complained greatly of feeling cold, and never seemed to get warm even when hot bottles were applied, or after a hot bath. Two days later the patient left the hospital, having persuaded her friends to take her home, though her debility was such that it seemed hardly safe to move her.

She was not seen again for nine or ten months, but during that time she had lost her rash, but had gained neither strength nor flesh. In the month of October she became an out-patient at St. Bartholomew's, and was shortly afterwards admitted. The prominent feature about the case was the extreme debility and prostration; the patient was pale and flabby, yet not emaciated, but was so feeble that she could hardly stand. Examination disclosed no definite organic disease, except that the radial artery was thickened, the pulse-tension low, the beats regular, 90 in the minute; the urine was 1010, showed a thick cloud of albumen and many crystals of triple phosphates, but no casts. There was slight dilatation of the heart, the apex being nearly in the nipple line; there was slight cedema of the ankles and legs; the temperature was subnormal, and the eyes showed no ophthalmoscopic change. The only other point of interest was that the patient had some oozing of blood from the gums.

She rapidly got worse after her admission, and after two or three days lay constantly in a heavy, apathetic, torpid condition, from which she could be roused with difficulty, though she was not unconscious. She seemed too feeble to move, and lay in that curious condition which resembled the asthenic form of uramia. She had a foul, somewhat urinous odour from her breath, but the urine was passed in fair quantity,

about 30 ounces in the day, and was of fair specific gravity.

The only diagnosis that could be made was that the patient had granular kidney and was dying of uramia. She was given strychnia and brandy, but she was able to take but little food because of obstinate and persistent vomiting. Small subcutaneous injections of nitrate of pilocarpine were given but without advantage; and finally, when everything seemed to have failed, inhalations of oxygen were tried but without success.

On the morning of the 20th, the third day after admission, the

following note was taken :-

"The patient had been very sick last night, and complained much of frontal headache. A twelfth of a grain of nitrate of pilocarpine was injected, but the patient sweated very little; she vomited constantly, the vomit being of a yellowish colour, and smelling very foul. She slept very badly all the night, but this morning was very drowsy and dull. In the afternoon the pulse became very weak; strychnia was injected and produced a temporary improvement, but only for a short time. The patient died somewhat suddenly, after a few gasping respirations at long intervals."

The diagnosis was one that presented very great difficulty. I do not know that I ever saw a patient so ill with so little obvious cause for it. She was dying like a patient in the last stage of malignant disease or Addison's disease, or as diabetics sometimes do, apparently from sheer exhaustion. Granular kidney seemed to be the only disease she had, and it appeared to be sufficient to explain her condition; but the thickening of her arteries and the slight dilatation of the heart and the albumen in the urine were all the symptoms that she displayed.

On post-morten examination this diagnosis was confirmed. Beyond the anæmia no disease was found in the body, except in the kidneys.

Post-mortem examination.—The body was very pale, but not very thin. Some small petechial spots were seen on the legs; no ædema. The heart was pale and weighed 12 ounces; left ventricle hypertrophied, but not dilated. There was a slight degree of atheroma of some of the large vessels. The liver was soft and pale, and weighed 49 ounces. The spleen weighed 2 ounces, capsule slightly thickened and pitted. The kidneys were extremely small, weighing only 4 ounces together; the capsules were thickened and adherent, and several small cysts the size of small marbles were visible on the surface.

The kidneys had undergone the most extreme contraction, and were even smaller than they looked, for the cortex was reduced almost to a thin line, and the pelvis was considerably dilated. The microscope showed the most extreme fibrosis; malpighian bodies were mostly degenerated, and a few only here and there were left; every stage of degeneration was present; round some the capsules were very thick, others were surrounded by a small-celled infiltration. Besides the larger cysts on the surface many others of smaller size were visible on microscopical section. The cells that were left in the tubes stained well, so that there was no evidence of acute renal degeneration.

### AFFECTIONS OF THE SKIN 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 cedema or not.

Where the subcutaneous tissue is distended with ædema the nutrition of the skin will naturally suffer, and from very slight local causes rashes are likely to be produced. Where there is no ædema 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 where there is much cedema in places 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; these 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 occur it will produce very grave effects. This used to be so far recognised that puncture or drainage of cedematous limbs was regarded as a very dangerous proceeding from the liability to phlegmonous inflammation, or even gangrene. Under the use of strict antiseptic precautions this danger has almost entirely disappeared.

These rashes, as stated, are usually limited in extent, transitory in duration, produce few, if any, symptoms, and except where they are caused by local infection, are of but little clinical importance.

Where the rashes are more widely spread or become universal the prognosis is graver, and the more unfavourable the more general the eruption is.

### 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, except so far as they may be the commencement of the general eruption.

The general rashes vary in character. They may be described as:—

- (1) Erythema.
- (2) Pityriasis.
- (3) Dermatitis exfoliativa.
- (4) General eczema.
- (5) A discrete, papular eruption, sometimes lichenous, sometimes resembling chronic urticaria.

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, or on the extensor surfaces of the arm and leg, and on the hands and feet.

In Le Cronier Lancaster's cases the development of the rash seems to have been remarkably uniform. It began as an erythema on the extensor surface of the hands, arms, and legs, rapidly spread over the whole body, and assumed a papular form. It was usually followed by extreme desquamation, and, especially when it had become eczematous, presented the characters of dermatitis

exfoliativa. In some instances pustules or large bullæ with seropurulent contents developed and were followed by abscesses. This was the result no doubt of secondary infection.

The following cases have come under my own observation:-

## (1) Erythema.

This occurred in a patient who was under treatment for uncontrollable diarrhœa.

Profuse diarrhæa; erythematous rash; death; post-mortem, granular kidney.—Man, aged 42, was on a holiday when, without reason, he was suddenly attacked with vomiting and diarrhæa. This completely prostrated him, and when I saw him three weeks later he was in a condition of extreme asthenia.

The diarrhea continued and was extremely frequent, liquid motions being passed almost every hour for days together. Treatment had but little effect, and after about six weeks' illness the man died of exhaustion,

having been wandering and delirious for the last few days.

The diagnosis of the case presented considerable difficulties during life, but on the patient's death nothing but a granular kidney was found. In the fourth week of illness an erythematous rash appeared on the trunk and spread rapidly over the whole body. It itched abominably, and subsequently peeled with fine branny scales. It resisted all treatment and continued with little change till the patient's death (cf. p. 117).

# (2) Pityriasis rubra.

Of this I have seen two instances, one in a man of 47 and the other in a woman of 42.

The eruption was universal, and affected the face, scalp, feet, and hands, as well as all other parts. The scales were fine and branny, and the skin beneath vivid red. It produced no symptoms except that of tension, stiffness, and soreness about the eyes and angles of the mouth.

What was most remarkable in both patients was their extreme debility, so that they could hardly stand or walk. Both cases came under treatment for the skin eruption.

The rash disappeared in time, but the cachexia progressed until it ended in death, after a few weeks in the one case and after a few months in the other.

Granular kidney; extreme asthenia; general pityriasis; improvement; disappearance of rash; death from uramia.—Fredk. C., aged 47, was admitted into the hospital in a condition of most extreme weakness so

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that he could hardly walk, or, indeed, sit up in bed. He was suffering

from a general pityriasis.

The history which he gave was this: that he was perfectly well till six months ago, and then began to vomit after food and lost flesh rapidly. Three months ago the eruption appeared, first on the face and scalp and then over the trunk and limbs, and it peeled greatly. He had syphilis 27 years ago, but no symptoms of it since. He used to weigh 13 stones, but now hardly 9 stones.

The patient was a tall, thin man, extremely feeble.

The condition of the skin was that of general pityriasis, the scaling being not very fine but very free; the skin below was red and shiny when

the scales were removed; beyond this it had no characteristics.

Physical examination showed nothing in particular; the apex of the heart was in the nipple line in the sixth space; the urine 1010, acid, with a trace of albumen. Pulse 84; arteries remarkably thick and slightly tortuous; the tension very high. Granular and blood casts were occasionally found in the urine.

The eyes presented well-marked albuminuric retinitis; there were numerous white patches round the yellow spot, a few small hæmorrhages here and there, especially between the yellow spot and the disc, and the

disc itself was a little blurred, but not markedly swollen.

On admission the man was so feeble that he could not raise himself in bed without assistance, but after a few weeks' rest and treatment improved so much that he could walk about without fatigue. The rash also improved, and ultimately disappeared, and after about six weeks' stay the patient went home, where, however, his health again rapidly deteriorated. Two months later he developed uraemia, and died comatose. No post-mortem examination was made.

A similar case is described under the heading of cachexia, the cachexia being the prominent symptom throughout (cf. p. 124).

# (3) Dermatitis exfoliativa.

This may be perhaps but an extreme degree of the preceding form, from which it differs chiefly in the fact that there is greater desquamation, that the skin is redder and becomes eczematous in parts, and that in places blebs form.

The following is a case of the kind: -

Dermatitis exfoliativa; granular kidney; progressive asthenia; death.—William S., aged 48, a cook, began to be troubled about Christmas time with itching of the feet and scrotum, and two blisters appeared on the palm of his hands. The irritation about the penis and scrotum became intolerable and kept him from sleep. The itching gradually extended over the whole body.

At the end of January the skin of the trunk began to scale, and in the beginning of March the face became affected and also the scalp, from which the hair came off. The eyebrows and eyelashes also fell out, and

there was a good deal of swelling of the face.

A fortnight later a few blebs formed in different parts of the body, and when these burst the skin peeled off in large flakes.

Until the skin affection appeared the patient believed himself a healthy

man, and did not look his age.

The whole of the body was covered with scales, which did not readily rub off, but where they had been removed the skin beneath was glossy-red and parchment-like to the feel. There was a good deal of subcutaneous infiltration, and the lower part of the legs and feet pitted on pressure. Parts were eczematous, viz., the back of the ears, the scrotum, penis, and insides of the thighs, as well as some other parts of the trunk. The face was greatly swollen and of a vivid red colour. The eyelashes were short and stubbly, and of the eyebrows only a few scattered bristles remained. The eyelids were cedematous, and there was some conjunctivitis and lacrymation. The scalp was full of dry scales, and the hair scanty, dry, and lustreless. The desquamation, which was general, was most marked over the trunk and lower part of the abdomen and on the thighs, where the epidermis peeled off in large flakes. On the sole the skin seemed almost raw.

The urine had a specific gravity of 1010, and contained a thick cloud of albumen. The arteries were somewhat thickened and the tension high. All the other functions seemed to be performed satisfactorily, and the

temperature was normal.

The patient was treated with simple bathing and inunction of carbolated oil, and a few days later was given baths of sulphide of potassium in the strength of about 15 grains to the ounce. This was followed by a good deal of general improvement. The subsequent notes of this case are lost, but the patient died soon after.

Another case of this kind I was asked to see in a surgical ward.

Dermatitis exfoliativa; tumour of breast; granular kidney; progressive asthenia; death.—The patient had been admitted for a simple tumour in the breast. The rash developed in the hospital and rapidly became universal. The peeling was extreme and occurred in large flakes, the surface beneath being in many parts eczematous. Albumen was found in the urine, and the patient evidently had granular kidney.

She shortly after died of asthenia without any operation having been

performed.

# (4) A General Papular Eruption.

Papular, urticaria-like eruption; granular kidney; death.—The first case occurred in a man of about 40 years of age, whose skin was covered with small papules of varying size, somewhat like those of chronic urticaria; but they were persistent though they itched. They were spread over the trunk, and were present on the backs of the hands, and feet, and wrists, and on the face. The case occurred during an epidemic of smallpox, and as the patient had a papular eruption with a slight elevation of temperature, the diagnosis was a matter of some importance.

This patient also died, and granular kidneys were found post mortem.

Epistaxis, vomiting, diarrhæa; papular eruption; coma; death; granular kidneys only.—The second case occurred in a woman 52 years (9772)

of age, who had had several children and considered herself healthy till lately. She had been in poor circumstances for about two years, and during this time had been troubled with acid dyspepsia and occasional epistaxis.

One month before admission she was attacked with vomiting and diarrhoea, which reduced her so much that she could do no work. The diarrhoea then ceased for a time and was followed by constipation, but both vomiting and diarrhoea recurred and were not absent for long.

On the day of admission, *i.e.*, 14 days before death, a rash appeared on the backs of the hands and arms, the feet, and face, causing intense irritation. The woman was thin, looked pale and careworn, but, except for the rash, presented no definite physical signs. The pulse was 80, weak and regular; tension not raised; the cardiac dulness normal. The urine contained a small amount of albumen.

The rash consisted of red papules, almost like urticaria, hard to the touch, mostly discrete but some confluent, scattered thickly over the hands and forearms on both sides. On the sole and dorsum of the feet as well as over the lower part of the legs the papules were smaller. Small papules were also abundant over the chest and abdomen, the face was covered with blotchy red patches, which on the chin were also papular. They all itched intensely, especially at night.

Three days later the rash had further developed, and the large papules had spread far up the arms. Rest had been greatly disturbed by the burning and itching, especially of the feet. The patient complained of great thirst and pain in the abdomen and back. The vomiting was less troublesome, but the bowels had been moved frequently, six liquid motions of large size being passed during the night.

Three days later still the rash had further developed, and the legs were covered with discrete papules, many as large as a split pea. The vomiting and diarrhea continued with slight variation from day to day, and the strength failed rapidly.

A fortnight after admission the patient passed into a drowsy, semiconscious state, with occasional twitching of fingers and arms. The urine became very scanty. The drowsiness deepened into coma, and in this state she died.

The post mortem revealed little but extremely granular kidneys, which weighed 6 ounces only together. The heart weighed 9½ ounces. The stomach showed an hour-glass contraction, but muscular only and without any lesion. There were a few calcareous nodules in the apices of both lungs. The stomach and intestines were somewhat congested, but showed no other lesions.

Vomiting; diarrhea; asthenia; albuminuric retinitis; papular rash; death from asthenia.—The third case of this kind occurred in a young unmarried woman 20 years of age, who had been ailing for four years, since an attack of scarlet fever followed by dropsy.

For the last two months she had suffered from vomiting and diarrheea. She was admitted with general edema. The urine contained one-third of albumen, and had a specific gravity of 1010. The ophthalmoscope revealed well-marked double albuminuric retinitis. The diarrheea and vomiting continued, she became extremely asthenic, and died unconscious.

Twelve days before her death a small red papular eruption appeared on the backs of the hands and forearms and on the insteps. It rapidly spread over the whole body, retaining its papular character, and continued the same till death, causing much irritation and distress.

## (5) Hamorrhagic Eruptions.

It is strange, considering the frequency with which hæmorrhage occurs in connection with granular kidney, that hæmorrhagic eruptions are so rare. I have seen one or two instances of small hæmorrhages into the skin (petechiæ), usually on the legs; they were probably due to failure of the heart and mechanical in origin.

