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ORIGINAL ARTICLES.

BRIGHT'S DISEASE, HYPERPIESIS, AND HYPERPIESIA.*

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I THOUGHT it might be suitable on this occasion to make some observations on one of the most baffling problems of medicine and pathology, viz., the relations existing between the different members of a threefold partnership which often comes under notice—kidney disease, high blood pressure, and arterial changes. The connexion between high pressure and arterial changes is comparatively easy to understand, though it was at one time misinterpreted; but the nature of the relationship between kidneys and high pressure remains obscure, in spite of the enormous amount of research which has been devoted, during many years, to the elucidation of the mystery.

I do not profess to add anything to what is already known. My aim is rather to discuss the subject in your company, so that our knowledge of the facts will be as accurate and up

* Honorary President's Address to the Glasgow Southern Medical Society, 10th January, 1929. A few alterations have been made in the paper since it was submitted to the Society.

to date as circumstances will permit. But no attempt can be made to mention all the theories or arguments which one comes across in the literature of the subject.

As I shall often have occasion to speak of arteriosclerosis, I must at the outset indicate the sense in which the term is used in this communication. The literal meaning of the word, of course, is arterial hardening, but there are different kinds of hardening of arteries, and different writers use the word arteriosclerosis in very different senses. Thus, Sir Clifford Allbutt recognized three classes of arteriosclerosis, viz., (1) high pressure arteriosclerosis (observed in hyperpiesia and in certain forms of renal disease); (2) involutionary or decrescent (senile); and (3) infectious or toxic (observed in enteric, syphilis, diabetes, lead poisoning, &c.). In his posthumous little treatise on *Arteriosclerosis* (published in 1925, the year of his death) he seems inclined to use Marchand's term, atherosclerosis, in preference to Lobstein's term, arteriosclerosis.

Professor Robert Muir, on the other hand, uses the term arteriosclerosis to indicate a hardening of the arteries due to increase of the fibrous tissue of the arterial wall, which is usually accompanied or preceded by hypertrophy of the muscular and elastic tissues of the wall. This development is generally due to excessive blood pressure, and this excess of blood pressure may be secondary to kidney disease or may be primary. This high pressure arteriosclerosis, it will be noted, corresponds to the first of Allbutt's three classes. Arteriosclerosis used in this sense of the word is, of course, an arbitrary and not perfectly satisfactory expression. For instance, it does not include calcification of the media, which gives rise to very marked hardening of arteries. Nevertheless, it will be convenient, on this occasion, to follow Muir's terminology.

What, then, is arteriosclerosis? It is a hypertrophy which the arterial system undergoes, to the best of its ability, under the pressure of excessive work; the heart, which is similarly involved, likewise undergoing hypertrophy. The muscular hypertrophy in the arteries is particularly seen in the media, but it also involves the longitudinal muscle cells of the intima. The elastic tissue hypertrophy is most marked in the intima

and adventitia. In course of time, however, this compensatory process begins to fail. The hypertrophied tissue degenerates and disappears, particularly in the media, and becomes replaced by connective tissue. At the same time the intima becomes thickened by increase of connective tissue. Thus the compensatory hypertrophy gives place in course of time to fibrosis, with thickening of another kind, which is of inferior functional value. Moreover, the tissues which have thus deteriorated may become the seat of further changes of more advanced degenerative character.

Of arteriosclerosis and its associated cardiac hypertrophy there are two well recognized causes—one renal, the other non-renal. In connexion with Bright's disease the renal variety often comes under observation.

Bright's Disease.

Passing over, with a mere mention, the observation of Saliceto in 1476 [1] that dropsy, scanty urine, and hardened kidneys might be found in association, and the observation by Cruickshank in 1798,[2] Wells in 1811,[3] and Blackall in 1813,[4] that dropsy and albuminous urine might go together, we come to Richard Bright's great discovery in 1827 that when a case of dropsy attended by coagulable urine is examined after death, some obvious derangement of the kidneys will generally be recognizable.[5] The characteristic features of Bright's disease then were these three—dropsy, coagulable urine, and structural changes in the kidneys. Nine years later, Bright himself showed that kidney disease with albuminous urine might run its course without dropsy at any time, and that fatal cases might be met with where anasarca, after being present for a time, had entirely disappeared.[6] The plates published in 1827 in his *Reports of Medical Cases* show that Bright was familiar, anatomically, with a large, soft, white kidney, and with a small hard, granulated kidney. He was also familiar, both clinically and anatomically, with the large congested kidney of febrile or inflammatory dropsy, or what we now call acute nephritis.

