Hunterian Lecture

ON

BRIGHT'S DISEASE IN SOME OF ITS CLINICAL ASPECTS.

Delivered before the Hunterian Society on Oct. 13th, 1915,

By SAMUEL WEST, M.D. OXON., F.R.C.P. LOND.,
CONSULTING PHYSICIAN TO ST. BARTHOLOMEW'S HOSPITAL, ETC.

GENTLEMEN,—An invitation to deliver a Hunterian lecture is a great compliment. I appreciate the honour highly, and I value it all the more when I read the list of those distinguished men whose names are inscribed upon the roll.

BRIGHT'S INVESTIGATIONS ON KIDNEY DISEASE.

In the choice of Bright's disease as the subject there is a historical appropriateness. The year 1915 is a sort of centenary in relation to Bright's disease, for it is exactly 100 years ago that Richard Bright began the work which was to make him famous.

In 1827, after, as he tells us, 12 years' study, he published his paper on Dropsy. In it he showed that in many cases of dropsy there were marked lesions of the kidney, the kidneys being large and soft, and that in them the urine was albuminous or coagulable by heat. He illustrated the paper by some excellent coloured drawings, which could hardly be improved on nowadays.

Carrying on his investigations for the next ten years from another point of view—viz., that of albuminuria—in 1837 he published another important paper, in which he showed that in many cases of albuminuria, in which there was and had been no dropsy, these were also kidney lesions, and that the kidneys were then small, shrunken, and hard.

These are the two groups as defined by him, which were subsequently called, in his honour, acute and chronic Bright's disease. With the large soft kidney he showed that the dropsy was well marked and the symptoms acute, and that with the small, hard kidney there was usually no dropsy, and the symptoms were often absent or indefinite. Clinically and anatomically, therefore, the two groups were distinct. Nor could Bright satisfy himself that they stood in any definite relation to one another.

So far as Bright's observations extended his work was complete, and subsequent observers did little more than confirm his conclusions. Some years later the view was dogmatically stated, notably by Frerichs, that the small kidney was simply the later stage of the large, but his statements were mere assertions, and entirely unsupported by clinical, or indeed any, evidence.

The term "Bright's disease" is nowadays often loosely applied to various forms of kidney disease. It should be strictly confined to the two groups which Bright described. Practically we now adopt this classification. The acute form with the large, soft kidney we now call acute nephritis, and the chronic form with the small, hard kidney we name granular kidney.

Bright's disease has now become a household word, but it is gradually becoming synonymous in the popular mind with the chronic form. It is a name which causes great alarm, for it is taken to imply an incurable kidney disease, resulting in serious illness and premature death.

No. 4812.

Bright made a real discovery. It depended on the combination of accurate clinical and pathological observation, and his classification, call we the different forms by what name we please, cannot be improved on.

Wilks wrote in the Guy's Hospital Reports for 1877 as follows:—

I think it may be safely said that dropsy must have been recognised as long as man had been seen to succumb to mortal disease, and also that for more than a century the urine was known to be albuminous in certain forms of this complaint, and for as long a period that persons died with symptoms of uræmia, where the kidneys were small and granular. It is clear, however, that renal disease was not recognised as an important malady until Bright's essays appeared or he would not have been hailed at once as a discoverer and the malady called after his name. He systematised and placed the disease on a satisfactory foundation, which was equivalent to having discovered it. He first showed there was a common disease amongst us, which was to be recognised by certain definite methods, and more than this that there were varieties of it. In this the merit of his discovery seems to consist.

Since Bright's time much work has been done in the study of both the acute and chronic forms, but it has been especially upon the latter, granular kidney, as it is now usually called, that interest has centred during the last half-century.

In this connexion an important advance was made when Gull and Sutton in 1872 drew attention to the widespread arterial changes which were associated with granular kidney, to which they gave the name "arterio-capillary fibrosis." The exact nature of the arterial change, whether muscular hypertrophy or fibrotic degeneration or both in varying degree, was the subject of active controversy for some years, and cannot be said to be settled yet.