Hamorrhagic blebs, followed by general crythema; chronic uramia; coma; death; granular kidneys.—The only case I have met with in which the cruption had marked hamorrhagic character occurred in a man of 44, who was under treatment for attacks of dyspnæa of cardiac origin. All the signs of granular kidney were well marked, and occasional attacks of

epileptiform convulsions occurred

About a fortnight before death some blebs appeared on the feet, which contained blood-stained fluid. At the same time the patient complained of general irritation all over the body, and in two or three days a general erythema, of the ordinary kind but not hæmorrhagic, developed, which was attended with great irritation, and followed quickly by free desquamation. The rash continued unchanged till death. He was at the time in a condition of chronic uræmia, had several fits, passed blood two or three times freely from the bowel, and finally died unconscious.

Post mortem.—The kidneys were markedly granular, and weighed

together only 7 ounces. The heart weighed 20 ounces.

I do not remember ever to have had a case under my own observation which could be fairly called purpura in the ordinary acceptation of the term, nor, as a rule, have the skin eruptions of granular kidney a specially hæmorrhagic character.

Dr. Colcott Fox\* has recently described a case of hæmorrhagic erythema in the course of granular kidney in a woman of 61. She had suffered from bronchitis and acute nephritis probably supervening on old mischief. She left an infirmary but returned a fortnight later (January 5th) with injected and swollen fauces, some erythematous maculæ on the face, and a few petechiæ on the legs. On January 10th a generalised eruption made its appearance. It was of an erythematous macular type slightly raised, with a tendency to rapid centrifugal extension. The eruption varied in size from that of a pin-point to that of a finger-nail, but tended to become confluent, forming patches and sheets. The colour was a vivid red, ineffaceable by pressure. The smaller lesions were dotted with distinct hæmorrhagic puncta, and the large older ones acquired a well-defined purple border enclosing bluish-red centres. The palms and soles were diffusely involved, but the fingers and dorsal surfaces were at first unaffected. The skin of the fingers, wrists, toes, and feet were cedematous. The joints of the wrists and hands were tender and painful. By January 12th the eruption had become almost universal, and looked at first glance like severe purpura. Over the abdomen the maculæ were mostly small

and erythematous, and not nearly as hæmorrhagic as elsewhere. The face was sallow, and the forehead was covered with a morbilliform eruption. The lips were swollen and blood-stained, and there were a few purpuric spots on the gums and palate. After a brief pause the lesions became increasingly hæmorrhagic and even more confluent. On the 15th a recent retinal hæmorrhage was detected. On the 16th a melæna occurred, and the patient died on the 17th. Before death the hæmorrhage was still increasing in the skin. Post mortem a good deal of congestion of the lungs was seen, with intense injection of the mucous membrane of the trachea, bronchi, stomach, colon, and especially of the jejunum and ileum, where it was hæmorrhagic. There was no endocarditis. The kidneys were small, red, and granular with a narrow cortex and adherent capsule. Microscopical examination of the affected portions of skin revealed distension of the lymph spaces and the blood-vessels of the papillary layer with a moderate cell infiltration. The sheaths of the larger horizontal vessels were, however, densely infiltrated with cells. There was apparently no plugging of the vessels and no micro-organisms were discovered.

### PROGNOSTIC VALUE OF SKIN AFFECTIONS.

Rashes of these kinds in granular kidney seem almost invariably to end fatally. Thus, all Le Cronier Lancaster's cases died, with the exception of one, and that a boy of 12, who recovered completely of the rash, and left the hospital, but the subsequent course of the case is not recorded.

All my cases also died, usually not long after the eruption appeared, but in two of the cases referred to the rash disappeared, and the patients lived for some months.

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 the rashes 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.

It is, of course, true that acute eruptions of the skin of an erythematous character are not unfrequently associated with a little albumen in the urine, especially if the temperature be raised.

Erythema with transient albuminuria.—I saw not long ago a little child of about 5 years of age, who was sent to me as a case of acute nephritis.

I failed to find any casts in the urine, and although there was a little blood as well as albumen still I did not think it was renal disease. The patient having a somewhat hæmorrhagic erythema I associated the albumen in the urine with the occurrence of the erythema, or perhaps it would be more correct to say that both the albumen and the erythema were consequent upon some other cause, possibly some defect in the food.

This proved to be correct, for in three or four days the patient was perfectly well. I saw the child subsequently, in the course of the next few months, on three or four separate occasions, and each time with the same symptoms, a temporary and transient erythema associated with

transient albuminuria.

The association of a generalised skin eruption with albuminuria is of great importance and justifies a much more cautious prognosis than might otherwise be given.

Evidence of granular kidney is often found if it is looked for, and then I believe a very grave prognosis is justified, for the patients die, either shortly with the rash still out, or if the rash disappears, before long of other symptoms connected with the disease.

### AFFECTIONS OF THE NERVOUS SYSTEM.

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

Headache, Giddiness, and Vomiting.—These symptoms are sometimes the first to cause the patient to seek advice, and when they are associated with optic neuritis the resemblance to cerebral tumour becomes very close. I have already given some illustrations of these difficulties in diagnosis (p. 115).

The vomiting is often of cerebral or nervous origin, for it stands in no relation with food, and is often periodic.

Headache is a very common and prominent early symptom; it is often of a neuralgic character, occurring in the most intense paroxysms, and is occasionally diagnosed as hemicrania—that is to say, that its association with granular kidney is overlooked.

The following two cases are good instances of this:-

Paroxysms of headache and cramp; granular kidney.—George B., aged 25, came to the hospital complaining of severe frontal headache and attacks of cramp from time to time, especially on rising in the morning. These symptoms had existed on and off for a period of about two years, and during this time he had also suffered a good deal from pain after food, with occasional vomiting. A short time ago his legs had been slightly swollen once or twice, but that had passed off. Micturition had been frequent; he had a considerable difficulty to hold the water during the daytime, and had to rise two or three times each night.

The artery was thick, the tension high; the urine contained one-eighth albumen, and was of low specific gravity. His chief present trouble besides his headache and cramps was thirst and dyspepsia.

Headache; giddiness; granular kidney.—George B., aged 58, a ship's carpenter, had been in active work and, as he thought, in fair health until the last two months, when he began to lose strength and to feel ailing. He suffered occasionally from headache and from giddiness. What brought him to the hospital was some trouble with the digestion.

He was a thin man, with a sallow, earthy complexion, some emphysema of the lungs, and some hypertrophy of the heart, the apex beat being in the seventh space, and the left ventricle obviously dilated, the artery thickened, the tension low, and the pulse beat somewhat irregular and deficient in force. The urine had specific gravity 1016, and contained a trace of albumen. He was not troubled with frequent micturition.

Respiratory Disturbances.—The respirations in uramic 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 dyspnæa. Or they may be rapid, noisy, and panting, not unlike what is sometimes seen in diabetes; in this form, again, there is no true dyspnæa.

Cheyne Stokes breathing is usually of cardiac origin.

Dyspnœa, even if paroxysmal, is often cardiac; and if not cardiac, is frequently due to emphysema and its attendant bronchitis, but the bronchitis itself may be of toxic origin.

Renal Asthma.—Any attack of the nature of true spasmodic asthma is very rare, and I must express myself sceptical as to its existence; at any rate, in my own experience I have certainly never met with a conclusive case.

Peripheral Neuritis.—Peripheral neuritis is a rare condition in granular kidney, but the following was, I think, an instance of it:—

Peripheral neuritis; albuminuria; probably granular kidney; sudden death in a fit; kidney disease in family.—A young man, aged 27, came under my care with the signs of peripheral nephritis, both his arms and legs being affected. Shortly afterwards he developed ædema and a good deal of albuminuria, the symptoms being apparently those of acute nephritis. He recovered from both his peripheral neuritis and most of his symptoms of nephritis, but he was left with a small amount of albumen. His arteries were a little thick, and during his convalescence he developed slight optic neuritis; but this passed off, and he was dismissed from the hospital fairly well, except for the small amount of albumen present. He remained, as it was thought, in fair health until a few months later, when he fell down in a fit in the street, and was picked up and taken into St. George's Hospital, where he died. There was, unfortunately, no post-mortem examination, but I considered it to be a case of granular kidney. It is interesting to add that a brother of his died about the same time with kidney symptoms; and one of his sisters also was brought to me with persistent albuminuria.

Another case is recorded in the Appendix (Case XI).

The next case is one which, though presenting some signs of

peripheral nerve disturbance, in some respects resembled a case of locomotor ataxia:—

Peripheral neuritis (?) with ataxic symptoms.—Richard H., aged 50, a warehouseman, came to the hospital complaining of numbness and tingling in the fingers of his right hand; this he had experienced for about a month, but during the last week he had similar sensations in the right leg, with occasional sharp pains starting from the back and shooting down the leg. With this leg he feels as if he were "walking on nothing." There was no loss of power or wasting in either leg, and no impairment of sensation; the knee-jerks were a little increased on both sides, and ankle-clonus was present on the right side.

The patient was a little unsteady when standing with the eyes closed and the feet together. There was also slight nystagmus, but no pupil changes. With these exceptions the patient presented nothing definite except the signs of granular kidney; for he had a thick artery, a high tension pulse, and a somewhat hypertrophied heart, and he was of a

cachectic, earthy complexion.

The urine contained a small amount of albumen, and was of low specific gravity.

The patient improved, but was subsequently lost sight of.

Fits (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 what is commonly understood by uræmic fits. This is an important point, for I do not think it is generally recognised.

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 stages.

Fits of this kind are, however, not peculiar to granular kidney, but may occur in chronic parenchymatous nephritis.

The attacks sometimes do not pass beyond the stage of unconsciousness, and may not be accompanied by convulsive movements.

Granular kidney; first symptom, attack of unconsciousness recurring every two or three weeks.—Arthur R., aged 40, was in good health until 18 months before admission. He then was attacked suddenly with a fit, the first he had ever had. He remained unconscious for 20 minutes, and on going to the doctor that evening he was told that he had "renal disease." Since then he has been subject to these attacks every two or three weeks.

When the attack is coming on he feels giddy and swimming in the head. Then he begins to sway backwards and forwards, and if he does

not support himself he falls down. After this condition has lasted for about 15 minutes he becomes unconscious. Though he says he knows what is going on about him he is unable to speak or move. This lasts about 10 minutes, and on coming to himself he breaks out into a profuse

perspiration.

He has been subject to occasional vomiting for years, which has continued since his illness, but has not become worse. Recently he has had severe attacks of headache. For 12 months he has been passing more water and has had to get up two or three times every night. Recently he has had a little epistaxis. Six months ago he was told he had renal retinitis, at Moorfields.

The patient was feeble but fairly well nourished. The cardiac dulness a little increased. The arteries thick and tortuous and the tension high. The urine was 1010; contained some albumen, one-ninth, and a few

epithelial casts.

The ophthalmoscope showed some pallor (? atrophy) of the discs, the edges of which were blurred, the arteries tortuous and thickened, some tiny patches of pigment here and there, and a few bright white patches near to left yellow spot.

No history could be obtained of convulsive movements during these

attacks, and the patient had no attack while under observation.

In many of the cases already recorded "fits" were a prominent symptom in the early history (App., Cases II, III, VII).

In another case, what the patient described as fits proved to be curious transient attacks of right hemiplegia with aphasia, the pathology of which could not be determined:—

Curious transient attacks of right hemiplegia with aphasia for eight years; repeated bleeding from gums, and occasional epistaxis; artery much thickened; tension high; white patches in right eye; no albumen in urine on many occasions .- Abraham W., aged 45, was admitted into the hospital on account of bleeding from the mouth. He had been seized in the afternoon with the bleeding, and had lost a good deal of blood from the mouth. An astringent lotion had stopped it, but in the night he was awoke by the return of the bleeding, he felt sick and vomited up a considerable quantity of blood; the bleeding evidently came from the nose and had been swallowed during sleep. On admission the gums were found bleeding. He had suffered from nose bleeding for some weeks. The artery was much thickened; the vascular tension was low; this was no doubt to be referred to the anæmic and feeble condition partly consequent on the recent loss of blood. The cardiac dulness was absent owing to the presence of emphysema, but the heart's action was very irregular and its rate varied greatly. It was 160 when seen in the waiting room, and 80 in the wards a little time later.

The urine contained no albumen, although it was repeatedly examined

on the two separate occasions when he was in the hospital.

So far the diagnosis might be thought to be uncertain; but ophthalmoscopic examination revealed two small patches of degeneration of the ordinary kind in the right eye. On the evening after admission he complained of feeling weak, and the next morning had a seizure. He stated that the right side of the body, arm, leg, and face felt drawn up; he became unable to speak, and passed into a condition of partial unconsciousness. The attack lasted about 10 minutes, and was followed by weakness of the whole side. He did not regain facility of speech for some hours.

These attacks he had been subject to for about eight years, and in five or six bad attacks he did not recover completely for two or three days. Sometimes he can tell that the attacks are coming on by a feeling of pins and needles in the whole side. The attacks occurred at very irregular intervals, and often came on without any obvious cause; at other times they would follow bleeding, as on this occasion. Though the patient said that the side appeared to him drawn up in the attacks seen no movements occurred; but the weakness was obvious enough, as well as the aphasia.

Cerebral Irritation.—In connection with fits may be placed the curious attacks of cerebral irritation, which are not at all uncommon. They may take the form of outbursts 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 (cf. p. 115, and App., Case X).

In this connection it is interesting to recall the great frequency with which granular kidney is found in patients who die in lunatic asylums.

#### ACUTE RENAL TOXÆMIA.—ACUTE URÆMIA.

Of acute renal toxemia—that is, of uremia as we commonly understand the term—much need not be said, for it is with uremia that so many cases of granular kidney suddenly end. The onset of the uremic attacks may be the first grave symptom of the disease from which the patient is suffering. Thus it is not at all uncommon in hospitals to find patients brought in unconscious, and dying without the diagnosis being certain as between uremia, epilepsy, or cerebral hemorrhage till after the autopsy, so suddenly may the attack come on and end, and so little clue may the patient's symptoms give as to the real cause and nature of the disease.

The symptoms of acute uramia 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. In other cases the condition almost resembles that of narcotic poisoning.

In some instances 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.

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 do 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 uramia in any of its forms 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.

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 may end in recovery now and then in granular kidney, as they more frequently do in acute nephritis.

In this connection the following case is of very great interest, for the attack was like one of apoplexy, though it proved ultimately to be uramia. What is still more remarkable is that this patient recovered completely, and has been at his usual work and in his usual health up to the present time, now many months after the attack. Such a result, it is hardly necessary to state, is extremely rare:—

Uramia, simulating apoplexy; granular kidney; recovery.—Samuel C., aged 43, a well-built and fairly healthy-looking man, was in good health and able to follow his usual occupation until May 1st. He then complained of feeling unwell, but of nothing definite; asked for food, but could not eat it; was extremely irritable, and his arms trembled a little. The next day he became somewhat rambling in talk, and by the evening was unconscious. He was brought to the hospital in this condition, and admitted as a case of apoplexy. The patient was quite unconscious, the face somewhat blue, the breathing stertorous, and the cheeks puffed out on expiration. The eyes and head had a tendency to turn to the right, but the legs and arms were both moved from time to time, so that the patient was not paralysed. The plantar and tendon reflexes were present on both sides. The arteries were thickened, tension high, pulse 120; there were slight traces of albumen in the urine, specific gravity 1020; the left ventricle was a little hypertrophied, the apex being in the nipple line. With these exceptions there was nothing to be discovered. The patient was treated in the usual way. In the evening it was thought the patient might be relieved by venesection, and accordingly about 20 ounces of blood were removed from the left arm; 5 grains of calomel were also given as a purge. The temperature on admission was 100.6°, falling that evening to below normal.