In the second half of last century three varieties of Bright's disease were recognized, one acute and two chronic—the chronic varieties corresponding to the large white and the

small red kidney. This was the teaching of Sir George Johnson, Sir Thomas Watson,[7] Sir William Roberts,[8] and my old teacher and chief, Sir William T. Gairdner, as well as of some leading German authorities. Many in Germany, however, held that the large white kidney would, if the patient survived, become red, granulated, and contracted.[9]

Now, Johnson and Roberts knew well that the large white kidney does occasionally become atrophic and granular, and Roberts pointed out that this change in structure is often accompanied by a corresponding change in clinical features, the symptoms then coming to resemble those of the small red kidney. Moreover, Johnson described the kidney which became granular and contracted after being enlarged, as being paler, firmer, and more coarsely granular than the small red kidney. He remarked, too, that it was often the sequel of the acute disease, though sometimes insidious. Thirty years earlier Sir Thomas Watson had noted that chronic Bright's disease might be met with in persons who had previously suffered and apparently recovered from an attack of febrile dropsy, and he suggested that the recovery had been incomplete in such cases. Now, this particular variety of Bright's disease —which, as these physicians pointed out, may develop, anatomically speaking, through atrophic changes in a large white kidney, or, clinically speaking, as the sequel of an acute attack (either directly or after a long period of apparently perfect health), or may develop insidiously—is generally recognized nowadays by the distinctive name of secondary, or better, secondarily contracted kidney. It is also called the small white kidney, though it may be neither small nor white. Both clinically and in its gross anatomy it may be regarded as intermediate in character between the large white and the small red kidney.

It is interesting to speculate why the early observers like Johnson did not raise the comparatively pale, secondarily contracted kidney to the dignity of a distinct variety. It was certainly not because they did not know about it. It is, indeed, possible that there has been some change in the prevailing types of Bright's disease since these men wrote. Thus, whereas Roberts said in 1865[10] that " these two types —the smooth large white kidney, and the granular red con-

tracted kidney—constitute the vast majority of cases of Bright's disease," I suspect that in this country, at anyrate, the small white kidney has been more common in recent years, in hospital practice, than the two other types put together. Of course, gout is rare among hospital patients in Scotland, and it is likely enough that the small red kidney, or so-called gouty kidney, has become less frequent even in England, through a diminished frequency of gout, lead poisoning, and other supposed causes. Moreover, in earlier years the tendency would be to be impressed by the contrast between the large white and the small red kidney, and to assign kidneys showing even minor degrees of granularity or shrinking to the small red group. Modern research shows that without a microscopic examination it may be impossible to say whether a granular contracted kidney is of primary or of secondary type, and, further, that the two types may be combined.

It should be noted that at the time when Roberts published his treatise in 1865, it was held by leading authorities in Germany, and the view had apparently gained common assent there, that the large white kidney would, if the patient survived, eventually become red and contracted; while in Britain, on the other hand, the evidence brought forward by Johnson, Wilks, and Dickinson was steadily gaining ground for the opposite and more correct view, that the small red kidney is not a more advanced stage of the large white kidney.

At this stage, then, we can recognize four types of Bright's disease—(1) acute nephritis; (2) the large white kidney; (3) the small white, or secondarily contracted kidney; (4) the small red, or primarily contracted kidney. This classification is very good in its way, but it does not please everyone, and it may be taken as certain that no classification of Bright's disease will ever be devised which will give universal satisfaction. This unfortunate state of matters is easily intelligible. In the first place, the well-defined types are connected with one another by intermediate cases. In the second place, two varieties may be combined in one patient, since an acute or subacute attack may be superimposed on chronic disease, or a case beginning as one variety may become transformed into another. In the third place, different workers look at the matter, naturally enough, from different points of view.

According to their individual temperaments, or their special lines of study, the basis of classification which they adopt may be clinical, or anatomical, or etiological. Now, in the present state of our knowledge it is impossible to make these different standards fit into one another. And so, while we have some classifications which are profuse in divisions and subdivisions, we have others in which this process is reduced almost to a minimum, though without exact correspondence to Frerichs's opinion that all Bright's disease is one and inflammatory, and that the three forms of anatomical change which he recognized (hyperæmia, exudation, and degeneration and atrophy) are simply stages of the same fundamental process. Nevertheless, classifications may be both interesting and useful. Each gives us in a condensed form the views held by the man who drew it up, and if perchance our own experience coincides with his, we may flatter ourselves with the reflection that our opinions on the subject must be correct, since such an eminent fellow-worker agrees with them.