The problem was further complicated by the study of arterial pressure. Upon the questions of the relation of this increased pressure to the arterial change, and of both to the kidney lesion, opinions are still almost as strongly divided as ever. Recently the view that raised arterial pressure is necessarily of renal origin has been actively challenged. Professor Clifford Allbutt has suggested the term "hyperpiesis" to indicate those cases of persistent high arterial pressure which are not associated with renal disease.

CLASSIFICATION.

In the remarks which follow I shall adhere strictly to Bright's original classification. Bright's disease I shall hold to consist of the two forms only which Bright originally described.

1. Acute Bright's disease, or what we now call acute—or acute parenchymatous—nephritis, an inflammatory affection with well-marked clinical symptoms and course.

2. Chronic Bright's disease, or what we now call granular kidney, a degenerative, non-inflammatory affection with few or very indefinite clinical symptoms.

Further, I shall maintain that there is no established relation between these two forms—in other words, that the chronic form is rarely, if ever, the later stage of the acute. That they are, in point of fact, entirely separate and distinct diseases.

The large white kidney, which we now usually speak of as chronic parenchymatous nephritis, Bright knew to be the later stage of acute nephritis, as many of his figures show. It belongs, therefore, to the category of acute Bright's disease, and not to that of chronic. Confusion might be avoided if we called it long-standing instead of chronic. The term "chronic" has a double meaning in

medicine. It may be used in reference merely to duration, and it is then only another way of expressing the fact that the affection has lasted some time. But it may also involve the pathological theory that long-standing acute inflammation ends in interstitial fibrosis, which as a general proposition is certainly not true. Facts and theories in medicine should always be kept distinct and terms avoided which confuse them, for even when the facts are right the theories may be wrong.

The general features of each form of Bright's disease are so familiar that I shall pass them over and deal only with certain points which appear to me either new, important, or interesting.

ACUTE BRIGHT'S DISEASE.

Acute nephritis is a truly inflammatory affection. It is not generally recognised that in the early stages it is attended with definite signs of fever. The temperature is raised, sometimes considerably. I have seen it as high as 104° F. in the first few days. The rise of temperature is, however, of short duration, rarely lasting longer than a week, after which time it falls and remains, as a rule, sub-normal.

The Effect of Cold or Chill.

Of the actual cause of acute Bright's disease we have but little definite knowledge. One fact is clear that *cold* or *chill* does not play by any means the important part which has been long attributed to it. The common text-book description—that the patient rode on a cold day outside a coach or on a motor-car, got greatly chilled, and next morning could hardly open his eyes for œdema—may be picturesque, but it is not correct, though there is no doubt an element of truth in the statement that a chill often precedes the onset of acute nephritis. The same is stated of pneumonia, rheumatic fever, peritonitis, and many other affections. If chill predisposes to any of them the actual attack requires the presence of some other determining factor, and we should probably be correct in saying that all cold can do is to reduce the general resistance of the body, so that it falls an easier victim to any infection which is lying in wait to attack it.

If cold and exposure could cause acute nephritis no conditions could have been more favourable to its production than life in the trenches during last winter. It was, I think, generally anticipated that acute nephritis would be frequent. Yet though frost-bite and other direct effects of cold were very common, there was little or no acute nephritis; and in the spring, when the great cold had passed and the weather had become milder, acute nephritis became common. The cases came in such a rush that it was thought they must be the result of an infection of some sort.

Several of the cases were sent to St. Bartholomew's Hospital, where a ward was set apart for their thorough investigation and placed under the competent direction of Dr. Langdon Brown. His report is an able record of thorough and systematic work, and is full of observations of great interest and importance. The figures which he gives of the incidence of the disease up to the end of June appear below. The highest number occurred in midsummer in the month of June when the heat was considerable.

Dropsy.

The signs of acute nephritis are obvious enough when dropsy occurs, but dropsy does not appear, except, perhaps, in the most severe cases, until

the nephritis has lasted some days. In mild cases it may not appear at all. This is especially the case in the course of scarlet fever or diphtheria, where, in spite of the absence of dropsy, the urine may contain blood, albumin, and casts, so that the diagnosis of acute nephritis is clear so soon as the urine is examined.

