localised, I felt that neither the Indian rhinoplastic or any of its modifications were indicated. Still less was the Taliacotian method.

The following procedure I adopted: The columella having happily remained unaffected, I was saved the trouble of making one. I commenced by making an incision a little to the inside of the right ala, and carried it across the extremity of the nose to a corresponding point on the left side. The incision extended as high up as the point corresponding to the lower margins of the nasal bones. This incision was passed through all the tissues into the anterior nares. We

J. B. Before operation

had thus a bridge of tissue attached at each side, and with the columella separated from the vomer and nasal bones. This bridge was then drawn downwards and kept in that position by a small ivory buttress, which separated it from the tissues of the upper part of the nose. The gap thus formed was somewhat lozenge-shaped, and to fill up this I dissected two triangular-shaped flaps, one from each side of

J. B. After operation.

the cheeks, with the bases above and the apices below, and these flaps were then turned downwards and inwards and their bases brought together in the middle line and carefully united by two or three points of suture of fine, carefully-asepticised silk. The upper margins of the transplanted flaps were also carefully sutured to the tissues above and the lower margins

to the bridge. The ivory buttress was left in for three days, until the edges of the flaps had become firmly united to the tissues above and below. The vitality of the triangular transplanted flaps was throughout satisfactory. In order to obliterate the defects caused by the detachment and transplantation of the flaps I performed a sliding plastic operation, which had the desired effect, and little or no cicatricial deformity on either cheek remained.

The cases applicable for such a procedure as that just described are, of course, exceptional; but in such a one it has, I think, great advantages over any of those ordinarily performed. The Indian rhinoplastic and its modifications are long and tedious in their performance and uncertain in their results; and the same may be said of the Taliacotian operation. These objections do not apply to the method described in the above case, which was done in a comparatively short space of time, was unattended with hæmorrhage of any moment, or the subsequent development of a disfiguring cicatrix.

REFERENCES.

¹ *The Works of that famous Chirurgion Ambroise Parey, London, 1649, p. 758.* ² *Clinical Society's Transactions*, vol. x, 1877, p. 1181. ³ *Dublin Journal of Medical Science*, May, 1882.

THE LETTSOMIAN LECTURES

ON

SOME CLINICAL ASPECTS OF GRANULAR KIDNEY.

Delivered before the Medical Society of London.

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LECTURE I.

THE invitation to deliver the Lettsomian Lectures before this ancient Society is a compliment which no one, and least of all myself, can fail to appreciate. It is one which 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.

Granular kidney is a disease of great importance on account of its frequency, a frequency which is by no means adequately recognised. *Post mortem* it is often discovered when not suspected. It is often in itself the cause of death, even of sudden death, and 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.

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).¹ Of these, 132 were in males and 84 in females, showing the frequency in males to be one third greater than that 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.

Ages.	Granular Kidney found in
10-20 ..	2.3 per cent
30 ...	3.0 "
40 ...	12.0 "
50 ...	38.5 "
60 ...	43.0 "
Above 60 ...	50.0 "

Nothing will better prove the importance of granular kidney than the following statistics obtained for me by Dr. Horderas,² 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.

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%
2. A concomitant cause of death in	19 cases=30%	2 cases=13.3%	21.6%
3. An accessory but doubtful cause of death in ...	6 cases=6.25%	2 cases=13.3%	9.77%
Totals	38 cases=56.25%	6 cases=40%	43.17%

Thus 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 10 death was due to hæmorrhage to which the interstitial nephritis may have directly or indirectly led. In 4 cases aneurysm of the aorta was present and its rupture was the cause of death. Of the others, in 1 there was hæmorrhage into the pons Varolii, in 1 pachymeningitis hæmorrhagica, and in the remaining 3, a ruptured aneurysm of the anterior communicating artery in 1 instance and of the Sylvian artery in 2, and the remaining case was one of hæmoptysis.

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 previously so clearly shown.

In 7 cases the cause of death was cardiac.

Acute endocarditis was found in	...	...	1 case.
" " with pericarditis in	...	...	1 "
Aortic incompetence in	...	...	3 "
Aneurysm of the heart in	...	...	1 "
Heart associated with atheroma of the coronary artery in ...	...	...	1 "

7 cases.

Of the remaining cases 3 had phthisis and 1 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, 8 of the heart, and 10 of the kidneys.

Sturges' 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.

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

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 them 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 $\frac{1}{2}$ 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 given in the St. Bartholomew's Hospital statistics 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 twelve 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.

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 the colour is referred.

None of these statements are, in my experience, quite correct; for small white kidneys are often 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 two forms certainly exist.

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 was 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.

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.

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.

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 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.

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.

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 white kidney passing into what may be described as a small white kidney, or even possibly ending in a small 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 does not occur. 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.

I have recently had 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 extensive fibrosis in the kidneys, though they were in neither case granular.

The first case, that of a woman, aged 29, appeared to be one of ordinary chronic parenchymatous nephritis, and so the kidneys appeared *post mortem*. I had the kidneys carefully examined 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.