During the night the patient was very restless and continually groaning, and in the early morning of May 4th he became somewhat quieter, but was still unconscious, and shortly afterwards had five fits, each lasting about three minutes, and confined to the left side. The temperature during the night rose to 104.2°, but fell again in the course of the day to normal.

On May 5th the temperature, which had risen in the latter part of the preceding evening to 102°, was found to be normal, and from this time

did not rise again. Breathing was quieter, and the patient now began to speak a little, and recognised his wife. He passed a fair amount of urine, which contained, as before, a small amount of albumen.

On the 6th he was better until the evening, when he became somewhat

wandering and was very restless.

From this time he began gradually to improve, though for the first

few days the improvement was slow.

On May 11th the patient, who had previously been taking hydrate of chloral and bromide, was now put upon nitrate of pilocarpin, one-sixth of a grain three times a day. From this time he rapidly improved, and on the 23rd was discharged well. He has been seen several times since, and continues well, and, though obviously the victim of granular kidney, has now no symptoms to trouble him.

This case shows that the acute uramia of granular kidney may be recovered from, just as that of acute nephritis; but it is hardly necessary to add that recovery is much less frequent, for in most cases of granular kidney uramia leads to death in a few hours, or at the most a few days.



PART IV.

PROGNOSIS.

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#### PROGNOSIS.

Many of the special points in prognosis have been already dealt with incidentally in discussing the various features of the disease. The general prognosis in granular kidney is closely identified

with the diagnosis.

## (1) GENERAL.

Duration of Life and Duration of the Disease.—Granular kidney doubtless shortens life, but possibly not as much as at first sight appears. The disease is rarely diagnosed until it has reached its later stages and symptoms are pronounced; at that time it is true that the prognosis is bad, and that the patient, as a rule, has not long to live. As it is not until the late stages that marked symptoms arise, and as the pathological process is a long standing gradual degeneration, it is evident that the real duration of the disease is much longer, and to be measured by years. Though it is true that the majority of fatal cases occur in the middle or later period of life, say, between 40 and 50 years of age, still there are good grounds for believing that the beginnings of the disease, even in these cases, is to be found in adolescence or early adult life, and that they may be recognised then with certainty in some cases and with much probability in many more. If then the disease, unrecognised and untreated as it usually is, permits of life to an average age of 40 or 50 years, there is fair reason to presume that an early diagnosis and appropriate treatment would tend to lengthen its duration, and thus improve the general prognosis.

General Risks of Life.—Apart from the general prognosis of the disease itself its presence largely increases the ordinary risks of life. Thus it greatly aggravates the dangers of intercurrent diseases, especially those of an acute character. This is well recognised in the case of acute pneumonia, for serious as this disease is in itself, post-mortem evidence seems to suggest that death in a large number of cases depends more upon the presence of some antecedent disease of other organs than upon the acute inflammation of the lungs alone, and among these antecedent diseases granular kidney takes a prominent place. Indeed, it is

tempting to conclude that if all other organs are sound the risks of pneumonia are not in themselves so very great, and that it is chiefly because as life advances the chances increase that the heart, kidneys, or other organs are not sound, that the danger of pneumonia increases so rapidly with age.

In respect of Surgical Operations.—With regard to the success of major surgical operations the gravity of chronic renal disease is generally recognised. The discovery of unsuspected granular kidney, post mortem, has often explained the miscarriage of an operation which otherwise might have been expected to run the usual favourable course. True as this is of surgical operations in general, it has a special importance in operations upon the kidney itself, or upon the urinary tract. Still the improvements in surgical methods, which have been so marked of recent years, has reduced even these risks, and now enables many operations to be successfully performed, to which not long ago the existence of chronic renal disease would have been considered a fatal bar.

Special Risks.—Lastly, the general prognosis largely depends upon the peculiar risks to which granular kidney predisposes those afflicted with it; they are cardiac, vascular, and renal.

Cardiac failure is serious enough in itself, but its gravity is increased in granular kidney, because even though the determining cause of the actual symptoms, e.g., overwork, general illness, &c., may be remediable, the predisposing cause, viz., the disease of the kidney, is irremovable on the side of the vessels.

The most serious risk is that of cerebral hæmorrhage, and the greater the thickening of the vessels—in other words, the more advanced the arterial degeneration—the greater the danger.

The importance of the arterial tension as providing a gauge of the patient's condition, I have already referred to, but I may repeat that though it is better not to have granular kidneys, still, having granular kidneys, it is best to have a raised arterial tension—in other words, that within limits low tension is worse than high.

In respect of the kidney itself it is obvious that when the kidneys are already unsound, any fresh acute inflammation of them is attended with especial risk. The existent renal disease not only predisposes to acute nephritis, but renders it more grave when it develops. The onset of acute uramia in the midst of

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apparent health, an event by no means rare in the history of granular kidney, may possibly be connected with changes in the cells of a kind hardly recognisable by our present methods, and of a degree which would not have made itself seriously felt had the kidneys been healthy.

### (2) Special Prognosis.

When symptoms are pronounced, the disease is far advanced and in its later stages, so that the general prognosis is bad, but of the particular symptoms some have greater gravity than others.

I need not refer further to uramia, which in granular kidney is almost invariably fatal, though I have previously quoted an exception to this general rule.

I have already considered in detail the prognostic value of albuminuric retinitis and of widespread eruptions of the skin, and reference can be made to the previous pages, where the question was dealt with.

Perhaps the best prognostic indication is given by the general condition of the patient. Where the general health has begun to fail, in proportion to the degree to which it has suffered the prognosis is bad, and it is worst of all where what can be fairly described as cachexia has developed. In such case, quite irrespective of what other special symptoms there may be, life cannot be long continued.

PART V.

TREATMENT.

#### 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.

When the disease is far advanced it cannot be cured, for scar tissue cannot be removed from the kidney by therapeutic means any more than it can 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 dis-Ease, *i.e.*, discomfort, he will not much mind the Disease.

We cannot cure myxœdema, but we now know how to relieve its symptoms. It is not too much, perhaps, to hope for similar success hereafter in the treatment of granular kidney.

The objects we should have in view in treatment are :-

(1) To relieve the damaged organ in every way possible, and so prevent the disease being aggravated.

With this end 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. Chief among 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 spot 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 correctly diagnosed, how much may be done to give relief.

I do not propose to enter into the details of the treatment of the multifarious symptoms of granular kidney, except incidentally, so far as the treatment is modified by the general conditions on which the symptoms depend.

It will be useful to consider how the conditions enumerated in the first two clauses can be best fulfilled.

I.—The first great indication is to relieve the damaged organs in every way possible.

There is a very close physiological relationship between the kidneys, skin, and bowels, and we know that when the elimination by the kidneys is defective, it is naturally supplemented by the skin and bowels. The treatment of the skin and bowels is recognised as the most potent means we possess of relieving the kidneys in attacks of acute nephritis, and it is of course equally important in the treatment of granular kidney.

The importance of the skin in the treatment of granular kidney is evident: First, because its healthy action relieves the kidneys; and secondly, because its defective action throws extra work upon the kidneys.

Therefore everything must be avoided which would check the action of the skin, and everything done which would promote it.

Clothing.—The body should be properly clothed. The patient should wear flannel next to the skin, winter and summer, day and

night; if not flannel and all wool, at any rate merino, or a mixture of wool and cotton or wool and silk, whichever can be the more easily obtained.

The clothing should be varied with the weather, for it is a great mistake to be too warmly clad, on account of the perspiration it causes and the risk of a chill. A flannel band should be worn round the loins, as is the habit in the tropics, and with women low evening dresses should be prohibited.

It is most important to keep the feet and legs warm as well as the body. This is often neglected, for the body is wrapped up warmly while the feet and legs are kept cold, yet the legs form in bulk nearly half the body, and more chills are caught through exposure of the feet and legs, perhaps, than of the body.

The socks worn, winter and summer, should be of wool or thick merino; the boots substantial, and lined with cork or felt socks. Cold or chilled feet especially should be avoided, and, above all things, if the feet get damp the boots or shoes and socks should be at once changed. These may seem trivial details, but it is astonishing how greatly these small matters are neglected, and how important they really are.

Everything must be done to avoid chill. Thus care must be taken not to check the perspiration abruptly when the body has been heated by exercise, or during hot weather, and great care should be taken of draughts after sitting in warm rooms, especially with women who are lightly clad in evening dress. More chills are acquired perhaps in hot weather than in cold, on account of the free action of the skin, and the draughts to which people expose themselves without sufficient care. Many of these precautions will depend upon the climate or season. What is especially to be avoided are abrupt changes of temperature, especially if the air be damp. It is for this reason, and to search after a more equable and drier climate than we have in this country, that patients with kidney disease are so often advised to spend the winter abroad.

Climate.—The best climate that could be devised would be the one which was most equable, i.e., in which there were fewest changes, and that whether the air were moist or dry. Madeira, the Azores, and the Canary Islands have an equable climate which is warm but is very moist, and often too relaxing, so that patients

do not feel well in it. The Riviera, which is a less relaxing climate, is at the same time one which is not altogether suitable for kidney cases, on account of the violent changes of temperature between the sun and shade, and between the morning and evening. Perhaps the dry climate of Egypt and Algiers is the best of all, but even these climates require care on account of the difference between the day and night temperature. According to my experience patients who have spent the winter in these last places have benefited most. It must be remembered that, with kidney disease, changes of temperature are felt of which the strong are not sensible, and it is on this account that care is necessary in every climate, and that a good climate is desirable.

Skin Toilette.—Everything must be done to keep the skin in good condition. For this purpose baths of every kind are useful, whether hot-water baths, Turkish, or vapour, provided that no chill be taken after them. A hot bath regularly two or three times every week on going to bed is advisable. Turkish baths are excellent if they are not found to be too lowering, and are not taken too frequently.

The question is often asked whether the patient should be permitted to take a sponge bath on rising in the morning. The answer to this must depend to some extent upon the patient. It is best as a general rule not to let the patient take the bath quite cold, but to have sufficient warm water to take the chill off. A cold bath is usually followed by a condition of reaction in which the skin becomes all of a glow, and in which the whole body feels warm and comfortable, but in some cases the opposite occurs; the fingers become chill and dead, and it may take an hour or two for them to recover. If this be so, it is evident the bath is unsuitable. Many patients who cannot take a cold bath in the morning find benefit from a hot bath; but as a rule if a sponge bath does not suit, it is better for the patient to be content with a rapid sponging over, and a good rubbing with a rough towel.

Bathing in the open, or even in swimming baths, is on all accounts to be prohibited. It may produce temporary albuminuria even in those who have nothing the matter with the kidneys, and it is fraught with mischief in every case where the kidneys are not sound. There is no better way of promoting healthy action of the skin than by muscular exercise, if this can be borne without

fatigue. It should be of such a kind and amount as to produce a gentle action of the skin rather than a violent perspiration. If there has been much sweating, a warm bath and a good rub down afterwards is a most excellent procedure.

Diet.—The next most important principle of treatment is diet. As it is by the kidneys that the products of nitrogenous waste are chiefly got rid of, and as the amount of nitrogenous substances in the urine depends largely upon food, it seems a natural conclusion to draw that the amount of nitrogenous food should be limited. In acute nephritis this indication is met by placing the patient upon a diet which consists chiefly of milk; but this kind of diet—milk and farinaceous food—should not be too long continued even in acute nephritis, and in the later stages, where that disease tends to become chronic, or where convalesence is delayed, a change to a more liberal dietary is often attended with very remarkable improvement.

In a long disease such as granular kidney too strict a diet cannot be insisted on, and the diet must be, in order to maintain the patient in good health, a properly mixed one. Although it is highly desirable that the amount of nitrogenous food should not be too great, still it is possible to err on the other side and make it too small. It is impossible, also, to prescribe one dietary which will suit everyone; idiosyncrasy must be considered in every case. The forms of albuminous food most especially to be avoided are the various meat extracts which are so popular. These contain a large amount of extractive substances, which are of little use as food, and have necessarily to be excreted largely by the kidney; the administration therefore of such things gives the kidney more work to do. The albumen is far best supplied in the ordinary form of well cooked meat, fowl, and fish, but it should be in moderate amount. Vegetables and salad are all good, and even a strictly vegetarian diet has been advocated, but of this I do not approve. Farinaceous foods of every kind are clearly indicated, and milk and cream can be taken in quantities; for such fattening things tend to counteract the loss of flesh, which is one of the tendencies of the disease as it progresses.

As the patients pass an excessive quantity of urine, they are often more or less thirsty. It would be well for such patients

to drink fairly freely of water. A popular remedy at the present time, and a good one, too, is a glass of hot water from time to time during the day. To the water may be added a little lemon juice, citric, or tartaric acid. Stimulants as far as possible should be avoided, and, above all, the rich and sweet wines of every kind. Dry sherry, Marsala, or light and sound claret are all admissible, but port, champagne, and even the heavier Burgundy should be avoided. On the whole, perhaps, a little whisky, well diluted, taken with the meals is the most suitable beverage, but if the patient can do entirely without stimulants it is best.

The Bowels.—It is important that the bowels should be kept in regular action, and that they should be moved every day, and perhaps have a tendency to be somewhat loose. This is best provided for, if necessary, by the use of one of the aperient waters, or of Epsom or Karlsbad salts, taken in the early morning. If stronger aperients are required, the favourite remedies are the compound jalap powder, or confection, or pills containing jalap, or even a little elaterium. A course of purgatives or purgative waters is distinctly to be avoided, for it lowers the general tone and reduces the general health too much.

To sum up what has been said:—The general health should be maintained in every way possible by appropriate dieting, by avoiding exposure, overwork, or worry, by fresh air and exercise. All this requires medical supervision and care, but not necessarily in special institutions or in special places; for if patients would only carry out the instructions given, they could often derive as much benefit by treatment at their own homes as at the fashionable baths of this country or abroad, except, of course, so far as climate is concerned. It is because they submit to rules abroad which they will not listen to at home that it is so desirable, in many cases, to send these patients for a course of treatment now and then in the year to foreign places, but if they would do what they are advised they might, in many cases, stay at home and avoid much expense.

II.—The second great indication is to recognise and guard against the accidents that are specially likely to occur in the

course of granular kidney; these are three—failure of the heart, rupture of vessels, and inflammatory affections of the kidney itself.

The Heart.—Heart failure is rarely sudden; usually some warning is given by the development of anæmia and by failure of the general health. If these symptoms appear everything should be done to bring the patient back to health again, for whatever affects the general health will affect the heart also, this being the weak organ. For this purpose all excessive strains should be avoided, all violent efforts, all excitement or anxiety, and all irritation of mind and body. The life that is led should be easy, both physical and mental.