The absence of dropsy does not therefore exclude acute nephritis, but it is unlikely that dropsy will continue absent except in the very mild cases, which quickly recover.

Cases of Acute Nephritis occurring in the British Expeditionary Force.

In the 6 months preceding } 92 in all—a monthly
February, 1915 } average of 15.3.

In February, 1915	72 new cases.	} Yielding a monthly average of 194.
In March, ,,	138 ,, ,,	
In April, ,,	223 ,, ,,	
In May, ,,	211 ,, ,,	
In June, ,,	326 ,, ,,	

Note.—The later figures are not yet available, but I understand that the number is still on the rise, and that in the last month for which there is a return it was nearly double that given for June.

ACUTE URÆMIA OF UNCERTAIN PATHOLOGY.

This is the most convenient place to refer to a remarkable group of cases, of which I have been able to find no record in recent literature, and I do not know exactly what name to describe it by.

The cases present themselves under the guise of acute uræmia in persons who have been hitherto in good health and free from any signs of kidney disease. The symptoms of uræmia develop with great suddenness, but are of the ordinary kind and unmistakable. The urine is greatly reduced in amount, contains some blood, much albumin, and many casts. There is no dropsy. After a few days, during which time the danger to life seems very great, the symptoms subside almost as quickly as they developed. In most of the cases I have seen recovery has been rapid and complete.

I saw a typical case of this kind in consultation with Dr. F. C. Evill.

The patient, who was about 40 years of age, had been under treatment for an attack of influenza a month previously. The urine was examined then and found normal. He returned to business a little earlier than, perhaps, he ought to have done, for he found his work a burden. A few days later he was taken ill rather suddenly in his office with headache and vomiting, and was brought home very ill. His headache became intense, and the most exhausting restlessness developed, which prevented sleep. Two days later typical uræmic convulsions set in for which he was freely bled with benefit. He remained in this uræmic condition for a week, with continued extreme restlessness and occasional fits. The treatment was active—venesection, diaphoretics, packs, pilocarpine, and finally inhalations of oxygen, which seemed very beneficial. He then began to improve, and in a few days all grave symptoms had disappeared and convalescence was established.

The urine, which during the attack contained much albumin, many casts, chiefly granular, and some blood, rapidly improved, and by the end of ten days was again normal.

No signs of kidney mischief had been present before the attack and none followed. I saw the patient several times subsequently and he remained perfectly well. Of course, I had examined him most carefully at the time for evidence of granular kidney, but no signs of it were present and none developed.

About the same time I saw also in consultation the following case.

The patient, a fine healthy young lady, had been confined at the normal time of her first child two days previously. The urine was known to have been perfectly healthy during the pregnancy. The confinement was quite normal, the

child was a fine healthy boy, and she had begun to suckle it. Two days after confinement, without any warning, she became strange in manner, and a few hours later did not recognise her husband. She was extremely restless, only semi-conscious, and had a good deal of twitching, though no actual fit. The urine was scanty and loaded with albumin.

The case was evidently one of incompletely developed uræmia and was treated on the usual lines. Her condition caused the gravest anxiety for the time, but by the end of the week the symptoms had all subsided. The albumin quickly disappeared from the urine, and the subsequent course of the case was satisfactory. She got quite well and was able to nurse the child.

A similar case was under my care in hospital.

The patient, a man of about 40, was admitted with acute symptoms of indefinite character, the nature of which was at first obscure. He was suffering with intense headache and frequent vomiting. When I paid my visit to the wards the prominent symptom was the extreme restlessness, for he lay in bed tossing himself about from side to side, never still for a moment, with frequent twitchings of the limbs and face, but no actual fit—clouded in mind but not delirious. The urine was scanty, loaded with albumin, and contained numerous casts. The arteries were not thickened, nor the tension raised. Except for the uræmic condition there was nothing to suggest granular kidney. The treatment was active and of the ordinary kind, but the patient was not bled.