Let me now call your attention to some of the lines upon which classification may reasonably proceed.

Starting from the fourfold division already referred to (acute, large white, small white, small red), we may subdivide according to the particular element of the kidney which is principally involved — glomerular, tubular, interstitial or vascular. It must, of course, be recognized that acute inflammation cannot be strictly confined to one of these tissue elements, but it is possible for one of them to be the part specially attacked in the first place, and if the disease persists, it may spread to other parts.

1. Of the acute varieties, there is *glomerulo-nephritis* as met with in scarlet fever and other infections, where the Malpighian bodies are chiefly involved; *catarrhal nephritis* where the tubules are specially involved; and *interstitial nephritis*, an uncommon form met with in scarlatina, where the interstitial tissue is mainly affected. But if the disease continues for a time, it may spread, and so a glomerulo-nephritis may become a *glomerulo-tubular nephritis* with enlargement; and still later, through added interstitial changes, it may develop into the *secondarily contracted kidney*. The *epidemic* or *trench*

nephritis which attacked the troops in the European war was in its early stage a glomerulo-nephritis, and in its fully developed form a glomerulo-tubular nephritis. From ordinary glomerulo-nephritis we may detach the special form known as *embolic nephritis*. In the former all the glomeruli are affected, but in the latter, which may occur in septic infections, such as ulcerative endocarditis, the glomeruli are only involved here and there, in an irregular way, as a result of plugs of thrombus and organisms settling in their vessels. The *hæmorrhagic nephritis* which occurs in connexion with tonsillitis, particularly in children, is possibly of embolic origin. In *tubular, desquamative,* or *catarrhal nephritis* it is the epithelium of the tubules which is chiefly involved. This is due to the influence of various toxins, and in many cases the changes are of a degenerative character, without any inflammatory reaction in the connective tissues; and accordingly some authorities, especially in Germany and the United States, follow Friedrich Müller and style this condition *nephrosis* so as to avoid the termination "itis," which implies inflammation.* Nephrosis is met with in acute infections, pregnancy, and acute yellow atrophy of the liver, and in poisoning by turpentine, cantharides, and numerous metallic salts. The lesion in pure nephrosis is a toxic-degenerative disease of the tubules, but in some instances inflammatory reaction may follow and thus a variety of genuine acute nephritis will be produced. Some recent writers are of the opinion that the nephrosis or toxæmic kidney of pregnancy is, in part at least, a glomerulo-nephrosis.[11] Nephrosis is characterized clinically by the presence of two striking features, viz., marked œdema and marked albuminuria, while the other well-known phenomena of Bright's disease, such as hæmaturia, nitrogen retention, increase of blood pressure, and cardiac hypertrophy are all absent. The presence of hæmaturia and cardiovascular

* Müller suggested in 1905 that for such cases the word nephrosis should be used instead of nephritis, or in German Nierenerkrankung instead of Nierenentzündung. Nierenerkrankung corresponds nowadays, not to nephrosis, but to nephropathy, as used by Dr. Barker. Both nephrosis, as now understood, and nephritis are varieties of nephropathy. Müller noted that the terms hydronephrosis and pyonephrosis were already allotted to other diseases, but he considered them unsatisfactory. (*Verhandl. d. deut. path. Gesellschaft*, 1905, S. 65).

changes would point to actual nephritis. In these cases of nephrosis with dropsy and intense albuminuria there is often an excess of cholesterol in the blood, and the renal tubules are the seat of lipoid degeneration, whence the disease is sometimes spoken of as *lipoid nephrosis*. It is possible that the so-called myelin kidney, which is characterized by accumulations of doubly refracting fat in the glomeruli and tubules and even more in the interstitial tissue, is an extreme development of this lipoid degeneration. It would appear, however, that while pure cases of nephrosis do occur, the condition is often accompanied by evidence of glomerulo-nephritis, past or present, and in these circumstances either the nephrosis or the glomerulitis may have come first, and been subsequently complicated by the addition of the other. Many workers, however, do not accept the theory of nephrosis, even though some of them employ the expression "toxæmic kidney" to signify the same thing. They would say that all forms of Bright's disease are of toxic origin, and that degeneration is an inflammatory phenomenon which may or may not be followed by tissue reaction. As to the occurrence of pure nephrosis in the sense of a merely degenerative alteration in the tubular epithelium, it is noteworthy that Professor John S. Dunn [12] states that though the glomeruli when examined only by ordinary staining may appear perfectly normal, nevertheless, in his experience, a close examination of a large number always reveals some stigma of an antecedent glomerulitis. Dr. Elwyn, of New York, likewise, while admitting the occurrence of pure nephrosis, emphasizes the frequency with which it is an accompaniment or sequel of glomerulo-nephritis, or is associated with amyloid disease; and in his view the first step towards the evolution of nephrosis is the escape of albumen through previous damage to the glomerular and capsular epithelium.[13] Still more recently, Dr. Henry A. Christian, of Boston, has lent the weight of his authority to the view that nephrosis is "a form of chronic nephritis (Bright's disease)." [14]