The Vessels.—Rupture of vessels and consequent hæmorrhage is the most serious danger, and it is a risk which is constantly present, and one which it is difficult to take precautions against except, so far as possible, to guard against worry and mental excitement, violent physical effort, and straining. In the hæmophilic condition, which develops in the latest stages, the hæmorrhage, which is rather a general oozing from the mucous spaces than free bleeding, often yields to opium, digitalis, or ergot. Ergot, especially, is a very valuable remedy, which I have not unfrequently found successful when other means have failed.

The vascular tension may supply indications for treatment.

The tension is normally raised in a granular kidney; it is best that a patient should not have granular kidney, but having granular kidney it is better that the tension should be somewhat raised. It is a mistake to attempt to reduce this increase of tension if it is only moderate, for granular-kidney patients are not so well when the tension is low. Yet the vascular tension may be too high as well as too low, and should then be treated.

If the tension be abnormally low it should be raised. This can be easily done by a richer and more stimulating diet, by stimulants, and by drugs, especially by digitalis or even by ergot.

Where the tension is very high it should be reduced, but this is not so easy without affecting the general health as well. This result is best attained by diminishing the amount of stimulants, placing the patient upon a bland and somewhat reduced diet, regulating the bowels, and keeping up the action of the skin.

For a case of this kind a course of baths and laxative waters under proper supervision is frequently very beneficial.

In intercurrent diseases, especially if acute, it is most important to watch the weak spots, especially the heart and the vascular tension. Thus, should a patient with granular kidney be attacked with pneumonia it would be necessary from the beginning to use stimulants freely, such as alcohol and strychnia, as well as stimulating cardiac drugs like digitalis and especially caffein. The association of granular kidney with pneumonia is a very serious matter, but if the treatment be directed to the weak spots it is often successful.

Surgical Operations.—In cases where surgical operations have to be performed upon patients with granular kidney a good deal of care is necessary. The patients require to be carefully prepared, and got into as good a condition of health as possible before operation, but if this be done an anæsthetic may be safely given and the operation satisfactorily performed. A great deal depends in these cases upon choosing the proper time for operation, but now that operations are more generally successful and attended with so much less risk than formerly, the importance of properly preparing the patient is often forgotten, and thus risks are incurred which might be avoided. On the other hand, with proper care and preparation, operations may now be safely performed in chronic renal cases to which not long ago the renal disease would have been considered a fatal objection.

Intercurrent Acute Nephritis.—I have already referred to the frequency with which acute nephritis occurs in the course of granular kidney, and to its importance in respect of diagnosis and prognosis, but it calls for no special or peculiar treatment.

III.—The symptoms and complications, and their treatment, fall conveniently into two groups—cardio-vascular and renal.

The cardio-vascular must be treated on general principles, and it is not necessary to add to what has been already said on this subject.

The renal are of prime importance, and deserve fuller consideration.

The Urine.—The urine provides many indications for treatment in granular kidney. The specific gravity and constitution of the urine, the amount of urea and albumen should be carefully watched, and treatment modified according to what is found. In this way much can be done to avoid the serious renal complications, which it should always be remembered are easier to prevent than they are to cure.

If the quantity of urine is greatly reduced it may indicate some congestion of the kidney, and therefore require some appropriate treatment.

On the other hand, if the quantity of urine be excessive the kidney is somewhat overworked, and therefore liable to break down. Both conditions, though for opposite reasons, call for freer action of the skin, which will be obtained by baths and diaphoretics.

The specific gravity gives an indication of the renal activity, and if inadequate the elimination must be assisted.

An occasional analysis of the total solids, especially those containing nitrogen, is useful, but many of the substances which are so toxic do not betray their presence to chemical tests.

Hæmaturia, if it come from the kidney, may be a serious sign, as indicating congestion of the kidney. This may be often relieved by dry-cupping. But hæmaturia may be a sign of little importance, especially if the blood come from the bladder, and even a considerable amount of blood may be passed in the urine from time to time without evil results or any other symptoms. It appears in these cases to be a mere accident of the disease, and not to require any special or active treatment. Still, as in other hæmorrhages in granular kidney, digitalis and ergot are often serviceable.

Casts are of little importance in respect of treatment. So long as they are merely hyaline, they have but little significance. Epithelial casts are rarer, but are of greater importance, because they indicate some progressive mischief in the kidney. Granular

casts are often spurious—that is to say, they are hyaline casts upon which phosphatic granules or some other granules have been deposited from the urine.

Albumen, perhaps, is the least important of all the signs which the urine yields from the point of view of treatment. It shows that there is some mischief of the kidney, but it fluctuates greatly from day to day; it may be absent or vary greatly in amount without any corresponding change in the patient's condition, or apparently in the condition of the kidney. Where, however, it is in large amount, and especially if associated with casts and a little blood, it may, of course, be the indication of acute nephritis, which will then require its own treatment.

Late Symptoms.—The late symptoms are, for the most part, toxic in origin. They are often very misleading, but if their connection with granular kidney be rightly recognised, much may be done by treatment for their relief.

Thus the headache, vomiting, cramp, and other symptoms, after resisting ordinary treatment, are often rapidly relieved by appropriate renal treatment, e.g., baths, purgations, and pilocarpin.

Of single drugs I do not know of any one more useful than nitrate of pilocarpin given in small doses by the mouth two or three times a day, or, in urgent cases, in larger doses sub cutem. Thus the beadache, irritability by day and restlessness by night, vomiting and digestive disturbance, the foul tongue and dry skin, may all rapidly yield to a dose or two of pilocarpin, and the patient be restored to comfort, and that even when uræmia seemed to threaten.

There is one noteworthy fact about pilocarpin in chronic renal disease, viz., that it often does not produce the sweating which under normal circumstances and in similar doses it usually causes. Yet, without the sweating, its effect is striking.

Restlessness, sleeplessness, or delirium may be treated in various ways. Chloral and bromide of potassium are advocated by many writers, but I am not very fond of these remedies, because of the depressing after-effects they produce if persisted with.

Opium and its preparations may be employed without the risks which were once supposed to attend their use. Indeed, if this drug is indicated, morphia (by the mouth or *sub cutem*) may be given without fear, and often with striking benefit, especially at night time.

As a hypnotic and general sedative, the drug to which my experience leads me to attach the highest value is Cannabis Indica. This is best given in the form of tincture, in a dose of 30 minims or more, at the time of sleep, in chloroform or pimento water.

Uramia.—When the more commonly recognised toxic or uramic symptoms develop, more active measures become necessary. First, an attempt may be made to supplement the action of the kidneys by working other excretory organs, such as the skin and bowels, by free diaphoresis, hot water or vapour baths, and copious purgations, and by the active use of pilocarpin. All these are lowering and depressing methods, and cannot therefore be too long persisted in.

If acute uramia develop and the fits be severe, bleeding may be employed, but bleeding has its own disadvantages, for it is useless unless free, *i.e.*, unless many ounces of blood are removed, and copious bleeding such as this leaves the patient more weak and feeble afterwards, though it may give relief at the time. Bleeding is therefore reserved for extreme and urgent cases.

As an alternative to bleeding, intravenous injections of saline solutions have been used, but without any permanent advantage. The inhalation of oxygen has been advocated, but in my experience has not proved of much use, though it seems to have a sedative action in some cases, for which purpose also chloroform inhalations have been employed with temporary benefit.

Renal Extracts.—There remains 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, viz., 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 bears a striking resemblance to 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.

In the case of myxœdema, there was the same absence of conclusive evidence 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 do 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 loss of nutrition and general cachexia are pronounced.

The first question is whether renal extracts administered by the mouth have 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 24 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.

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A striking instance of the effect of the renal tabloids occurred in the following case:—

Ellen B., 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 diarrhœa, 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 grains twice a day. Coincident with this she began to improve; the quantity of urine a few days after the first administration increased and reached 47 ounces—the largest amount she had ever passed while under treatment, the usual average hitherto having been not more than 15 or 20 ounces. With the increase in the urine the amount of albumen greatly diminished and the cedema began to disappear. In the course of a month the urine averaged 40 ounces in amount, 1012 specific gravity, and not more than 0.5 per cent. of albumen. Soon after 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 again left the hospital, except for the albuminuria, well. A third time she was brought to the hospital, this time in 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.

#### CONCLUSION.

It is evident from what has been said how much room there is in the treatment of granular kidney for good judgment, experience, and skill.

The great difficulty to be contended with is the belief that granular kidney is an incurable disease and that nothing can be done for the patient—a lamentable error often shared alike by doctor and by patient, and one which has cost many a patient some years of his life. So far from granular kidney being a disease so fatal and incurable that the patients have nothing to do but to fold their hands and wait for death, it is one which, when properly recognised and treated, is compatible with a fairly long life, and with a fairly comfortable life too.

The damaged kidney cannot, of course, be restored ad integrum, for scar-tissue cannot be removed from the kidney by drugs or other treatment any more than it can be removed from the skin or liver. Yet a patient may live a long time with comparatively little kidney substance.

Patients may live for years with a weak heart, and why should they not with weak and damaged kidneys. Sudden and unexpected death may occur in either case, but it is rare enough, and could often have been avoided with proper care.

If a patient has granular kidneys it is best for him to be told so, so that he may know his weak spot, and protect it; at the same time he may be assured that with ordinary care he may have many years to live; and he should be warned against a belief in the hopelessness of his case, lest becoming desperate he might throw off all restraint, and by thus aggravating the disease hasten his end.

Granular kidney is so fatal a disease, not because nothing can be done for it, but because it has not been recognised till too late, and nothing has been done to protect the patient against its dangers.

If a diagnosis were correctly made in the early stages, I believe statistics would show vastly improved results.

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## EPILOGUE.

I have now finished the task set me. My choice of granular kidney as the subject was inspired by the hope that what had interested me would prove of interest to others also. I trust I have not 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.

# APPENDIX.

INTERESTING CASES.

#### INTERESTING CASES.

I.—Granular kidney, presenting as subacute parenchymatous nephritis; extreme ascites, with peculiar fluctuation in intercostal spaces; abdomen tapped through pleural puncture; frequent paracentesis; death from asthenia; post mortem.

Charlotte H., aged 31, a housemaid, was admitted into the Royal Free Hospital on January 28th, 1889. She was in good health until five months ago, when she first began to complain of pain in the back, which came on without obvious cause, and continued more or less ever since. There had been amenorrhoea for the same period. Two months ago she first had swelling of the ankles, worse at night, and the swelling gradually extended up the legs; but during the last month there had been swelling also of the abdomen and face, especially round the eyes, and most marked in the morning.

During the last month she had passed more urine than normal.

Since the commencement of her illness she had become paler, had lost flesh, and had felt very much weaker; and during the last two or three months her sight had become impaired. She described a darkness which came before the eyes, and prevented her from reading or doing fine work. During the last 12 months she had occasionally had attacks of epistaxis.

The appetite had been good, and the bowels regular; she had slept well, and there had been no sickness or headache. Her breath had been short on exertion, and she had suffered sometimes from beating at the heart; but this had been so for some years, and was not much worse since the illness began. She was at work until January 23rd.

The patient was a well-developed young woman, with a white puffy face and characteristic renal appearance, and general edema of the legs and body, but not of the arms and hands. The arteries were much thickened; the pulse 100, regular, and of very high tension. The urine was acid, 1013, containing a third of albumen and a number of hyaline and granular casts.

The area of cardiac dulness was somewhat enlarged, the first sound a little prolonged at the apex, the second accentuated at the base, especially over the aorta; there were no murmurs.

The abdomen was distended, contained much fluid, and measured 391 inches round.

Dulness extended on the right side of the chest some distance up the back, but was thought to be in great part due to the displacement upwards of the liver, though in part also to the presence of fluid in the pleura.

Both eyes showed well-marked *albuminuric retinitis*; the optic discs were blurred and indistinct, and there were some large, irregular, retinal hæmorrhages as well as white patches near the yellow spot.

The patient evidently was suffering from a subacute attack of nephritis; but the character of the urine, the hardness of the artery, and the changes in the discs showed that there was something more than chronic parenchymatous nephritis.

The amount of dropsy and the history of the onset of the affection

suggested that a great deal of the anasarca was of cardiac origin.

The chief complaint of the patient was of the swelling, of pain in the back, and of failing vision.

In the course of the next few days the dulness on the right side of the chest increased, and reached up to the second rib. The intercostal spaces

were wide and bulging.

It was decided to tap the right pleura; an exploring needle was inserted, and serous fluid was easily obtained. A trocar was then inserted in the sixth space in the mid-axillary line, and the fluid withdrawn by syphonage. It flowed readily; 150 ounces, 200 ounces, and 300 ounces, and ultimately 505 ounces were withdrawn. It was then found that this result was due to the fact that the abdomen had been emptied through the puncture in the pleura. This was very extraordinary, because the needle had been inserted in the usual place and passed only a very short distance through the chest walls, and it seemed difficult to understand how, if the diaphragm had been penetrated, the liver could have been avoided.

After the tapping the right side was found to have fallen in considerably, so that the ribs were close together and the bulging had disappeared. The liver could now be felt in its usual place, somewhat below the ribs. The fluid withdrawn was of the usual character, and contained about one-sixth of albumen and 0.05 per cent. of urea.

The case ran a very slow course. The patient was in the hospital seven months, getting gradually weaker and more dropsical. The chief feature of the case was the recurrent ascites, which required frequent tapping, about once a fortnight, so that she was tapped 14 or 15 times. The patient suffered frequently with severe headaches and from occasional attacks of epistaxis and vomiting.

The only important event to note was that on April 15th the patient had a slight attack of pericarditis, but this subsided without special

symptoms.

The temperature was normal throughout. The pulse tension was interesting on account of its constant variation, so that it was hardly the same on two consecutive days.

The albuminuric retinitis slowly progressed, but was throughout more

marked in the left eye than in the right.

In the middle of March there was extreme optic neuritis of the left eye, so that the disc could hardly be made out, and round about it were several small hæmorrhages. The central part of the retina also was a good deal blurred, but the white patches were not so numerous as in the opposite eye. The right eye was not so much affected, but there were numerous hæmorrhages scattered about over the retina, and many very characteristic white patches.

The vision was as follows:—Right eye: J.  $\frac{6}{12}$  at 20 feet, with -7.5 D.; type 8 at 11 inches. Left eye: J.  $\frac{6}{36}$  at 20 feet, with -5 D.; type 10 at 12 inches. There was no marked diminution of the field of vision.

The urine remained throughout of much the same character; it averaged about 70 to 80 ounces daily; the specific gravity 1010, contained about one-third of albumen and about 1.5 per cent, of urea with numerous casts, chiefly granular, but occasionally epithelial. Even to the last the urine retained these characters without change.

The patient died of exhaustion on August 6th, after having been in

the hospital nearly seven months.

The chief peculiarity of the case was the ascites, which was out of all proportion to the general anasarca, so that the abdomen required to be tapped, as has already been stated, about every fortnight. The girth of the abdomen was considerable—40 to 43 inches—and the amount of fluid removed very large; thus, on the first paracentesis it was  $25\frac{1}{4}$  pints, and on other occasions it measured 26, 27, and even on one occasion as many as 33 pints.

The thoracic organs were, of course, greatly displaced, so that the heart was pushed up to the second rib, and dulness on the right side reached as far as the second rib in front. This was thought to indicate a large pleuritic effusion on the right side; but when the pleura was tapped on the first occasion the abdomen was emptied; and with the return of ascites, the dulness in the chest became the same, and no other evidence of fluid within the chest was obtained.