For two days the condition remained the same, the most prominent feature of the case being the extreme restlessness, which was most distressing. After this the symptoms rapidly subsided and by the end of the week had vanished entirely. The urine rapidly cleared up and became normal. On his discharge from the hospital he seemed quite well and showed no signs of the critical illness through which he had passed. There was no evidence of granular kidney.

I have seen one or two other cases of this kind in private. The only fatal case I have met with occurred in private, and no post-mortem examination could be obtained.

I am at a loss to explain the nature of these cases. Uræmia may set in without warning in granular kidney, but the signs of granular kidney are then obvious enough. It is generally fatal, and in the rare cases in which it is not the signs of granular kidney, of course, persist, and before long either another attack of uræmia or some other complication ends the story.

In the cases I am describing granular kidney may be excluded, for there were no signs of it before or after. Acute nephritis also will not explain them, for uræmia is not an early, least of all the first, symptom in acute nephritis, and convalescence is much more tedious and prolonged. The condition is obviously renal in origin, but it is not one that is met with in any of the recognised forms of kidney disease. I have wondered whether it was for cases of this kind that the old-fashioned term, which has now dropped out of our nomenclature—viz., acute congestion of the kidneys—was invented.

CHRONIC BRIGHT'S DISEASE—GRANULAR KIDNEY.

I now pass to the second or chronic form of Bright's disease, which we now generally speak of as granular kidney.

Granular kidney is a disease *sui generis*. It has signs and symptoms by which it can be recognised with precision, and definite pathological lesions of the kidney associated with them. It is true that it is often overlooked, chiefly because the symptoms are so variable and may point to any part of the body rather than to the kidney; but for all that the diagnosis is in most cases easy enough. The thickening of the radial artery felt when examining the pulse may be the first thing to arouse suspicion.

Examination of the urine shows the presence of albumin, and suspicion once aroused the correct diagnosis is soon made.

The morbid anatomy of granular kidney falls into two parts: (1) the renal; and (2) the cardio-vascular.

Renal Changes in Granular Kidney.

Of the renal changes there are only one or two points to which I wish to refer.

Granular kidney is a *bilateral affection*. Both kidneys are always involved, and to much the same extent. Consequently no unilateral affection belongs to the category of Bright's disease. For example, I recall a typical contracted kidney on the left side only, which was the result of the pressure of an abdominal aneurysm on the renal vessels. But there were none of the symptoms of granular kidney, the other kidney being sound. Similar cases are not uncommon as the result of impacted calculus.

The morbid process in the kidney is essentially an interstitial fibrosis, but to regard granular kidney as synonymous with *chronic interstitial nephritis*, even when bilateral, leads to confusion, for similar changes are met with as the result of other affections. Complicated as the structure of the kidney appears to be, its ultimate constitution is simple when it is unravelled and its essential units studied. The combinations of pathological changes, therefore, in the kidney are limited, so that similar anatomical changes do not prove identity of cause.

The Contracted White and Contracted Red Kidney.

The only other point upon which I desire to dwell in relation to the morbid anatomy of granular kidney is the distinction so commonly drawn between the white and the red contracted forms. The two forms, of course, exist, and are, perhaps, equally common in the post-mortem room. Still a classification by colour is very indefinite and unsatisfactory, for the results would differ with different observers.

What I desire to protest against is the theory implied that the difference of colour connotes a different origin; that the small white kidney is the later stage of the large white which had its origin in acute nephritis; and that the small red kidney is the result of other, so far unknown, causes.

Frerichs, to whose writings so much of the pathological confusion is due, asserted dogmatically, but without adducing a scrap of clinical evidence to prove his assertion, that granular kidney was in all cases the chronic and later stage of acute nephritis. His theory has been now so far modified as to limit this assertion to the contracted white form, but equally without evidence.