One can usually, with care, recognize clinically a case of acute nephritis, but the results of repeated examination and the course of events may ultimately show that the attack is really an implantation upon underlying chronic disease.

2. The *large white kidney*, known also as *subacute nephritis*, *chronic tubal nephritis*, and *chronic parenchymatous nephritis*, may be subacute or chronic in its course, and may in its beginning be either a glomerulo-nephritis or a tubal (or catarrhal) nephritis. It is often the sequel of an acute nephritis (usually glomerular, occasionally tubal or catarrhal), but it may set in insidiously without obvious cause. It is sometimes called the " hydræmic " or " hydropigenous " form of nephritis, because dropsy is a marked feature. Albuminuria also is well marked. Along with the dropsy there is a diminution of urinary chlorides, but why this should be is a matter of controversy. According to one theory, it is because of the diminished power of the kidneys to excrete chlorides. According to another theory, the retention of chlorides is secondary to diminished power of the kidneys to excrete water. A third theory is that there is increased permeability of the capillaries and that the chlorides are thus diverted, along with the excess of water, into the tissues. Some of these cases belong to the nephrosis type, and it is to them in particular that the remarks already quoted from Dunn apply. When this disease proves fatal, it is generally through some intercurrent infection.

Other cases of large white kidney are quite definitely inflammatory, with marked changes in the glomeruli and tubules, and in these there may be some tendency to uræmia and cardiac hypertrophy.

3. The *small white kidney*, on the other hand, is not associated with œdema unless through cardiac failure. Its leading characteristics, in addition to the absence of dropsy, are slight albuminuria, nitrogen retention, low specific gravity of the urine, increased blood pressure, cardiovascular changes, and a tendency to uræmia. This type is sometimes called " azotæmic " because of the nitrogen retention in the blood, and it is also sometimes known as *chronic interstitial nephritis*. The condition is a chronic glomerulo-nephritis. It may occasionally develop out of the acute or subacute form, but very often the patient comes under observation only when the disease has entered upon its terminal phase, or when an acute or subacute exacerbation takes place. Sometimes there is a

history of one or more acute attacks which seemed to pass off completely, leaving the patient in good health for many years. Though there may be a moderate degree of increased blood pressure and cardiovascular hypertrophy, the terminal stage is usually reached while the patient is still in the prime of life, and death is not so likely to be due to cerebral hæmorrhage or cardiac failure as to uræmia or some intercurrent infection.

4. The *small red kidney*, called also the *gouty*, *granular*, *cirrhotic*, *primarily contracted*, and *genuine contracted* or *arteriosclerotic kidney*, is also described as *primary fibrosis of the kidney*, *primary chronic interstitial nephritis*, and (by Dr. Barker) [15] *arteriolar nephropathy*. Gout and lead poisoning are recognized causes, and high living and hereditary tendency have probably some influence, but the etiology is really very obscure. This disease of the kidney gives rise to, or at anyrate becomes associated with, high blood pressure and cardiovascular hypertrophy.

(At this stage it is well to detach *two other forms of renal fibrosis* as distinct from this primary fibrosis or gouty kidney. (*a*) In the first place, in some high-pressure cases with generalized arteriosclerosis, small portions of kidney substance become starved of their blood supply and undergo fibrosis, without causing any noteworthy shrinking of the organ. Here the high pressure is the first departure from the normal and causes the arteriosclerosis. This kidney is appropriately called *arteriosclerotic*. (b) In the second place, in old people, as a consequence of atheroma of the renal arteries, and often without increased blood pressure, there may be well-marked atrophy of the kidneys, distributed in an irregular manner, and due as in the other case to starvation of blood supply through the arterial changes. This *senile contracted* kidney is sometimes very small.)

In the *granular*, *gouty*, or *small red kidney*, arterial disease of a peculiar severity, as Allbutt puts it, is a primary and invariable feature. This involves the interlobular and afferent arteries of the kidneys and often, too, the splenic, pancreatic, and cerebral arteries, but it spares the intimate vascular network of the myocardium, liver, and skeletal muscles, even

though larger trunks, such as the coronaries, may be greatly altered.