After the first paracentesis the liver could be felt in its usual place below the ribs, but on subsequent occasions it was not to be detected at all.

The next point of interest was the curious fluctuation that was obtained on several occasions between the intercostal spaces and the abdomen. The lower intercostal spaces were all dilated, and bulging, and they felt tense and elastic.

Very distinct fluctuation could be obtained in the intercostal spaces between the sixth in front and the tenth behind, on the same level that is to say; evident though much less distinct fluctuation could be obtained in the lower intercostal spaces behind by percussing the abdomen. This is a very remarkable condition, and one which I have never seen in any form of pleuritic effusion, or indeed in any other case of ascites.

On March 15th, when paracentesis was performed and 240 onnces of fluid removed, the intra-abdominal pressure was + 7 inches of water, and what was curious was that, although the fluid was removed from the abdomen, no change was made in the lines of dulness on the right side of the chest which reached up to the third rib; but the bulging of the lower intercostal spaces disappeared, and there was after the operation marked inspiratory recession of those spaces.

As the fluid reaccumulated, the symptoms described all returned more or less according to the distension of the abdomen, and disappeared with each paracentesis.

Although the case was regarded throughout as one of granular kidney, still it was thought there must have been some other supplementary condition to account for the predominance of ascites. Cirrhosis was thought to be a possibility, but there was no evidence of it, for the veins of the abdomen were not distended, and there was no history of alcoholism.

Although rare, it is well known that in general dropsy the stress of the effusion may fall on one or other of the serous cavities.

As in this case it seemed to fall upon the peritoneum, so in another case I can recall, I remember it fell chiefly upon the right pleura, which had on several occasions to be tapped. This was a case of morbus cordis, and though the patient ultimately recovered and lost all the general cedema, the fluid persisted in the right side of the chest for some time, and required paracentesis two or three times after all general signs of dropsy had disappeared. In the end this disappeared also, and the patient recovered so far as the morbus cordis permitted.

The patient died, as stated, on August 7th, having been troubled during the last few days with frequent diarrhœa and vomiting, but there were no other signs of uræmia.

On the post-mortem examination there was some general anasarca, and the abdomen was found greatly distended with fluid. The diaphragm on the right side reached up to the third rib. The spot where the paracentesis was made on the first occasion was in the sixth space in the midaxilla, and in this line the diaphragm reached well up into the fourth

space.

There was no adhesion of the lung or pleura in this part, and the lung was collapsed, but not diseased; there was no fluid actually in the pleura, or any signs of there having been any there. The liver was normal, except for one or two little streaks of capsular thickening. The heart was greatly hypertrophied, and weighed 1× ounces; there was no valvular disease, but there were a few firm pericardial adhesions here and there. The kidneys were very granular, but irregularly so; in some parts the whole of the cortex seemed to have been completely destroyed; in the other parts there were coarse and fine granulations, and the cortex in these places was very considerably reduced.

This case illustrates an important clinical fact, viz., that in adults granular kidney not unfrequently presents itself under the guise of acute nephritis; in other words, that what appears to be a first attack of acute parenchymatous nephritis is really but an intercurrent acute nephritis in the course of chronic disease, i.e., granular kidney. Hence it follows that if in a case of granular kidney a history of antecedent acute nephritis be obtained, it must not be assumed that the acute nephritis has caused the interstitial nephritis, for the relation between the two conditions may very probably be the exact converse, viz., that the patient had an attack of acute nephritis, because the kidneys were already diseased, i.e.,

granular. The importance of this conclusion from a pathological point of view is obvious.

II.—Granular kidney; patient had worked with lead for 20 years, gout only during last few months; first grave symptom angina; occasional fits for three years before; rash, bulla, and erythema; hamorrhage from bowel; restlessness, noisy delirium, coma, death; post mortem; remarks.

William W., aged 44, was admitted into the hospital on account of attacks of dyspnœa, which seized him suddenly at night. He gave this history:—He had been a maker of lead pipes for 20 years. During the last 15 years he had suffered three times from lead colic, being ill for about a week. The last attack was three years ago. One year ago he had his first attack of gout, and he had had two or three slight attacks since. One month ago he began to notice that he was passing rather more water, having to rise five or six times during the night. In other respects he was well until one month ago (September 30th), when, having gone to bed well, as he thought, he was awoke in the middle of the night with a violent attack of dyspnæa; he awoke fighting for breath, and continued to suffer for half an hour. He was able to go to his work next day, and felt well for a fortnight, when he had a similar attack at night; and again, a fortnight later, he had a third attack, for which he came to the hospital, and was admitted.

The patient was a well-developed, strong-looking man, except that he appeared rather pale, and his hands were a little tremulous. There was a well-marked blue line on his gums, both on the upper and lower jaw. The pulse was 92, a little rapid, and of high tension; the artery considerably thickened, and rather tortuous. The heart's apex was in the normal place, the cardiac dulness not obviously increased, and the sounds normal. The urine was clear, 1008 specific gravity, contained a cloud of albumen, and about 1 per cent. of urea. There was a little rhonchus over the chest, and a little crepitation at both bases. There was also some grating in the joints of both great toes. Examination of the eyes showed early albuminuric retinitis in the form of small white patches round the yellow spot. There was one hæmorrhage not far

from the disc in both eyes.

The case was evidently one of granular kidney, and the attacks of

dyspnœa cardiac in origin.

The patient improved, and nothing special occurred until November 18th, when the patient, who had not been feeling very well the day before, was seized during the night with a violent attack of cardiac pain, but without any shortness of breath. This lasted some time, and did not completely pass off for the whole of the next day. The following night he was attacked with a similar spasm. Three days later an attack of gout in both great toes showed itself.

These attacks were, no doubt, cardiac in origin, and of the nature of angina. The occurrence of gout a few days later throws a light upon what is sometimes called "gout of the heart," which, no doubt, in the majority of cases is anginal. The gout rapidly subsided under the use

of salicylate of soda and iodide of potassium.

Nothing further happened until December 7th, when the patient was attacked by a fit of an ordinary epileptic character, which lasted about four minutes. Inquiry then elicited the fact that he had been occasionally

subject to fits at irregular intervals during the last three years, and that the last fit occurred 14 days before admission. For the last few days the patient had been complaining of pain over the dorsum of the right foot, and on December 7th some small bulke were found there containing a blood-stained fluid; these were incised and dressed with boracic acid ointment.

On the 13th the patient seemed to be weaker and to be a little wandering. On the 14th he began to be sick, and vomited from time to time. On the 17th his tongue got dry, and he complained of great thirst.

That evening he had another fit.

At the end of the month the cardiac dulness was found to be increased and the apex outside the nipple line, showing that some dilatation of the

left ventricle had occurred.

On January 2nd and 7th he had other fits. On January 14th the patient began to complain of general irritation over the whole body, which was followed in a few days by an erythematous eruption. The temperature now began to rise. Bullæ continued to form upon the

feet, which were opened and dressed in the way described.

On January 18th the patient complained again of great thirst and of drowsiness. The albumen was somewhat increased, and the urea continued, as it had been for some time, at 1.4 per cent. On January 19th the patient became very restless and more drowsy; he passed water in bed, and began to suffer from diarrhæa. That evening he passed a large blood-clot, and the next day a considerable amount of blood from the bowels, which, apparently, was not due to piles. The temperature, which had gradually risen to between 102 degrees and 103 degrees, now began to fall.

On January 22nd the patient was very feeble, passed but little water (19 ounces in the 24 hours), became *delirious* and noisy for a time, and subequently passed into a condition of *coma*, and died unconscious on

the 23rd.

There had been no change in the character of the urine throughout, except one, which was rather an improvement, for on admission the urea was I per cent., but during the whole of the later stages of his illness it had reached 1'4 per cent.; the quantity of urine averaged between 50 ounces and 60 ounces daily, the specific gravity was 1008 to 1010, and the amount of albumen about an eighth. It was only during the last two days of life that the quantity of urine fell much, and even then averaged about 18 to 20 ounces. The general erythema, which began on the 14th, and spread all over the body, caused a great deal of irritation and distress. It presented no special characters, but was of the ordinary kind, and attended with a fair amount of fine desquamation. The usual treatment was adopted throughout, but was of little permanent benefit.

The post mortem showed nothing except the ordinary lesions of granular kidney. The kidneys were small and contracted, granular on the surface, with small cysts; they weighed only 7 ounces together. The stomach and small intestines were congested, but showed no evidence of the source of hæmorrhage. The heart was a good deal hypertrophied, and weighed 20 ounces. The liver was rather large (4½ lbs.), but otherwise

normal.

The points of interest in the case are the following :-

1. The fits, which had developed during the last three years,

were of an ordinary epileptic character of only occasional occurrence, and not very severe. So little importance was attached to them that they did not transpire in the history until the occurrence of the first fit in the hospital caused special inquiry to be made. Granular kidney as a cause of epileptic fits in the adult is not generally recognised; yet not infrequently they are the first grave sign of illness.

- 2. With the exception of these fits, the patient thought himself to be in good health until the attack of dyspnœa developed a month before admission.
- 3. The attack of dyspnœa was evidently cardiac in origin, and of the nature of angina; it had nothing of the asthmatic character about it, and could not properly be called asthma.
- 4. General rashes are rare. The rash in this case was of the kind that is common in the later stages of granular kidney, viz., an erythema, and, except for the irritation it caused and its grave significance, it was not serious in itself. The bullous eruption which occurred upon the feet is very unusual, and in this case the contents were blood-stained, though the erythema itself was not hæmorrhagic.

The rash was probably of a septic or toxic character, and this is confirmed by the rise of temperature which accompanied it, for the tendency in the last stages of granular kidney is for the temperature to be subnormal—often remarkably so.

- 5. The later symptoms could in no way be connected with any obvious change in the urine. There was more albumen and less urea on the patient's admission than subsequently, and until the last two days of life elimination by the kidneys seemed to be satisfactory. Though the patient had had fits previously, and died comatose, nothing of the nature of uræmic fits occurred.
- 6. The albuminanc retinitis, though slight, was characteristic. The hæmorrhages which were noticed on admission were slowly absorbed, and no fresh ones occurred, but the white spots remained as they were.

It is interesting to note that the albuminuric retinitis was what is often called "early," though the granular kidney was in its last stages. The patient complained of no defect of sight; the field of vision was taken, and found normal in both eyes.

7. The association with granular kidney of both lead-poisoning and gout raises the question of the relation of these lesions to each other.

The man had been working with lead for 20 years; the gout had only developed during the last few months, so that it was obviously subsequent to the granular kidney. Except for the lead-line and the history of one or two slight attacks of colic, the evidence of lead-poisoning was not marked, and the working with metallic lead does not usually lead to lead-poisoning; so that in this case the development of granular kidney was probably quite independent of the lead. In many cases it is not so much that gout and lead-poisoning cause granular kidney as that patients suffer from gout and lead-poisoning because their kidneys are already granular and elimination defective.

- 8. Hæmorrhage from the bowels is of very rare occurrence, although the general tendency to bleeding is so marked a feature.
- 9. Gradual cardiac failure is common, as shown by shortness of the breath, ædema of the feet, &c.; yet for angina to be the first symptom is rare.
- 10. This case illustrates an important fact in the clinical history of granular kidney, the suddenness with which grave symptoms often develop in the midst of apparent health, for this patient thought himself well, or, at any rate, in his usual health, up to two months before his death; yet from the time the angina developed his fate was sealed.
- III.—Gradual loss of strength, colour, and sight for three years; first definite symptom fits; hæmaturia early; blood seen passing down ureters; well-marked albuminuric retinitis; blood from bowels; vomiting; diarrhæa; death from asthenia; post mortem, granular kidney, hypertrophy of heart, extensive atheroma, ulcers in rectum and cæcum.

Eliza W., aged 43, was admitted into the hospital on account of pain on micturition and the frequent passing of blood. She had been a healthy child, had been long married, had had three children (the last 10 years ago), and the pregnancies had given her no trouble. She had been, as she thought, in good health until three or four years ago, when she began to lose strength and colour, and her sight had begun to fail. During the

last year or two she had suffered a good deal from headache.

In June, 1898, she was suddenly seized with a fit of an epileptic character, the first she ever had had in her life. A second fit followed shortly after. In September, 1898, she began to pass some blood in the urine, and to suffer from pain in the back; the frequency of micturition also became increased, especially at night. In October she again came to St. Bartholomew's Hospital, complaining of the passing of blood, which was thought to come from the vagina, and she was admitted. Mr. Bruce Clarke examined her with a cystoscope, and observed blood passing into the bladder through the ureters. The instrument probably produced a small

fissure in the ureter, for after that time she experienced a good deal of pain on micturition, which she had not suffered from before. While in

the hospital she had two epileptic fits.

I was asked to see her in December, 1898. At that time she was an extremely pale woman, with very thick arteries and a large-amount of albumen in the urine (about one-third); the heart's apex was just outside the nipple, the second aortic sound a good deal accentuated, and the first apex sound prolonged, but no murmur; there was no edema of the feet.

The eyes were examined, and extreme albuminuric retinitis with numerous white patches and small hæmorrhages were found. There were white streaks on the vessels, especially of the right eye, and a broad reflex on some of the veins. The blood having stopped and the patient being much better, she was then discharged from the hospital and became an out-patient.

In February, 1899, she had well-marked epileptic convulsions at

home.

On March 24th she was admitted into the Royal Free Hospital because her health had been failing rapidly, and she had been getting much weaker and more anæmic. On admission she was found to be extremely pallid and anæmic, and looked very ill. The pulse was regular, of high tension, the artery very much thickened. The heart's apex was in the nipple line, in the fifth space, and the cardiac dulness increased upwards and outwards; the first apex sound was clear but somewhat prolonged; the second aortic sound accentuated. The tongue was red and raw, and the appetite very bad. The urine, acid, 1014, contained rather more than 1 per cent. of albumen; no casts were discovered.

Ophthalmoscopic examination showed extreme albuminuric retinitis in both eyes. The vessels, both arteries and veins, were very tortuous, and the veins distended to more than twice their usual calibre. Numerous small flame-shaped hæmorrhages were scattered over the fundus in both eyes, especially in the right, in which also were some large irregular patches of hæmorrhage. Some of the arteries had a bright silver streak, and there was a broad central streak in many of the veins. The discs were blurred, and the edges indistinct, but no distinct swelling.

The patient complained of a good deal of pain on micturition, which was frequent both night and day, but she was not then passing blood. She had also a good deal of pain in the back. A vaginal repository gave

her a good deal of relief.

On March 28th (four days after admission) she became wandering and very restless at night, wanting continually to get out of bed, and passed her water involuntarily.

A few days later the vagina and ureter were examined, but nothing could be found, and a soft catheter was passed easily without any pain.

On April 8th she passed a little blood by the bowels, and on the 9th a larger quantity, with some clots. On the 10th she vomited a few times,

and on the 11th passed more blood by the bowel.