If the theory were true it should be readily capable of clinical proof, for there would be no difficulty: (1) in showing that the small white kidney gave a history of acute nephritis while the small red did not; and (2) in obtaining a series of cases in which the progress of the disease could be followed from the original attack of acute nephritis, through the chronic stages up to the ultimate condition of the contracted white kidney.

The figure (see next page) shows the theory in a diagrammatic form, and the dotted line where the evidence is lacking. The theory depends, not upon pathological possibilities, but upon clinical evidence, by which it must stand or fall, and the clinical facts are absolutely opposed to the theory. Wilks said that in the whole of his experience he had never seen a conclusive case, and my own experience has been the same.

If the acute and chronic forms of Bright's disease are identical it is remarkable that in their morbid anatomy, as well as in their clinical course, they have hardly a point in common.

Granular Kidney as a Cause of Acute Nephritis.

In dealing with the question of the relation of granular kidney to acute nephritis it must be borne in mind that granular kidney, so far from being the end results of acute nephritis, is itself not an uncommon predisposing cause of acute nephritis. Indeed, we may lay down the general proposition that as in children the chief cause of acute nephritis is an infection like scarlet fever or diphtheria, so in adults it is granular kidney. In other words, the adult gets his attack of acute nephritis because his kidneys are already unsound, that is, in most cases, granular.

The distinction drawn between the small white and the small red kidney is not established by clinical evidence, and this false theory by suggesting a connexion which does not exist hampers progress.

The Cardio-vascular Changes.

I should prefer to call them arterial, for the cardiac changes I regard as in the main consecutive or secondary. Here, again, in our classification of arterial changes we must rely mainly upon clinical and not purely anatomical criteria.

Putting aside the acute, for the most part infective, lesions commonly described as acute arteritis, we find that the chronic forms fall into two well-defined groups: (1) those associated with advancing years, which are commonly called atheroma; and (2) those connected with granular kidney, met with at a much earlier period of life. Syphilitic affections are local, though they may be multiple, and do not require to be considered in this connexion.

Atheroma, though widespread, is not universal. It affects the large vessels, notably the aorta and main trunks, and among the smaller vessels those of the brain and heart especially. It may also affect the renal vessels and lead to degenerative changes in the kidney.

In *granular kidney* the arterial changes are universal and involve all the arteries throughout the body, especially the middle-sized and smaller vessels. Though associated with degenerative changes, it is largely muscular hypertrophy, at any rate in the early stages, as the effect of nitrite of amyl shows.

As age advances the two conditions may be associated, but to suggest the use of the term "athero-sclerosis" is to confuse together two lesions which should be kept distinct. Atheroma is the recognised term for the one. It is to be regretted that there is no accepted term for the other. Arterio-sclerosis, which is sometimes used, is the mere translation of "thickening of arteries," and is a general term which covers both forms.

The difficulty is still further increased by the fact that while the one form, atheroma, presents more or less definite pathological changes, there is no agreement yet as to the exact nature of the

pathological changes in the other; but, as I have said, we must not expect pathology by itself to settle a question which is largely clinical.

Besides these two forms there is a third general arterial change, which perhaps ought rather to be regarded as physiological. I refer to the thickening of the arteries which is often observed in healthy young men of great physical power—e.g., in athletes in training, especially gymnasts and oarsmen. In them the arteries seem to hypertrophy just as the heart does. The condition in both heart and arteries is transient and passes off as the need for it disappears. It occasionally raises questions of clinical importance, so that it should be better known than it appears to be. I have not infrequently been consulted by young athletes in the height of physical fitness who have been alarmed by being told that their arteries were thick and that they might have kidney disease.

Clinically the significance of arterial thickening varies with age. Thus in elderly persons it may be the simple common degeneration due to advancing age. In early middle life its significance is much graver, and the suspicion is at once raised of granular kidney—a suspicion which becomes greater the younger the patient is—for granular kidney occurs, as is well known, in the quite young, even in small children, and in them, too, arterial thickening may be well marked.

Arterial Tension.