The disease of the arterioles in the kidneys causes narrowing of their lumen, amounting, it may be, to complete occlusion, and this leads to sclerosis of the glomeruli and loss of function of their tubules. Muir thinks that "the appearances suggest the action of some mild poison or irritant on a kidney and its vessels," and Allbutt likewise regards the granular kidney as "a slow irritative process." There is reason to suspect that the poison attacks other tissue elements in the kidneys, here and there, in addition to the blood-vessels, so that the damage to those other elements is not entirely due to deprivation of blood. The other striking feature of this disease is the early and great rise of blood pressure, with great hypertrophy of the left ventricle. The excessive pressure leads in course of time to arteriosclerosis, which may involve the larger vessels as well as the smaller, just as in a case of non-renal hypertension. Whether the high pressure is immediately related to loss of function of the glomeruli, or of the parenchyma, or of the renal tissue as a whole, or whether it may be due to the poison which causes the change in the arterioles, is not clear. Some would fix their suspicions on the glomeruli.

In his posthumous essay on *Arteriosclerosis* (1925, p. 17), Allbutt says :—"It seems probable that the primary contracted kidney is itself a long protracted result of an infection, such as of scarlet fever, diphtheria, streptococcal or pneumococcal sepsis, and so forth, creeping forward in latency for years after an apparent recovery from the acute attack." He also speaks of the infective cause damaging both arterioles and glandular elements in the kidney. This history and description, it will be observed, are remarkably like what one is prepared to meet with in connexion with the small white kidney as distinguished from the small red kidney. In a case of small red kidney there is usually no history of an antecedent acute attack, and the patient usually comes under observation later in life than in the case of the small white kidney. It is true that Dunn has pointed out that some kidneys which seem to be characteristically small red kidneys do on microscopic examination reveal evidence of old focal disease which might conceivably have caused or at anyrate initiated the

fibrosis. But Muir thinks that in most of these cases the fibrosis came first and the inflammation later. In the typical granular or small red kidney the arteriolar change is so early and so striking as to mark the condition off pretty completely from the typical small white kidney. On this question there is an extraordinary diversity of opinion among pathologists, but it may be mentioned that Lorrain Smith and Dunn regard the small red kidney as a product of old focal glomerulitis, not recognized at the time, and sparing many of the renal units to undergo compensatory hypertrophy and carry on the function of the kidneys for many years; while they regard the small white kidney as the result of a diffuse glomerulitis involving practically all the glomeruli.

To sum up the history of the small red kidney, it may be said that a poison—known, it may be, or suspected, or entirely unknown, either imported from without, or produced by infection or by perverted metabolism within the body—causes disease of the arterioles of various organs, including the kidneys, and that the arteriolar disease of the kidneys leads to such changes in the structure and functions of the glomeruli and tubules as to bring about a great increase of blood pressure. The destruction of the secreting elements may lead to death by uræmia; while the high pressure and resulting cardio-vascular changes may lead to death by cardiac failure or cerebral hæmorrhage.

Before leaving the subject of classification, it may be noted that Professor Hugh MacLean keeps to the original division of Bright's disease into three varieties, one acute and two chronic, but he follows the lead of French workers and distinguishes the two chronic varieties, not on the ground of difference in the physical characters of the kidneys, but on the basis of defects of function, as recognized clinically. The more common by far is the *azotæmic type* (interstitial nephritis), in which the defect is in the excretion of nitrogenous waste products. It is characterized by increased blood urea, defective urea concentration in the urine, cardio-vascular changes, absence of œdema, moderate albuminuria, and a tendency to uræmia. This, of course, corresponds in the main to the small white and the small red kidneys. The other is the *hydræmic type* (parenchymatous nephritis), in

which the defect is in the excretion of salt and water. This is characterized by dropsy, marked albuminuria, and diminished urinary chlorides, but there is no nitrogen retention, impaired urea concentration, cardiovascular hypertrophy, or marked tendency towards uræmia. While working on the basis of this simple classification, Dr. MacLean himself points out that the two types are frequently found combined in one patient, and that a case which seems clearly to belong to one variety may be lacking in certain features which are usually present. Thus, in a case of the azotæmic type there may be no recognizable cardiovascular changes.