All this time she was getting rapidly weaker, the restlessness at night was extreme, the pulse became rapid and weak, and reached 120. On the 13th very troublesome diarrhea set in. On the 15th she became unconscious, and gradually passed away that night without regaining consciousness, but without any fits.

The post-morten showed nothing of importance, except in the kidneys,

heart, and vessels.

The heart weighed  $13\frac{1}{2}$  ounces; the left ventricle and septum were

considerably hypertrophied, with slight atheromatous thickening on the valves of the aorta. There was extensive atheromatous degeneration throughout the thoracic and abdominal aorta, as well as in the branches of the smaller vessels.

The liver weighed 44 ounces, the spleen 3½ ounces; both seemed normal. The kidneys weighed 3 ounces; they were pale in colour, of a firm consistency; the capsules stripped readily off over the greater part of the surface, but were somewhat adherent in parts; the cortex was diminished

in size, the surface granular.

The other facts of importance were that there was ulceration in the large intestines, a little round the ileo-cæcal valve, three ulcers in the mucuous membrane of the cæcum, but the last 4 inches of the rectum were completely covered with ulcers, all superficial, and in one or two places only extending as far as the muscular coat. The walls of the rectum were a good deal thickened, and the surface was covered with one or two greyish sloughs, suggesting that some of the ulceration at any rate was of recent origin.

This case, it will be observed, was admitted into a surgical ward on account of hæmaturia, and it was not until later that the true nature of the case was recognised by Mr. Bruce Clarke. The more careful investigation of the history then disclosed early symptoms of the disease as much as three years before, but the first serious symptom was the occurrence of fits.

Hæmor hage occurred from the bowels several times, and in this connection it is interesting to note the ulcers which were discovered post mortem in the rectum and cæcum. Hæmorrhage from the bowels, however, is not an uncommon symptom, while ulceration in the bowels is a rare lesion. It follows, therefore, that the hæmorrhage from the bowels must be put into the same category as epistaxis, and cannot be referred in most cases to an organic lesion. Lastly, the real nature of the case would very easily have been overlooked had it not come under the care of a surgeon familiar with the condition.

IV.—First symptoms six weeks before death; headache and insomnia; epistaxis, abdominal pain, diarrhæa, hæmorrhage from bowel, vomiting; sudden dyspnæa and coma; post mortem.

Jane B., aged 21, was admitted into the hospital, suffering from shortness of breath, pain in the abdomen, vomiting, and diarrhea. She was obviously very ill, but the nature of the case did not seem clear.

The history was somewhat defective, but she appeared to have been in good health until about a month ago, when she began to complain of some headache and insomnia. However, she continued at work until September 21st, when the headache became worse. On the 24th she had an attack of epistaxis, and again on the 25th, and then vomiting and diarrhæa and abdominal pain developed, and she came to the hospital.

There was no history of any illness during her life of any importance,

except influenza four years previously.

She was extremely anæmic, pallid, and looked very ill; the tongue was moist and red; the cardiac dulness was a good deal increased outwards and to the left, the apex in the fifth space half an inch outside the nipple line. There was a systolic apex murmur, not audible in the axilla, which was attributed to the dilatation, and not to valvular disease. The temperature was low, the abdomen somewhat distended and tender, especially in the epigastrium. There was no ædema. The urine was 1008, and contained a cloud of albumen.

On September 30th she vomited nearly two pints of a brownish fluid, partly beef-tea and milk which she had taken; there was considerable epistaxis. The colour of the vomit was probably due to blood which had been swallowed. The motions were frequent, loose, and dark-coloured; anæmia became very much more marked. The diarrhea continued for the next day or two, and the epistaxis too, though not to the same extent.

On October 3rd she seemed in the same condition until late in the day, when she was rather suddenly attacked with dyspnæa, became unconscious,

and died rapidly.

The post mortem showed the body to be well nourished, really almost plump, but extremely anæmic, and there was no ædema. The lungs showed several small infarcts of recent date, and a small group of pleural adhesions on the right lung; otherwise there was nothing in the body, except in connection with the heart and kidneys.

The heart weighed 16 ounces. There was a great deal of hypertrophy of both ventricles, but chiefly of the left ventricle; the ventricular wall

was pale. The vessels were free from atheroma.

The kidneys were very greatly reduced in size, the two together only weighed 3 ounces, the colour whitish-yellow with red medulla, and the whole organ tough and hard, the cortex was greatly contracted, the pelvis much dilated, the surface very granular, and the capsule was firmly adherent and puckered. The kidney was described by the pathologist as "contracted white." The microscope showed the ordinary lesions of advanced granular kidney.

The nature of the case was not recognised until shortly before death, when the diagnosis of granular kidney was suggested; so that, unfortunately, the eyes were not carefully examined, nor the urine either. The notes were kindly supplied me by the doctor in charge, who stated that there was nothing at all during the case which suggested that it was a case of granular kidney.

It is interesting to note that the patient regarded herself as a healthy woman, and that apparently she had no symptoms until six weeks before her death.

V.—Granular kidney; puerperal eclampsia, without adema, eight years previously; white patches observed to develop, at first unilateral; silver-wire arteries developed after the white patches.

Louisa M., aged 36, had been married for some time, and had had one miscarriage and nine pregnancies, eight of which were premature; there

was only one child living. Eight years ago she had an attack of fits, and was unconscious three days; she was pregnant then, and the child was born while she was unconscious, but she had no cedema at the time.

She first came to the hospital on February 3rd, 1898, complaining of feeling dazed and lost when she was walking about, and that her urine had been giving her some trouble. The urine then contained a fair cloud of albumen. She was only under observation at that time for

a few days, and did not again come under observation for a year.

During these 12 months she said she had been pretty well, except that about three months ago she had spent a week or two in bed because "her kidneys were bad." She had suffered frequently from headache, especially in the morning, over the frontal and temporal region, and chiefly on the left side; this was sometimes very severe, and made her feel very ill. The micturition had been frequent at night for a good long time; she had to rise generally twice. The eyesight had been failing for the last 18 months a little, chiefly in the left eye, but she could read well with either eye.

The case was a clear one of granular kidney. The arteries were thick, the tension high, and there was a small amount of albumen in the urine. Ophthalmoscopic examination showed commencing albuminuric retinitis

in both eyes.

On February 3rd, 1898, in the left eye there was a series of minute white points on both sides of one of the large vessels in the upper segment of the eye, close to the disc. The right eye showed no lesion at all. On April 4th these white patches had become somewhat larger and more numerous. On May 2nd their number had still further increased, and some fresh ones appeared round the yellow spot. A few white patches were now found in the right eye.

By August 11th the changes in the left eye were still further advanced; there were more larger white spots, and there were some white spots also in the left eye half-way between the disc and yellow spot, and the yellow spot itself was indistinct and somewhat cloudy. The arteries had been

getting streaky for some little time.

The changes slowly progressed, and by December were well marked in both eyes, though still a little further advanced in the right. The lesions were now fairly symmetrical. The retinal arteries had been gradually becoming streaky, and by February many of them were characteristically "silver-wire."

The patient is still under observation and in statu quo, nearly two years after being first seen.

It is interesting in this case to have watched the white patches of degeneration develop before the arteries showed the characteristic streak.

- VI.—Granular kidney; first symptom, right hemiplegia and recovery; paroxysmal headache; attacks of blindness; detachment of retina (blood); left hemiplegia and recovery; large hæmorrhage into globe; occasional fits; death nearly six years after the albuminuric retinitis was observed.
- J. K., a married woman, aged 51, came under observation in December, 1894, complaining of pain in the temples. She was a large, well (9772)

nourished woman, and presented so little that was striking that her case, in the press of work, was passed by until the next visit, when she was found to have the signs of granular kidney and well-marked albuminuric retinitis. She stated that she had been in good health up to 12 months ago, when she was suddenly seized with loss of power on the right side, incomplete right hemiplegia. This, however, she had completely recovered from at the time of her visit. She presented the usual signs of granular kidney, the thickened artery, high-tension pulse, a small amount of albumen in the urine, and well-marked albuminuric retinitis. Her only complaint was of neuralgic headache, which came on in violent paroxysms, the pain being chiefly felt in the temples.

In the right eye there were numerous small white patches round the yellow spot, and abundant hæmorrhages, partly outside partly above it; the disc was normal, but one of the main vessels near the disc had a long white streak, perivascular, extending some distance along it, perhaps for the distance of a quarter of the retina. In the left eye the optic disc was a little blurred, but there was no marked swelling, and its edges were fairly distinct; there were some white patches at the yellow spot,

but no streaks as in the other eye.

There was nothing special to note about the case; the headache was greatly improved by means of salicylate of soda, and the eye condition remained unchanged, except that the white streaks progressed, still being confined to the right eye; they gradually approached the discs, and involved some of the other branches of the same artery; the other vessels were normal in appearance. Nine months later she became suddenly quite blind in the right eye, and this, she stated, persisted for about six weeks. She was not then under observation. When she returned in October she was able to see fairly well with that eye, and there was no change in the ophthalmoscopic appearances; we may presume that her loss of sight was due to hæmorrhages, which had been completely absorbed.

In the beginning of January, 1896, she suffered much from headache for a week, and in the middle of January woke up suddenly one night again completely blind in the right eye, as before. On examination the media seemed to be opaque and the fundus was not visible. It appeared that there was a detachment of the retina by dark coloured fluid behind it, viz., blood (Mr. Bowater Vernon). In the course of two months the sight gradually improved, and in March she was again able to see fairly well with that eye. She then had an attack of hemiplegia on the left side and disappeared from observation for more than three months. It appeared that about this time, viz., in March, 1896, beside the hemiplegia she had occasional fits, and since that time her speech has been a

little defective and her memory failing.

In November, 1896, she had recovered her usual health, there was very little trace of the hemiplegia left, nor had her general appearance much altered; her nutrition was still fairly good, she still passed a certain amount of albumen, and had a high-tension pulse, and there had been no special change in the condition of the eyes.

In February, 1897, she ceased to attend the hospital and was not again seen until February, 1899, when I wrote for her, but hardly expected to hear that she was living. To my surprise she presented herself in much the same condition as before. She had gone on in much the same way, having occasional fits, but no further paralysis. Her memory had deteriorated and her speech was not very clear. On examining her with

the ophthalmoscope the left retina was found little altered, except that several of the vessels showed well-marked silver-wire streaks, and the white patches had increased in number; the disc itself presented no abnormality. The right eye, however, was found full of blood-clot right up to the back of the lens. This eye, it transpired, had been completely blind for some time, but one month previously she had been seized with pain in it, which had continued for a few days, getting gradually less, and I presumed that it was at this time that the hæmorrhage had occurred. When I saw her, the tension was slightly raised, the clot evidently consolidated; its colour dull red. In the course of the next few weeks the clot gradually contracted and was partly absorbed.

When last seen she was in good health and looked rubicund. Her chief complaint was of a varicose ulcer below her right calf. About six months later I was informed that she had had another fit, probably apoplectic, in which she died. She had lived for more than five years

from the time when the albuminuric retinitis was first observed.

This case is one of very great interest: first, in respect of the number of attacks of hemiplegia she suffered and recovered from more or less completely, and secondly, in respect of the intraocular hæmorrhage.

A hæmorrhagic detachment of the retina, of slight degree, occurred three and a half years before ber death, from which recovery was complete without impairment of sight. Two and a half years later an enormous hæmorrhage occurred in the same eye, filling the whole vitreous chamber, a condition of the greatest rarity and the only instance, to anything like the same degree, I have ever met with. This case was shown at the Medical Society in illustration of the lectures.

VII.—First symptom a fit, but asthenia previously; ascites due to cirrhosis of liver; albuminuric retinitis only a few weeks before death; death from asthenia; post mortem, kidneys very granular, ascitic fluid very rich in extractives.

Elizabeth J., aged 38, married, was admitted on June 3rd, 1898, to St. Bartholomew's Hospital complaining of vomiting blood and of swelling of the abdomen. Up to a year ago her history had been good. She had been married 20 years, had had nine children and two miscarriages, and, except for typhoid fever eight years previously, considered herself to be in good health until about 12 months ago. She admitted she had taken spirits sometimes, but denied any excess. A year ago she had a fit, and was unconscious for about half an hour. She dated her illness from Christmas, 1897, i.e., six months before her admission, when she vomited blood at intervals, and had bleeding from the mouth and nose while asleep. This occurred on several occasions subsequently, but there had been no return of it for the last five weeks.

A month ago she had a fit in which the left side twitched and she was semi-unconscious for 24 hours. Three weeks ago the abdomen became swollen (ascites) and there was pain in the left side. For the last week

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she had had very troublesome diarrhaa, the motions being very dark. The catamenia had been irregular for about the last 12 months; the last period was about five weeks ago, the one before that having occurred three months previously. Her mother died in a fit, one brother died of a ruptured blood vessel, and six of her own children died of bronchitis.

The patient was much emaciated, extremely anæmic, and somewhat sallow. The abdomen was greatly distended and contained a large amount of fluid; the liver was enlarged and there were a good many piles; the bowels had been relaxed for the last week. The heart was a little dilated and there was a systolic murmur over the pulmonary artery. The lungs were normal. The tongue was clean, but the breath had a somewhat urinous odour. The pulse was 104, small in volume but regular, the artery a good deal thickened, and the tension somewhat raised. The urine was 1008, acid, showed a cloud of albumen, contained some blood and some blood casts. The blood was examined and found to present the signs of extreme anæmia, red cells 1,620,000, white 6,000, hæmoglobin 27 per cent. The diagnosis was made of cirrhosis of the liver and granular kidney. Paracentesis abdominis was performed a week after admission, and 13 pints of serous fluid removed.

The patient remained in the hospital until her death on September 19th, and required paracentesis frequently at intervals of every two or three weeks. The symptoms were those of gradually increasing anæmia and asthenia, and during the last two months of life, although the patient had ascites which required to be frequently tapped, the symptoms were those of chronic uræmia, and depended more upon the condition of her kidneys than upon that of her liver. The urine throughout was much the same; it averaged 25 ounces daily, 1008 to 1012 specific gravity, contained a fair amount of albumen, and from time to time casts and a little blood. Towards the last the patient was frequently wandering at night, and somewhat also during the day; the delirium was more marked when the abdomen was much distended and was relieved by paracentesis.

Another point of interest was that during the last two weeks the patient had a good deal of bleeding from different parts of the body; occasionally she lost a little blood from the bowel, but there were no evident piles. What troubled her considerably for a time was her repeated loss of blood in small amount from the vagina, but this had nothing to do with the catamenia, which, as stated, had been absent for These symptoms were ultimately controlled by the administration of ergot. The most troublesome and obstinate symptom was oozing from the gums, and though no large amount of blood was lost in this way still it was almost continuous for several weeks, though much worse at one time than another. The artery was markedly thickened, but the tension was almost invariably low. Great variations of tension occurred from time to time within short intervals. I endeavoured to fix these by sphygmographic tracings, but the tracings obtained only showed a pulse of low tension, and not that characteristic of chronic renal disease. The eyes were frequently examined, but presented no changes until within the last four or five weeks of life. Then the discs began to get a little cloudy, but there was no obvious effusion. About a month before death some white spots were discovered in the right eye, and a few very minute ones a little later in the left in the neighbourhood of the yellow spot, as well as one or two small hæmorrhages.