From arterial thickening it is natural to turn to arterial tension. The blood pressure is generally high in granular kidney and may be well over 200 mm., but there is often no distinction drawn between the systolic and diastolic pressure. The systolic depends largely upon the force of the heart. It is the diastolic that it is most important to determine, and this is where the difficulty lies in the absence of any reliable apparatus. The educated finger is often a far better guide than any instrument. It is, no doubt, the fact that the diastolic pressure is markedly raised as well as the systolic.

The pressure having been high it may fall, even below the normal. Such a fall is an indication that the patient is not so well. It were better for a patient not to have granular kidney, but having it, it is best that the pressure should be raised. The pressure cannot be materially reduced without the general health suffering, and it is not until the pressure has risen again to the former height that the patient begins to feel in his usual health.

The rise of blood pressure is, as a rule, persistent, but it may vary to some extent, being higher at one time than another. What I desire to draw attention to is the fact which is not generally known, that, in the later stages especially these oscillations are frequent, and may recur so rapidly as almost to deserve the name of waves. While the finger is resting on the pulse these waves may often be clearly observed if watched for, and the character of the pulse may be felt to change even in consecutive half-minutes. I have often tried to obtain tracings to demonstrate these changes, but hitherto without success. I am inclined to regard these variations as vaso-motor in origin rather than cardiac.

Hyperpiesis.

High tension is not necessarily of renal origin. For these cases Clifford Allbutt has suggested the name "hyperpiesis," and it is well to have a term to describe them by, for they constitute a definite clinical group of great interest, though I doubt if

they are as common as they are sometimes thought to be.

The condition produces the same secondary effects upon the heart as are the result of granular kidney, and no doubt in the end may lead to arterial degeneration, so that cardiac failure or cerebral lesions may develop in time. Yet there is no albuminuria, and where a post-mortem examination has been made no kidney lesions have been found. In some persons this raised pressure seems to be their normal state. They are usually of robust, full habit, of great energy and powers of work, both mental and physical, and they live literally at high pressure and without that high pressure they cannot live the life which seems natural to them and which they enjoy. To attempt by active means to reduce that pressure has generally little, if any, effect on the pressure, but it succeeds in making the patient ill and miserable.

Many years ago Mahomed described what he called the pre-albuminuric stage of chronic Bright's disease, cases in which the blood pressure was high, but in which albuminuria or other signs of renal disease were absent. Some of them were probably cases of hyperpiesis. Mahomed, however, assumed that the high pressure was the precursor of renal disease, but the clinical evidence he adduced did not prove his theory.

The Relation of Arterial Thickening, High Tension, and Kidney Lesion to One Another.

Given the three factors in granular kidney—the arterial thickening, the raised blood pressure, and the kidney lesion—the question of the relation between them has given rise to prolonged controversy.

Is the arterial thickening the cause or consequence of the high pressure? Do they stand in any direct relation to the renal lesion? Or are the three factors coördinate results of some general, and so far undetected, morbid state? We know that there are cases of high arterial pressure without arterial change or renal lesion, and cases have been described of granular kidney without arterial change or high pressure.

My own belief is that, so far as granular kidney is concerned, the primary change is renal, that the raised arterial tension is the result of the renal lesion, and the arterial changes are the consequence of that, the heart changes being secondary and consequent on the arterial. The cause of the primary renal disease is still unknown. One thing seems abundantly clear—that these problems can only be solved by clinical observation.

Albuminuria.

The amount of albumin in the urine in granular kidney is as a rule small, but it may be considerable, even as much as a half or more. The more important fact is that it may vary from time to time in the same case. Though small at one time it may be large in another. It may even vanish altogether for a time for days or even weeks.

Albuminuria is a symptom, and no diagnosis should be made upon a single symptom. Thus in young persons the question of physiological albuminuria would arise, and in the absence of all other symptoms and signs would probably be the correct diagnosis. Any other sign, especially thickening of the arteries, would render its significance more serious, though even then in a young athlete the question of the thickening being a physiological hypertrophy would have to be considered, especially as in such cases the albuminuria itself might be the result of the muscular effort.