The second case, that of a girl of 14 is a more remarkable one, for on the child's death after about twelve 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 they do 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 know of a woman who has had several attacks of parenchymatous nephritis in the course of thirteen years, and who has never at any time lost the albumen from the urine; yet now, at the end of thirteen years, her arteries are thin and her heart not hypertrophied; she appears in fair health, and her retinae 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, twenty-five 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, too, 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 any 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 see a patient hitherto believed to be healthy with the symptoms of acute parenchymatous nephritis, and yet for that patient to present 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 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.

In cases of granular kidney, therefore, 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.

It is evident from what has been said that it is only in a very small number of cases 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.

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

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 regarding the matter too much

from an anatomical, that is, pathological, instead of clinical point of view. Pathologically, of course, such 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.

I do not know that I should have spent so much time in discussing 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 distinction made between the two forms of granular kidney, the white and the red.

I now turn to the arteries. 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. Now, there are only two forms of general arterial change recognised in pathology, namely, atheroma and that connected with 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.

As to the nature of the vascular lesions in granular kidney 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.

So far as the hypertrophy of the arteries is concerned, it 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 therefore in the small peripheral arteries or capillaries.

If the changes in the vessels be 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 kind are described, but they are very rare.

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.

THE SYMPTOMS 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 definite 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 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, cardiovascular and renal. Speaking generally, the cardiovascular 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

rhage 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 frequently described as chronic and acute uræmia respectively. I should prefer to call them acute and chronic renal toxæmia. Both alike are to be connected with the wasting in the kidney and its consequent defective action.

The gradual and progressive wasting of the kidney is attended with the gradual and progressive development of the chronic forms of uræmia. Renal cachexia is the name that I should prefer to give to chronic uræmia. 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 consisted in a gradually increasing anæmia and asthenia, associated with various miscellaneous symptoms.

The symptoms are similar in kind, and differ from them 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.

The symptoms in all these cases are similar, but differ from those which are usually described as acute uræmia, and the difference is probably not one of degree only but of kind, so that I think they ought to be distinguished by different names; for the first I should 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.

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, that is, the disease is far advanced, and death may be near. The disease, however, must have commenced long before, perhaps years, so that even in these cases in middle life the onset of the disease is to be traced back, it may be, to quite early life.

Not only is the disease in many cases to be referred to early life, but it may be advanced and fatal even in quite early years. 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.

Guthrie has recorded several instances in small children. The following figures give the general age-distribution above 20 years.

Table of Age at Death.

Age.	Dickinson.	Fagge.	Bartels.*	Galabin.	St. Bartholomew's Hospital	Total.
About 20	1	—	4	2	3	10
20-30	17	—	4	6	15	42
30-40	38	18	9	12	25	102
40-50	73	39	4	19	59	189
50-60	55	36	7	21	56	175
60-70	43	24	5	16	36	124
Above 70	15	4	—	3	12	34

* One death at 18, one at 19.

† One death at 19, one at 20.

Table showing Age Distribution at the time of Death of 203 Cases at St. Bartholomew's Hospital.

20		20-30		30-40		40-50		50-60		60-70		70-80	
M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
3	—	6	9	11	14	33	26	42	14	27	9	7	5
3		15		25		59		56		36		12

Diagram constructed from the combined statistics given, showing the percentage age-distribution at time of death.

I propose to 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 EARLY STAGES: THE PHYSICAL SIGNS.

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? Or, if the arteries are 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 exhibition to-day, but this failing me, I have no fresh facts of my own to bring forward.

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. I show a case from the St. Bartholomew's Hospital Museum, in which the heart weighed 28 ounces.

In the early stages it is of very little assistance, because of the difficulty in diagnosing 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, is really valueless, for it will occur wherever the 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.

THICKENED ARTERIES.

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

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

This is not simply 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 even when the tension is low, as it may be in the later stages, the thickening of course 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. 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 granular kidney, and the effect of nitrate of amygdal upon it is the same.

We are thus driven to this conclusion, that if it is not an early indication of granular kidney, then 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 high-tension artery as rolling under the finger, but attributes this to high tension only. Really it is due to arterial thickening and high tension.

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 microscopical, as do Gunn's ophthalmoscopic, observations on the retinal arteries show the same thing.

HIGH TENSION.

In well-marked (that is, advanced) granular kidney the high-tension pulse as well as the thickened arteries are well recognised. The sphygmographic tracing is characteristic; it has a round or square top to the wave, 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 fulness 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; thus the long wave with its square or roundish 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 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. It may also, by diminishing the amount of blood driven into the arteries at each beat, reduce somewhat the tension, 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 still be easily made out, and is as characteristic as ever.

A persistently high tension, under ordinary conditions is of itself mischievous, but not so with granular kidney, paradoxical as this may seem. The patient is best without granular kidneys, but if the kidneys be granular it is better that the tension should be high rather than low; in other words, the patient is worse with a low tension. This explains the use of digitalis in such cases, which does so much good 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 by what has just been said, is not generally recognised, although 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 be felt to vary considerably even in very short spaces of time; for instance, even while the finger is placed upon 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 diagnosable 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 Broadbent³ and Dr. Goodhart⁴; and if we go back fifteen years, we come to a series of papers written on this subject by the late Dr. Mahomed.⁵ 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 view.