Let us now look through the list of varieties of Bright's disease and collect those which are associated with high blood pressure. In *acute nephritis* there may be a speedy and marked rise of blood pressure with enlargement of the heart, but if recovery should be complete, these phenomena pass off after the acute attack subsides. The increased pressure has been attributed to heightened activity of the vasomotor system under the influence of a toxin. In the acute glomerulonephritis of scarlet fever the rise of pressure may sometimes be detected before the appearance of albuminuria, hæmaturia, or œdema. In *nephrosis* or *toxæmic kidney* (the toxic-degenerative disease of the tubule epithelium which stops short of inflammatory reaction in the connective tissue), increased blood pressure is not a feature; but in severe cases of the toxæmia of pregnancy (*pregnancy kidney*) the blood pressure may be raised, and this has been attributed to glomerulonephrosis with resulting hypertonus of the arterioles.[16] The *large white kidney* (*chronic parenchymatous nephritis*) corresponding to hydræmic or hydropigenous nephritis is not in its pure form attended by any marked rise in the pressure, or by marked cardiovascular changes. In azotæmic or *chronic interstitial nephritis*, on the other hand, these features are present in moderate degree. In actual experience, however, intermediate cases may be found connecting the two types. In the *small red kidney* or *renal fibrosis*, high pressure and cardiovascular changes show themselves in high degree. It should be added that in some cases of hydronephrosis and of polycystic disease in adults, with atrophy of the kidney tissue, high pressure and cardiac hypertrophy develop. It might

therefore be suggested that in chronic nephritis the degree of cardiovascular hypertrophy is roughly proportional to the amount of interstitial change or fibrosis in the kidneys; but perhaps it is still more accurate to say that it is proportional to the amount of damage to the glomeruli. In glomerulonephritis, acute or chronic, the glomeruli are, of course, the principal parts to suffer; in the small red kidney, the thickening of the walls and narrowing of the lumen of the arterioles gradually deprive the glomeruli of their blood supply, and as a consequence they undergo atrophy, and their related tubules are thrown out of action.

The question whether the increased pressure is due to the mechanical obstruction of arteries in the damaged kidneys, with consequent diminished capacity of the renal arterial system, can apparently be answered in the negative, on experimental and clinical grounds. The whole renal area is too small for this. Whether the increased pressure is compensatory in the sense that the heart is trying to force an increased quantity of blood through the damaged kidneys to compensate for the partial loss of renal function, is very doubtful. The available evidence seems rather to point to impairment of the specific function of the glomeruli by toxic and/or mechanical agencies, with consequent retention of a pressor substance which causes constriction of the arterioles of the body.

HYPERPIESIA.

Let us now look at the subject of high pressure apart from kidney disease, *essential* or *idiopathic hypertonus* or *hypertension*, as it is sometimes called, as distinguished from nephritic hypertonus. This is a disease whose features were first clearly explained by Allbutt. Allbutt uses the term "hyperpiesia" to signify the disease, and the term "hyperpiesis" to signify the increased blood pressure which, in the first stage of the disease, is its only recognizable manifestation. In course of time the hyperpiesis leads to hypertrophy of the heart and arteriosclerosis of the hypertonic variety. Allbutt in his posthumous treatise has given us the history of the interpretation of cause and effect. In the first place, Von Basch, studying arterial disease and high pressure in Marienbad and Vienna, attributed the rising pressure to the resistance offered by

thickened arteries. In the second place, Huchard in Paris (1893), reversing cause and effect, attributed the disease of the arteries to the damage done by the excessive pressure. In the third place, Allbutt pointed out that in a half or more of the cases of arterial disease, pressures were not, and had not been, excessive. Von Basch said : arterial disease causes high pressure. Allbutt said : arterial disease does not of itself cause high pressure. Huchard said : high pressure causes arterial disease. Allbutt said : high pressure is not the only cause of arterial disease. Allbutt remarks that many years elapsed before what he terms his crucial distinction between arterial disease with high pressure and arterial disease without high pressure was admitted or even seriously considered. This distinction was published in 1894, and it was not until 1904 that the opinion of clinicians began to lean towards the position that arterial decay does not of itself set up cardiac hypertrophy. Allbutt's teaching, now generally accepted, is that cases of arteriosclerosis with high pressure are cases either of renal disease or of hyperpiesia, the arteriosclerosis being not the cause but the consequence of the high pressure. Cases of arterial disease with high pressure die sooner than those without high pressure, often through cardiac failure or apoplexy. Before Allbutt's views were generally accepted, observers who encountered or admitted the two kinds of case, viz., arterial disease with and arterial disease without high pressure, were inclined to regard them as cases essentially of arterial disease in which the pressures differed in accordance with differences in cardiac energy or other accidental circumstances.