The subject of physiological albuminuria cannot be dealt with in this communication, but it may be interesting to observe in this connexion that the same variations in the albuminuria which has given rise to the various names given to it—viz., cyclic, postural, dietetic, orthostatic, &c.—may be all observed in the convalescent stages of acute nephritis, so that they do not necessarily exclude a renal origin.

The only other remark I would here interpolate is that where albuminuria persists long after an attack of acute nephritis, so that it is in all probability due to incomplete resolution in the kidney, it does not follow, as seems to be so frequently assumed, that the whole kidney is left in a stage of incomplete resolution, still less the whole of both kidneys. It may be, and it certainly is the fact in many cases, that while the great mass of the kidneys on both sides has been restored to perfect health some small part has not, and this little patch of permanent mischief may be quite sufficient to account for the albumin found.

The Ophthalmoscopic Changes.

These I propose to deal with a little more in detail, because I think their significance is not as fully recognised as it ought to be. Yet some of them are pathognomonic, and frequently make a diagnosis certain which without them might remain in doubt. The changes are: (1) silver-wire arteries; (2) pressure on the veins; (3) hæmorrhages; and (4) albuminuric retinitis.

Changes in Retinal Arteries and Veins.

Silver-wire arteries I consider, when well marked, pathognomonic, for though the retinal arteries may show a broad white central streak in some other conditions, especially in the graver forms of anæmia, it never has that peculiar metallic lustre which makes the name so appropriate. Moreover, it is not seen with the other forms of arterial thickening—for example, with atheroma, perhaps for one good reason that atheroma does not attack, so far as I know, the retinal arteries. It is not, however, constant, for it may be absent in otherwise well-marked cases of granular kidney, and is not necessarily seen even when albuminuric retinitis is well marked. Several arteries may show the silver streak, but it often happens that it is well marked in only one or two of them, but in every case it is equally significant.

Closely associated with silver arteries is the *compression of the veins* where the arteries cross them, and their consequent distension on the distal side. This is an inconstant sign and therefore not of the same importance, for it may be absent when the silver streak is well marked.

Tortuosity of arteries is sometimes seen and may be so extreme as to resemble small aneurysms. But tortuosity of any kind is not common, and extreme tortuosity such as that very rare indeed. Some of the most marked cases of tortuous retinal arteries I have seen have not been in granular kidney cases at all.

Retinal Hæmorrhages.

These vary greatly in size, number, shape, and distribution. They may be flame-shaped or like the form of irregular blotches. The latter have their favourite seat in or above the yellow spot. The former lie nearer the disc, extending radially from it as a centre. Of themselves they are not characteristic, but in granular kidney they do not occur without other more definite retinal changes.

The smaller ones may resolve and completely disappear, and even large ones may leave but little trace behind.

If small they may be numerous, and yet affect the sight but little. Much will depend upon the seat, for on the yellow spot even a small hæmorrhage may, of course, affect vision seriously. Sometimes they lead to peculiar ocular symptoms, as in one case which I recall, in which with quite a few small hæmorrhages the patient in certain positions of the eyes saw all things green.

Albuminuric Retinitis.

This is the most important of all the retinal changes, but the most curiously contradictory statements are made about it by different authorities, the reason being that there are two forms which are not generally distinguished from one another as they ought to be. The two forms, to which I drew attention now many years ago, I endeavoured to distinguish by the names of exsudative and degenerative.

The *exsudative* form is similar to that seen in ordinary optic neuritis, such, for instance, as may be associated with cerebral tumour, with which I have more than once seen the diagnosis confused. This form is not rare in acute nephritis, and may completely resolve as the acute nephritis gets well. In granular kidney it is, of course, except in the rarest instances, persistent, and it is a sign that the end is not far off.