I do not think Mahomed's work has been estimated at its 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, there is general agreement, but opinions differ as to whether these results are to be referred to granular kidney or not. 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 a significant fact which 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 mentioned 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 so far 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 point. At any rate, a larger number of these cases can now be proved to be granular kidney than has been hitherto supposed.

REFERENCES.

¹ For these figures I am indebted to Mr. Woodbridge. They will be published *in extenso* in the *St. Barth. Hosp. Reports*. ² This paper will be published *in extenso*. The short abstract now given of it is of the nature of a preliminary report only. ³ BRITISH MEDICAL JOURNAL, August, 1883. ⁴ Bradshaw Lecture, 1885, BRITISH MEDICAL JOURNAL, ii, 327. ⁵ *Lancet*, January 11th, 1879, etc.

PROFESSOR VON ESMARCH has resigned the Chair of Surgery in the University of Kiel, in which he has been succeeded by Professor Helferich, late of Greifswald.

THE late Sir William Gray, shipbuilder, has left the sum of £2,000 to the West Hartlepool Hospital.

SOME UNCERTAINTIES IN THE DIAGNOSIS OF CEREBRAL TUMOUR.

By ERNEST SEPTIMUS REYNOLDS, M.D. LOND., F.R.C.P.,
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IN looking over the records of brain surgery one is struck by the very large proportion of cases in which no tumour was found at the operation. Thus in Starr's¹ list of 162 cases no tumour was found in 48; in Knapp's² list of 405 cases none in 92, and Bergmann³ only found a growth in 1 case out of 6. Besides these there are many isolated cases of the same kind scattered through literature. It seems therefore to be important and interesting to inquire into the causes of these deficiencies.

Uncertainties in the diagnosis of brain tumour may be grouped into two large classes. (A.) When no tumour exists, but other diseases are mistaken for it. (B.) When a tumour is present, but (a) the symptoms are ascribed to some other disease; (b) there is a mistake in localisation; (c) there is uncertainty in the nature of the tumour.

A. DISEASES WHICH MAY SIMULATE BRAIN TUMOUR.

1. *Chlorosis*.—Very rarely optic neuritis, generally of rapid onset, is present in this disease; and if it is associated with intense headache and perhaps with hysterical motor or sensory symptoms, a mistake in diagnosis may easily occur.

2. *Uræmia* with intense headache, optic neuritis, convulsions, and coma may simulate brain tumour, especially if the convulsions are unilateral in character. The unilateral form of uræmic convulsion, without cerebral hæmorrhage, is spoken of by Sir William Broadbent in his book on the pulse, and I remember seeing a case of the kind at the Manchester Royal Infirmary (under the care of Dr. Graham Steele) some years ago. The character of the optic neuritis, together with the history and symptoms of Bright's disease, should of course make the diagnosis clear.

3. *Chronic lead poisoning*, if associated with lead encephalopathy, with convulsions, delirium, sometimes acute mania, and coma with optic neuritis and severe headache, may suggest the presence of brain tumour. This idea may be strengthened if hemianæsthesia is present, and particularly if there is any paralysis of the cranial nerves. Buzzard (quoted by Gowers) has described paralysis of the third cranial nerve in lead poisoning; and I have at present under my care a man suffering from chronic plumbism with gout and paralysis of both sixth cranial nerves; a few weeks ago the right nerve was totally paralysed, the left slightly so; this has now almost recovered, so that he has no apparent strabismus, but there is double vision when strain is put on to either of the external recti.

4. *Hysteria* may of course simulate brain tumour, particularly when there is headache, vomiting, convergent strabismus, and various motor and sensory disturbances.

5. So-called *reflex epilepsy*, in which the convulsions are unilateral, is sometimes difficult to distinguish from symptoms due to coarse irritation of the cortex of the opposite side. These convulsions may be caused by irritation of the dura mater due to old injury, by subdural hæmatoma, or by irritation (in dogs) of the inner surface of the exposed dura mater (Franck quoted by Mills⁴). In many of these cases the convulsions are on the same side of the body as the irritation, and are considered to be due not to irritation of the cortex but to irritation of the fifth cranial nerve supplying the dura mater, and especially distributed to its inner surface. Similarly reflex epilepsy, unilateral in character, may be set up by pressure on old scars in the region of the fifth cranial nerve, or by any peripheral irritation of the fifth nerve as from lesions of the ear, eye, nose, teeth, face, or scalp. Injuries of nerves or an isolated fibroma on a nerve in other parts of the body have been known to set up these unilateral reflex epilepsies.

6. Many *anomalous cases* have been reported from time to time in which there were symptoms apparently due to coarse irritation of the brain cortex, but in which the patients have either recovered without operation or after an operation in which nothing was found. Thus Pearce Gould⁵ reported a