Excessive blood pressure, then, or hyperpiesis, is met with either as a result of certain forms of kidney disease, or apart from any recognizable disease of the kidneys or any other organ. The latter condition is what Allbutt raised to the dignity of a disease *per se*, under the title of " Hyperpiesia." In both cases the high pressure leads to arterial hypertrophy and ultimately to arterial degeneration; and in both there is the danger that the heart will become unfit for the greatly increased task thrown upon it, or that grave consequences will ensue to important viscera such as the brain, the kidneys, or the heart itself, through obstruction or rupture of degenerate vessels.

What the cause of this hyperpiesia is, no man knows. As

Allbutt proved by abundance of evidence, it is certainly not a result of disease of the arteries. It is not, properly speaking, a senile disease, though its age-period tends to overlap the age-period of senile atheroma. Allbutt thinks that the usual age-period of hyperpiesia is 45 to 60, with an average duration of 10 or 15 years, ordinarily terminating in apoplexy or cardiac failure; whereas the age-period of atheroma would begin about 55. Hereditary tendency must be admitted, to explain how members of a family, perhaps in several generations, will be cut off, at about the same age, by cerebral hæmorrhage. There is good ground for suspecting lead to be a cause. This seems to operate by causing vaso-constriction, but it may also impair renal function. The position of gout is doubtful, but we need not hesitate to accept the widely-held opinion that habitual excess in eating or drinking is harmful. Other suggested causes, such as plethora and excess of adrenalin or of cholesterol in the blood, are either disproved or unproved or insufficient. The same may be said of the theory that high pressure is a result of modern civilization and the mental strain of a high-pressure life causing over-activity of the vasomotor system. An inability of the liver to destroy, or of the kidneys to excrete, certain pressor substances is a speculation which must be mentioned. Allbutt alludes with some evident sympathy, which is shared by Batty Shaw, to the observations of Abelous (1906) and others that there are two pressor substances which are normally excreted in the urine, the one derived from leucin and the other from tyrosin. These pressor substances appear to be produced in the intestine, from protein, by the agency of bacteria. If the liver allows these substances to pass unchanged, "the tyrosin derivative especially," says Allbutt, "must aggravate blood pressures by acting locally on the vessels, and herein," he says, "may lie the secret of the malady of hyperpiesia. Such poisons," he adds, "may not only crimp up the arterioles, but also do some direct injury to their walls." William Bain claims that since isoamylamine is the most abundant of the pressor bases in normal urine, its retention in the body plays the chief part in the causation of hyperpiesis.[17] This seems to be as far as we can go in the way of theorizing in the meantime. Whatever be the pressor substance, and whether it acts on the arterial wall

directly, or through the agency of the vasomotor centre, the first thing that happens is widespread and persistent hypertonus or constriction of the smaller arteries, and then follow increased blood pressure, hypertrophy of the heart, hypertrophy and afterwards degeneration of the arteries, until in the long run, perhaps after many years, something gives way. Allbutt watched one case for eighteen years. It may be that the toxin which causes the hypertonus may also cause proliferative change in the intima and thus intensify the peripheral resistance.

It is natural to inquire whether hyperpiesia and kidney disease have anything in common besides the high pressure and its effects. The answer for the present appears to be in the negative. It is indeed curious that kidney disease, including acute nephritis, should be alone among the organic diseases in giving rise to increased tension, and yet in hyperpiesia, so far as the examination of the structure and functions of the kidneys can guide us, these organs may be perfectly sound.* Batty Shaw has gone the length of suggesting that pressor bacterial derivatives may usurp the whole position, and be the cause of hyperpiesis both in hyperpiesia and in kidney disease, but this speculation does not carry us very far forward.

It may be difficult to decide clinically between hyperpiesia and chronic nephritis. Hyperpiesia is likely to come under notice at a more advanced age than nephritis. A normal blood urea and a normal specific gravity of the urine would favour a diagnosis of hyperpiesia. Moreover, until some disaster occurs, the hyperpietic subject may look and feel remarkably well, whereas kidney disease at a corresponding stage may be causing loss of flesh, strength, and colour, as well as headache and digestive disturbance. I do not think that ophthalmoscopic examination will help us if all other clinical considerations leave us in doubt, because the changes in the fundi are likely in both cases to be results of rupture or obstruction of minute vessels. If only we could see the kidneys in the living subject it might help us greatly, because the kidney of hyperpiesia is usually of full size, whereas in chronic Bright's disease

* The high pressure which may be caused by increased intracranial tension stimulating the vasomotor centre, and the high pressure met with in some cases of erythræmia, are not evidently relevant to this question.

with similar clinical phenomena the kidney is very likely to be shrunken. It is noteworthy that some degree of uræmia may occur in hyperpiesia though the kidneys are normal or at most congested, and that such uræmic attacks may be recovered from once or oftener.[18, 19] It would appear, therefore, that uræmia may develop in hyperpiesis, whether renal or non-renal.