The treatment was chiefly symptomatic; thus iron was given for the anæmia, bismuth for the dyspepsia and diarrhea, and ergot for the

hæmorrhage. The ergot seemed, as stated, to control the hæmorrhage from the vagina, but had no effect upon the oozings from the gums. Bromidia, Cannabis Indica, and one or two other remedies were given to procure rest at night with more or less success. What seemed to do some good for a time was nitrate of pilocarpin in doses of one-sixth of a grain three times a day, together with a draught containing citrate of caffein

and strychnia.

In this case, as is frequent with chronic renal disease, the nitrate of pilocarpin did not produce the characteristic sweating. For about the last six weeks of life the patient was taking two or three tabloids of renal substance, supplied by Burroughs and Wellcome, twice a day. These produced no symptoms, but at the same time did not appear to have any effect upon the general condition of the patient, and yet that they had some effect is shown by this curious fact, that whereas the nitrate of pilocarpin had previously produced no sweating, as soon as the renal tabloids were administered, as well as the nitrate of pilocarpin, copious sweating was produced, so much so that it became a distress to the patient and the pilocarpin had to be suspended. When the renal tabloids ceased to do any good they were left off and the nitrate of pilocarpin resumed, but being no longer combined with the renal tabloids as before, no sweating was produced.

The following analysis was made of the ascitic fluid by Mr. Cam-

madge :-

A faint, yellowish green, slightly opalescent, fluid which did not spontaneously coagulate; reaction, faintly alkaline; specific gravity, 1011.

Total proteids—					in which Kidneys were not Affected.	
viz., Serum	globulin, albumen,	$\binom{5}{3}$ g1	rammes	per litre	8.0	$\begin{Bmatrix} 10 \\ 5 \end{Bmatrix} 15.00$
Urea			"	,,	4.0	12.0
Extractives			"	"	11.87	6.76
Metallic ash			,,	"	5.97	5.26
Glycogen					trace.	

It contained no uric acid, sugar, or blood, but gave the ethyl-diacetic acid reaction. Microscopically it contained a few epithelial cells only.

As compared with another case of ascites due to cirrhosis of the liver but not associated with granular kidney, analysis showed that this fluid contained a-much smaller amount of albumen and a much smaller amount of urea, but a very much larger amount of extractives.

Post-mortem report.—The body was pale and wasted; the lungs cedematous; the cesophagus showed some varicose veins near the cardiac end; the heart weighed 10 ounces, was flabby and pale; the abdomen contained eight pints of ascitic fluid; the liver was markedly cirrhotic,

and weighed 2 lbs. 10 ounces.

The kidneys were extremely granular, and together weighed 8 ounces, that is to say, they were not much below the normal weight; there were many cysts, some as large as marbles, close beneath the capsule, which tore off with difficulty, leaving the surface markedly granular beneath. Evidently the weight of the kidney was largely due to the cysts and their contents.

The microscopical examination showed the usual changes characteristic of granular kidney.

Asthenia was in this case the prominent symptom throughout. It was evident that cirrhosis as well as granular kidney was present, and the condition of the œsophageal veins explains the hæmatemesis. In the last stages the cachexia was extreme, and was greatly aggravated by the hæmophilic condition which developed. The hæmorrhage per vaginam was very difficult to check, but the most troublesome symptom was the continuous, uncontrollable oozing from the gums during the last few weeks of life.

VIII.—Chronic parenchymatous nephritis; great anamia and dilatation of heart; albuminuric retinitis two months before death; death after 10 months' illness; post mortem, kidneys large white, capsule adherent, patchy cortical fibrosis.

Charlotte M., aged 29, a hospital nurse, was in good health and at work until the beginning of April, when she began to have pain in her chest, of dyspeptic character. She continued poorly until the beginning of August, when her legs began to swell and became quickly of great size. She had some frequency of micturition, passing but little water at a time, and this was dark in colour. She became very pale, had much pain all over the chest and difficulty in breathing, but for a month or more previously she had been so short of breath when walking that she had frequently to stop and stand still to recover breath. The catamenia

had been quite regular till May, but had not occurred since.

The patient was a well-developed woman, rather above the average size, extremely pale, and somewhat puffy about the face, with a considerable amount of cedema of the legs and the lower part of the body. The tongue was furred and the breath offensive, but not urinous. The pulse 76, of high tension, but regular; the artery somewhat thickened. The heart was considerably dilated; there were no murmurs, but the first sound was prolonged at the apex, and the second sound accentuated, especially at the left base. There was a little rhonchus over the whole of the lungs, with some crepitation and a little dulness at both bases behind. There did not appear to be any ascites. The urine was 1008, one half albumen, contained a number of blood and granular casts; the quantity of urine passed varied a good deal from day to day, but averaged about 20 ounces. The only other point to notice was that her hair had been falling out very rapidly since her illness.

The eyes were examined carefully with the ophthalmoscope, and found

to present nothing abnormal.

On September 2nd she vomited a good deal, and was much troubled with diarrhea, the bowels being opened eight times in the 24 hours. This continued for the next day or two, and was associated with a considerable diminution in the amount of urine, the total quantity passed being not more than 8 to 10 ounces. She was then treated with vapour baths, which produced a good result, and she seemed to improve considerably. The condition remained much the same until September 16th, when constipation had taken the place of the diarrhea.

Her mental condition now became peculiar. She developed delusions

of persecution, and it was difficult to get her to take food, as she fancied some one wanted to poison her.

On September 17th the discs were examined again and found to be perfectly natural. Upon the administration of pilocarpin the quantity

of urine considerably increased up to 30 or 40 ounces daily.

On October 31st the patient was suddenly attacked with very acute blenorrhæic conjunctivitis with great ædema and discharge; the eyelids also were discoloured and stained, as if from hæmorrhage. The pain was very acute. The condition was evidently a septic conjunctivitis, but no cause for it could be discovered. For a few days the condition of the eyes gave very considerable anxiety, but in the end the symptoms subsided, and ultimately the patient recovered sight completely. In this connection it is interesting to state that 12 months previously a case of granular kidney, in another ward, had had a similar attack, but this patient also had recovered without any loss or impairment of sight.

On November 20th another ophthalmoscopic examination was made, and then both eyes were found to present a marked condition of albuminuric retinitis. There were many recent hæmorrhages scattered over the retina, white spots round both yellow spots, a good deal of swelling of the discs and of the retina around. The eyes had been on many occasions previously examined ophthalmoscopically, but there is no note made exactly of the date when this was last done. The condition of the retina is last noted on September 17th, but there is no doubt that the eyes were examined more than once subsequently to that and nothing

found.

The patient gradually got worse in every way. She was very restless at night, and did not take her food so well. She had several attacks of dyspnæa, and became quite livid; for these strychnine was administered subcutaneously, with much relief.

On January 1st on the back of the thighs, which were very cedematous, one or two blebs formed and broke, from which considerable leaking took

place for the next fortnight, after which the places healed.

On January 17th she had a slight fit. On the 20th she had another, and some blood reappeared in the urine. On the 24th there was another fit, and she was troubled a good deal with vomiting, which continued for the next two days. She was then seized with another convulsion, became extremely cyanosed, and died suddenly.

The case appeared to be one of chronic parenchymatous nephritis. The patient became rapidly asthenic, and died with the symptoms of uramia. It is to be noticed that at the time of her admission the arteries were stated to be somewhat thickened and the heart dilated. The dilatation of the heart was a marked symptom throughout the disease, and in part accounted for the exhaustion and dyspnœa as well as for the extreme anasarca. The arterial tension, which at first was raised, varied a great deal, but for the most part of the time was distinctly below normal, the artery being not contracted but dilated. In respect of treatment, a great variety of remedies was employed during the case. Iron, digitalis, caffein, strychnine in various combinations. Pilocarpin

seemed to do her good for a time. Renal tabloids were administered for several weeks, but without any apparent effect.

The post-mortem examination was incomplete, as permission was only granted to examine the kidneys. The body was very cedematous; the kidneys weighed 6 ounces each, and appeared typical large white kidneys; the cortex was much increased in size and very opaque, the medulla showing up very red against the pale cortex; the capsule was somewhat thickened and adherent; the surface was pale and mottled, and showed

some fine granulations and two or three small cysts.

The microscopical report was as follows:-The kidney presented the general appearance of chronic parenchymatous nephritis (large white), but the capsule was adherent. Patches of interstitial changes were found, especially beneath the capsule, in which there were some atrophied glomeruli with a great increase of nuclei. In some parts the cells were well preserved and the nuclei stained well; in other parts the cells were greatly degenerated, the nuclei stained but little, and the tubes were filled with casts. The interstitial tissue in some parts contained much smallcelled infiltration, the nuclei staining well; in other parts it was many times its normal thickness, and consisted of well-formed connective tissue. The malpighian bodies were for the most part well preserved, but some were atrophied, and presented an almost colloidal appearance. The interstitial changes were quite superficial, and limited to patches under and near the capsule, and became rapidly less in the deeper parts of the cortex, and were absent in the medulla. The case appeared to be one of contracting white kidney, that is, of interstitial changes following acute nephritis.

The occurrence of albuminuric retinitis in the later stages is interesting. In this connection it is to be noted that on admission the arteries were somewhat thickened, so that it is possible that after all the kidneys were not quite sound before the acute nephritis set in; but for all that I certainly regarded the case during life as one of simple chronic parenchymatous nephritis.

- IX.—Chronic parenchymatous nephritis; uramia; recovery; great improvement under renal extract; albuminuric retinitis nine months from commencement of illness; pericarditis; death in uramic convulsions; post mortem, kidneys large white, not granular, yet showing extensive general fibrosis.
- E. B., aged 14, was admitted into the Royal Free Hospital on March 17th, 1896, with considerable ædema of the legs and face. She had been in good health until six weeks before admission, when she was confined to bed with a sore throat, headache, and vomiting. The sore throat got rapidly better, but the headache and drowsiness continued up to the present time, and every two or three days she has had attacks of vomiting. Three weeks ago her face was noticed to be puffy, and she was brought to the out-patient department, and 10 days ago her feet and legs swelled. The child was a fairly grown child, with a pale puffy face, and considerable ædema of the legs. There were no other obvious

physical signs. The cardiac dulness was not increased. There was no ascites. The temperature was normal. The pulse was regular, about 80; the artery not thickened, and the tension moderate. The urine was somewhat cloudy, and gave a marked blood reaction with guaiacum. It contained a large amount of albumen, becoming almost solid on boiling, Esbach's test showing 1.2 per cent.; specific gravity 1025, urea 1.1 per cent. The character of the urine remained much the same for the next few days, except that the specific gravity was a good deal lower, about 1014, the total quantity passed daily being about 20 ounces. Microscopical examination showed the presence of numerous casts, granular and hyaline, as well as a few blood casts. The eyes were carefully examined, and no ophthalmoscopic change found.

The case was regarded as one of acute parenchymatous nephritis, and treated accordingly. The patient was placed upon a fluid diet and a diaphoretic mixture; the bowels were kept regularly relieved, and the sixth of a grain of nitrate of pilocarpin given by the mouth twice daily. A little later she also had hot-air baths, but it seemed very difficult to get the skin to act. During the next few weeks the condition appeared to be almost stationary, and to change neither for better nor worse. The urine

remained much the same, except that the blood disappeared.

In the middle of May the patient began to get worse; the quantity of urine was not reduced, but the amount of albumen increased considerably, blood appeared again, and the amount of urea fell to about 0.8 per cent. There was a good deal of *vomiting* and *abdominal pain*; then diarrhea set in, five or six copious liquid motions being passed in the

day, and some bronchitis developed.

On May 21st a rash appeared, spreading from just above Poupart's ligament down to the knee on the left side; it was a red erythematous rash, intense in colour, and looking at a distance somewhat like erysipelas, but it had no raised margin, and there was no elevation of temperature; this lasted for several days, and finally disappeared. At the end of the month, as the child was not making improvement and the asthenia was gaining ground, a change was made in her diet, and she was given a more liberal allowance of food; this seemed to do good.

On June 7th her face was more puffy than it had been; at 2 p.m. she woke from her sleep with a headache; at 3 p.m. she vomited, and at 6 p.m. she had a slight fit, which lasted about four minutes; she vomited freely after it; half an hour later she had a second fit, and vomited again; then a hot-air bath was given, and 3 minims of liquor strychninæ injected. A little later she had another fit, and 3 minims of pilocarpin were injected, and this, with the air bath, caused free perspiration, and

the air bath was then discontinued.

During all that night she had a succession of fits, and at 10 o'clock it was thought desirable to bleed her, and this was done to the extent of 10 ounces. At the commencement of the fits the temperature gradually rose in the course of a few hours up to 104°, and from that time it fell slowly throughout the day until it reached 97.8° on midday of the 9th—that is, in about 19 hours. All the night of the 8th the patient was semi-unconscious, and had frequent fits. On the morning of the 9th she began slowly to improve; the fits diminished in frequency and violence, and during the rest of the day nothing was observed except occasional twitching; consciousness returned. Under the action of the pilocarpin the skin perspired freely, and some slight salivation occurred. A little later in the day diarrhoea set in again, with tolerably large fluid motions;

but the child rapidly improved, and in the later part of the day had some

refreshing sleep.

On the night of the 10th she began to wander, complained of noises in the head, and seemed a good deal distressed, though she responded readily when spoken to. The night of the 10th was an extremely restless one; she was delirious the whole time, and did not sleep more than half an hour perhaps.

The urine was found to contain about 1 per cent. of albumen and 1.1 per cent. of urea; it was acid, and had a specific gravity of 1014, and was free from blood. These characters the urine had all through

the fits.

Cannabis Indica was given at night, and acted successfully for some

days as a sedative.

On June 14th the eyes were examined again and found normal. From this time the patient began gradually to improve, and by the end of the month she was much in the same condition as she was before the fits.

I now administered to her some renal tabloids prepared by Burroughs and Wellcome, giving her 5 grains twice a day. From this time she made great improvement. On July 3rd the quantity of urine reached 47 ounces, the largest amount she had ever passed since admission. With the increase in the amount of urine the amount of albumen greatly diminished, and the cedema at the same time began to disappear. Rapid improvement took place from this time forward; as the quantity of urine gradually increased, the amount of albumen gradually fell; the cedema of the feet and face entirely disappeared; the patient slept well, lost all her sickness and vomiting, and rapidly got well. For the next month or so the urine averaged 1012 specific gravity, 40 ounces in amount, and not more than 0.5 of albumen.

By the beginning of August she was well enough to get up. At the end of September she was discharged from the hospital. She still looked pale, but her nutrition was good, and she seemed in all respects well, except that the urine still contained albumen. During the last week or 10 days before she left the urine averaged between 70 and 80 ounces, the specific gravity 1008, the amount of albumen by Esbach's test 0'2 per cent.

From this time the patient was seen frequently at odd intervals, and at the end of December, nine months from the commencement of her illness, she appeared to be in very good health, and almost well, except that she had not entirely lost the albumen. About this time her eyes were examined, and she was found to have early albuminuric retinitis in both eyes, in the form of small white patches in the neighbourhood of the yellow spot. She had made no complaint of defect of vision; the artery had also become somewhat thickened, and the pulse was of high tension.