The *degenerative* form consists of white glistening patches, bright as cholesterin crystals or fish-scales. They are found for the most part round the yellow spot, but not infrequently in other parts of the retina. They may be quite tiny and need most careful looking for, otherwise they might be easily missed. In their most striking form (the cartwheel form) they occur as long, spoke-like streaks radiating from the yellow spot, or they run together into irregular areas of considerable size. In all cases alike, even where the spots are so tiny, this degenerative form is pathognomonic, for nothing like it is seen in any other disease than granular kidney. Although what have been also called white patches occur in the exsudative form, whether in connexion with granular kidney or some other disease, these are less defined in shape, dull grey in colour, and woolly in appearance, and in most cases easily distinguished from the sharply defined glistening white spots of the degenerative form.

In both forms alike the changes are bilateral and generally more or less symmetrical—that is to say, they occur in similar parts of the retina and to much the same degree in both eyes. To this there are some rare exceptions, in which the changes may be extreme on the one side, with very little on the other, but this is so unusual that it does not affect the general truth of the statement.

The two forms are quite distinct from one another, and the exsudative is not, as is often stated, the later stage of the degenerative. They may be associated together sometimes, but even then are essentially independent of one another, and if the exsudative form should resolve the degenerative form would persist.

Prognostic Significance of Retinal Changes.

It is generally stated that albuminuric retinitis is a late symptom in granular kidney, and that in most cases the patient has at the most not more than two years to live. This is true of the exsudative form; indeed, most cases die in a much shorter

time—within a few weeks it may be of its being discovered. But the exact duration even of this form is difficult to determine, for in most cases the eyes have not been examined until the vision has suffered, and then being found fully developed, it must have existed some time before it was discovered.

The degenerative form has a much longer lease of life. I myself know of cases of seven years' duration and more. If the eyes were examined carefully in a routine way in every case in which granular kidney was suspected the white spots would be detected much earlier, and the subsequent duration of life therefore found to be much longer than is usually stated.

The hæmorrhages even when large do not as such affect the prognosis in respect of the duration of life, except so far as they show rottenness of vessels, which may end in cerebral hæmorrhage.

I saw some years ago a very remarkable case. I have already recorded it, but on account of its special interest in relation to this part of my subject, I may be permitted to refer to it again.

The patient, about 36 years of age, met with a shooting accident in India and had to have his right eye removed. While recovering he suddenly had some fits, never having had any before. The urine was found loaded with albumin and casts, so that the diagnosis was made of acute uræmia, and he was treated accordingly. Shortly after this the remaining eye was examined and found to present the signs of acute optic neuritis which was thought to be characteristic. The diagnosis of granular kidney was made and a very gloomy prognosis given.

Shortly after his return to England I had the opportunity of seeing him. He seemed quite well. His arteries were not thickened, nor was the tension raised. There was no albumin in the urine. His only symptom was defective vision and a little headache if he tried to use his eyes. The ophthalmoscope showed what I regarded as quite characteristic and well-marked albuminuric retinitis. Mr. E. W. Brewerton saw the case with me and agreed that in spite of the absence of other signs the history of the case, together with the eye changes, made the diagnosis of granular kidney certain.

The patient remained under our observation for some months. Albumin was found in the urine while under my observation. Gradually the eye lesion resolved, and in the end the eye recovered completely, so that there was ultimately nothing to indicate that such acute mischief had ever been present. When I last heard of the patient he was well and in active work. He was careful not to overtask his eyes, but the sight of his one eye was excellent.

The optic neuritis was of the exsudative type, but being associated with many hæmorrhages and with white patches which closely resembled the degenerative form, it seemed fair to conclude that the acute symptoms had occurred in the course of granular kidney of date long antecedent to the accident. This view the subsequent course of the case did not confirm. On considering this case again in the light of those which I described in the early part of this lecture I cannot but think that it may have been one of those instances of acute uræmia of unknown origin, similar to that, for instance, of the primipara mentioned, the predisposing cause in his case being the gun accident as parturition was in her case.

My lecture has now reached its conclusion, and I trust it may have justified my choice of subject. Though 100 years have passed since Bright began his work some of the problems he propounded are still unsolved, while many others have evolved which our successors will have to find solutions for. Much as we already know, still more remains to be learnt.