She remained in fair health until about the middle of April, 1897, when she began to feel very tired and languid; her eyesight became dim every now and then, and she said she sometimes squinted. She could not sleep well at nights because of cramp in legs and hands; and she was sick several times. She then came up to the hospital, and was admitted on April 30th. When seen the next day she looked pale and ill, and had evidently lost flesh; she lay in a semi-somnolent condition, with her eyes shut, but she roused up to answer when spoken to. There was a little oozing of blood from the gums. The cardiac dulness was normal, and the apex in its proper place, but the first sound was somewhat forcible in character. The pulse was small, rapid, and of moderate tension, but the

artery slightly thickened. She complained of pain across the abdomen, and of cramp in the legs and hands, and itching in the soles of the feet. There was no cedema. She passed during the first 24 hours after admission 31 ounces of urine, which was pale and cloudy, with a slight deposit, specific gravity 1020, containing 2.5 per cent. of albumen, no blood, and a good

many granular casts.

On May 2nd she vomited a good deal, and was extremely restless during the night. The next morning she complained of pain over the sternum, and on examining the heart a loud to-and-fro friction was heard in the precordial region, and the cardiac dulness was somewhat enlarged. She vomited several times, and seemed very ill. Nitrate of pilocarpin was then ordered sub cutem, some brandy and a citrate of potash mixture administered.

On May 4th there was nothing further to report; she was in much the same condition, but complained now of dimness of sight. The oozing from the gums still continued. The ophthalmoscopic examination showed the presence of albuminuric retinitis, much as it was before. On May 5th the patient was worse; she vomited a good many times; she had lost her pain in the chest, but complained a good deal of feelings of suffocation, but without any dyspnœa; she passed water unconsciously; the cardiac dulness was somewhat increased still, and the friction distinctly heard. Irregular twitching movements of the hands and feet were observed.

On May 6th no special change had taken place, but the patient complained more of the suffocation feelings, and the twitchings were rather more marked, and she had still had some oozing from the gums. In the course of the afternoon the breathing became sighing in character; she was restless and very sick, and later had a violent convulsion, which lasted

three minutes, and ended fatally.

Post-mortem examination showed recent pericarditis, the pericardial cavity contained about 4 ounces of sero-fibrinous fluid with some stringy

lymph. The pleura had a few old adhesions.

The kidneys were pale, slightly above average size for the child; the capsules stripped off readily, and the surface was not at all granular. They presented the ordinary appearance of chronic parenchymatous nephritis, but on section they cut somewhat tough. The general colour was a mottled white. The cortex was not much, if at all, diminished. Microscopic examination revealed changes not at all suggested by the naked-eye appearance. There was found a remarkable and most extensive diffuse fibrosis, affecting the whole of the kidney medulla and cortex alike. The cells were extensively destroyed, and many small cysts were found. The malpighian bodies were for the most part of normal size and appearance, but a few here and there were wasted. The lesion may be best described as diffuse general interstitial fibrosis. It would be difficult to show any granular kidney with such extensive and general fibrosis, and the microscopical characters in many respects differed from those usually seen in granular kidney.

Even when first seen, though the diagnosis of chronic parenchymatous nephritis seemed justified, there was always something in the condition of the patient which made me regard the case as peculiar, and likely to run an irregular course, as it certainly did. After a few months symptoms developed such as are usual in granular kidney — attacks of cramp, headache, vomiting, hæmorrhage, pericarditis, albuminuric retinitis, and, at the last, drowsiness, coma, and fits.

The pathological lesions were as interesting as the clinical history, for the kidneys, though not granular, showed a remarkably widespread and extreme fibrosis. Indeed, it would be difficult to show any granular kidney with such extensive general fibrosis, and in this as in several other respects the microscopical characters differed from those usually met with in granular kidney.

From the therapeutic point of view the case is also interesting, as it was one in which renal extracts seemed to do good, at any rate in the earlier stage.

The case which follows was one seen by me, in consultation with Dr. Enraght, to whom I am indebted for many of the details:—

X.—Slight cardiac failure of one year's duration; attack of paroxysmal headache; thickness of speech; delusions; transient right hemiplegia and aphasia; acute mania; death from exhaustion.

Arthur L., aged 53, considered himself to be in good health until three months ago (about March, 1899), when he got a cold on his chest, and was troubled with some cough and expectoration. He went away into the country and came back much better, but was shortly after attacked with influenza, to which he really refers his illness; for since that time his breathing has been short, especially at night, and his sleep has been restless and disturbed, chiefly from the discomfort in breathing, and he had been losing flesh and strength. These symptoms gradually got worse, until he found he could not lie down at night in bed; so that the last few nights were spent in an arm-chair. The feet had swollen slightly during the last two or three days.

On cross-examination it transpired that, for the last 12 months, he had been troubled with shortness of breath and palpitation on exertion, but that he had not found it bad enough to attach any importance to it, or consult a doctor for it. For the last six months he had been disturbed at

night, once or twice, to pass water.

The physical examination showed some dilatation, and, probably, hypertrophy of the left ventricle, without evidence of valvular disease. The aortic second sound was markedly accentuated. The arteries were much thickened, but the tension low, and there was slight cedema of the ankles. The urine was of 1014 specific gravity, and contained a good deal (one-fourth) of albumen. The eyes were not examined.

The diagnosis was clear, viz., granular kidney with failing heart. The subsequent history of the case is as follows, and was furnished me by Dr. Enraght:—

The patient continued in much the same condition for a time, and then the heart slowly recovered itself; the cedema of the ankles disappeared, and the general strength increased. Still the patient remained short of breath on exertion, and the albumen persisted in the urine, though

varying a good deal in amount from time to time.

In June, i.e., four months from what he considered the commencement of his symptoms, while away from home, he was seized with acute pain in the head, which was attended by some thickness of speech and delusions. These symptoms lasted a few days and disappeared, but they returned, though in less degree, at intervals of a week or ten days. In these attacks, besides the acute pain in the head, there was a good deal of cloudiness of ideas, and he would do strange things, e.g., take his money out of his pockets and let it fall about the floor, without attempting to pick it up again.

On June 20th he had an extremely severe attack of headache, which made him cry out with pain, and was accompanied with delusions, thickness of speech, and excitement. This attack also cleared up in a few days, but left him with a constant vertical headache, and pain also down the back of the neck. The albumen at this time had somewhat increased, but there was only slight cedema of the ankles.

On August 20th he was suddenly seized with right hemiplegia and aphasia, with delusions. He was apparently in a dying condition for some days, but slowly recovered. In 14 days the paralysis had passed away, and there was nothing left but some thickness of speech and cloudiness of ideas. A few days later he was attacked with acute mental excitement and delusions. He thought he was going to be killed, and had people coming after him to take him; used to arrange cushions on the floor, and say they were corpses; was constantly in a state of terror; would catch hold of his wife and others, and say that he was saving them from some danger; would pour his medicine, &c., on the floor, and so on. This attack subsided for a week or so and then returned, and continued more or less up to the time of his death, which occurred on October 6th, and was due to gradually-increasing exhaustion and cardiac failure. During the last six weeks of life the patient was in a condition practically of acute mania.

This patient, again, thought himself well till but a few months (nine) before his death. The early symptoms, those of slight cardiac failure, rapidly improved under treatment, and were soon replaced by symptoms of another and much more serious kind. A succession of curious cerebral attacks followed of short duration, and attended with more or less psychical disturbance, and ended in an attack of right hemiplegia and aphasia. This, though grave enough to cause coma and threaten life for a few days, passed off completely in a fortnight. The last few weeks of life were passed in a condition of acute mania. The case is a good illustration of one of the most interesting and least recognised modes of termination of granular kidney.

## XI.—Peripheral Neuritis and Granular Kidney.

Eliza M., aged 30, married, was admitted into Hope Ward suffering from loss of power in the hands and weakness in both legs. She was married nine years ago, has had four children, and no miscarriages. She was in excellent health until after the third confinement, when, five weeks after the birth of the child, she was seized with pain across the loins and swelling of the ankles and eyelids. The urine was scanty and thick, and she was told she had "kidney disease." A week later she had a fit, and was unconscious for some time. She remained in bed for two weeks, and suffered much from headache. The legs and eyelids continued swollen for about six weeks, when she began to recover her health, but she has never been so well since, suffering from weakness, irritability, and occasional headache.

In September, 1898, the fourth child was born. There was no return

of any of her previous symptoms.

In February, 1899, she was confined to bed for three weeks with pain, redness, and swelling in the right great toe and leg, which the doctor called "rheumatic gout."

In June, 1899, she had an attack of influenza, and was in bed a week,

and recovered completely.

On August 5th she was troubled with much itching in the palm of the right hand, and on the 6th the hand became red and swollen, and the

swelling gradually extended up the arm to the elbow.

On August 8th similar patches developed on the legs. On August 9th she lost use in the little fingers of both hands, and by the following week the second and third fingers of the left hand, and the third finger of the right, became powerless.

In the course of the next five weeks all the power was lost in both hands, and by October 1st she was quite unable to extend the hand at

the wrist.

The legs began to get weak early in September, the loss of power being preceded for about a fortnight by severe shooting pains in the calves. Wasting took place from the first in the affected muscles, and was progressive.

There was no history of insomnia, of headache, or of increased frequency of micturition day or night, or of other symptoms before or after the attack of acute nephritis in June, 1897. There was no evidence or history of syphilis, potus, lead, arsenic, or other poisoning, nor of diphtheria or of any recent illness except the mild attack of influenza referred to.

The patient was a pale, thin woman, with double foot and wrist drop. The artery at the wrist was enormously thickened, and the tension high. The second aortic sound was greatly accentuated, but no increase of

cardiac dulness could be made out.

The urine was of 1012 specific gravity, and contained one-fifth of

albumen, but no casts were found.

The eyes exhibited well-marked albuminuric retinitis of the exudative and hæmorrhagic type. The disc was swollen, its edges frayed out and ill defined. Numerous white woolly patches and abundant hæmorrhages, some flame-shaped, others irregular, were scattered over the parts of the retina, especially round about the disc, between it and the yellow spot.

The condition of the paralysed limbs was as follows :-

In the arms there was general wasting, especially of the forearms and in the thenar and hypothenar eminences. The grasp was extremely

feeble in both hands. Elbow flexion and rotation good. Complete wrist-drop on both sides, the extensors being much wasted and completely paralysed, the flexors acting feebly. The digital extensors were completely paralysed, the flexors interessei, lumbricales, and opponen pollicis acting feebly. No tendon reflexes obtained.

In the legs there was but little obvious wasting. The loss of extension of the foot was considerable, but of flexion only slight. The knee jerks

were very feeble.

Electrical reactions:—The long extensors of the left wrist and fingers gave no response to either interrupted or constant current. Those of the right wrist and fingers reacted feebly to both currents, but with the constant current the anodal and cathodal closure gave contractions of equal intensity.

In the course of the next four weeks, the hands being placed on palmar splints and the limbs massaged, improvement took place. Power was regained to some extent in the flexors of the hands and fingers, and in the leg muscles, but no improvement was detected in extension of the

hands.

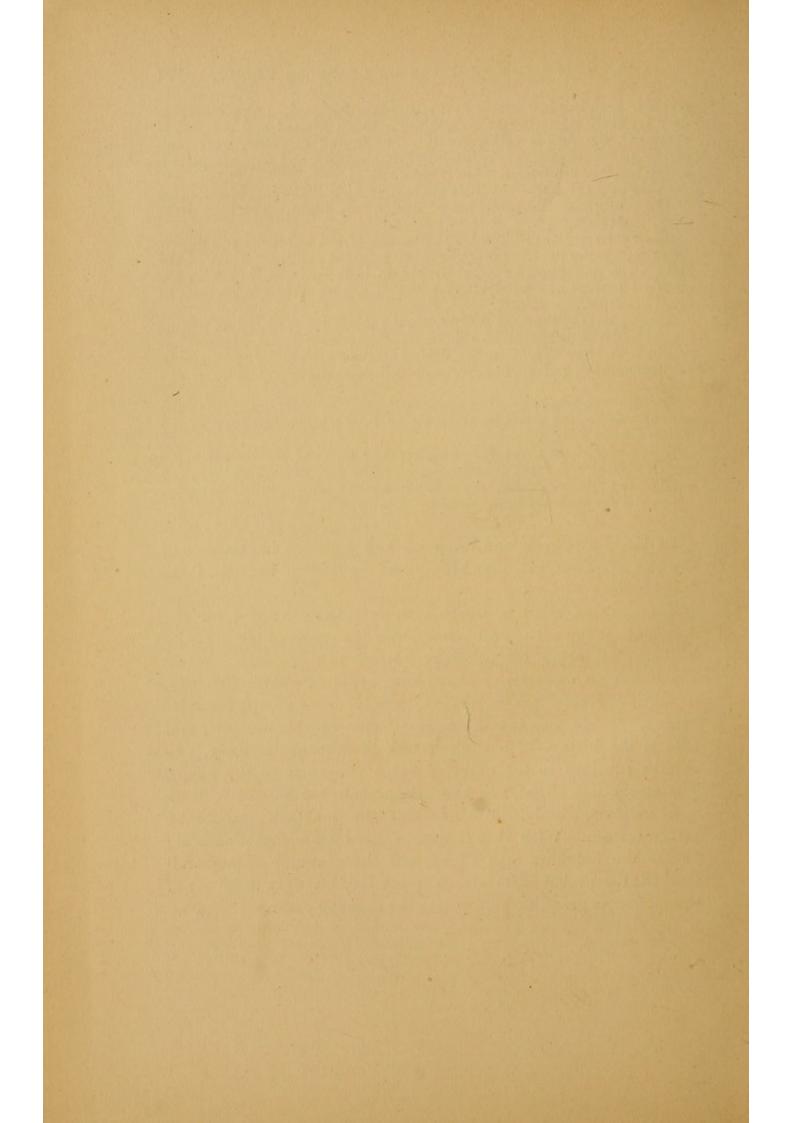
The albumen was reduced to a trace only, and in general condition the patient was feeling stronger and looking better. The condition of the retinæ altered slowly.

The exudation in great part disappeared; many of the hæmorrhages were absorbed, but fresh ones developed. The disc became whitish, and some of the arteries very small, as if there was some amount of atrophy.

The patient is slowly improving.

Of the coexistence, and order of, and sequence in this case of the two affections, granular kidney and peripheral neuritis, there is no doubt.

The only question is whether there is good ground for the opinion that the peripheral neuritis was the result of the granular kidney. All other causes of peripheral neuritis were absent. There was no evidence of alcoholism, syphilis, general diseases, or specific fevers—indeed, no other definite cause except granular kidney. There was one disturbing factor in the problem, and that is the history of a slight attack of influenza in June, two months previous to the onset of nerve symptoms in the hands. The attack was slight, and the patient believed herself to have recovered completely. But for this the conclusion would be pretty certain. With this it must remain somewhat doubtful; but as the influenza was slight, and the granular kidney well marked, the probabilities are, to my mind, strongly in favour of the view that granular kidney was the exciting cause.



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