In its first stage, then, *hyperpiesia* is not a cause of any distress or disability. It comes under observation, as a rule, only when the results of advanced secondary changes in the cardiovascular system have begun to tell on the functional integrity of important viscera, such as the heart, brain, or kidneys, or of the retinæ. Sometimes, however, an intercurrent illness or a proposal for life insurance, by leading to a medical examination, reveals the presence of the disease in the first stage. Some time ago I saw a lady of 28, a school teacher, who had a blood pressure of 240/160, with apex-beat outside the nipple line, and yet was feeling perfectly well and enjoying her work, and was anxious to resume her tennis and badminton.

To alarm these people would be cruel, but it may be practicable to give them useful advice. It may be possible to explain to them, even in the early stage, that the blood pressure is rather above the average, and that as this gives the heart more work to do, it may become old sooner than in the average individual. It will, therefore, be wise not to overtax it, and accordingly to avoid excesses in eating and drinking, physical exertion which causes palpitation or shortness of breath, and constipation. Late hours are undesirable. Fresh air, a sufficiency of sleep, and regular exercise in moderation are all worthy of mention. Whether septic processes in the mouth or elsewhere raise or depress the blood pressure, it is obviously wise to get rid of them, in case they promote disease of the kidneys. Short courses of calomel, grey powder or blue pill, in small doses, should be ordered. Vasodilators are not curative, though they may, like bleeding, be of service in an emergency; but, apart from emergencies, they are at least as likely to do harm as to do good. Medical diathermy was highly thought of by Allbutt. Once symptoms set in, the question of rest in bed and drug treatment calls for consideration.

As to the treatment of *Bright's disease*, it is no part of my plan, on the present occasion, to deal with this in detail, but I may be allowed to make a few practical observations. In acute nephritis it is a long-established practice to feed the patient on diluted milk. This is quite suitable if the urinary excretion is fairly good, but weak tea and toast are allowable in addition. If the urine is very scanty indeed, the quantity of fluid administered should be kept down to one or two pints a day. The juice of oranges and other fruits, with sugar and water, is an acceptable part of a restricted dietary. Rest and warmth in bed, and attention to the bowels, are, of course, parts of the routine therapy.

In the subacute, parenchymatous, hydropigenous, or hydræmic variety of Bright's disease, the dropsy is often difficult to deal with. There is no advantage in restricting the fluid intake. An occasional case may benefit by a salt-free diet; or a diet which is rich in protein and poor in fat and starch. In any case, in view of the great daily loss of albumen in the urine, there should be no restriction of protein in the diet. If the dropsy persists for a period of many months, great improvement or even an apparently complete cure will sometimes follow decapsulation of the kidneys.

Very little, as a rule, can be done for the small white kidney. It often comes under notice only when it has reached its terminal stage, but if haply we have to deal with an acute or subacute exacerbation, treatment may lead to much improvement. If, when the disease is already advanced, a septic focus is discovered which may be suspected of having been the original cause of the mischief, no drastic operation should be undertaken; first, because it is too late to do good; secondly, because a specially large dose of the toxin may be absorbed from the raw surface; and, thirdly, because the recuperative power of the tissues may be so poor that healing does not take place satisfactorily, if at all, and the patient's end may actually be hastened.

In cases of the small red or primarily contracted kidney, the principal danger that threatens is collapse of the cardio-vascular system. Some patients, it is true, die from uræmia; but in the main the aim must be to spare the heart and blood-vessels just as in hyperpiesia.

REFERENCES.

1 Saliceto, reference given by Garrison, *History of Medicine*, 1913, p. 353, footnote.

2 Cruickshank, chapter vi in John Rollo's *Cases of the Diabetes Mellitus*, London, 1798, second edition, pp. 447-448.

3 Wells, reference given by Garrison, *op. cit.*, p. 354, footnote.

4 Blackall, *Observations on the Nature and Cure of Dropsies, and particularly on the presence of the Coagulable part of the Blood in Dropsical Urine.* London, 1813.

5 Bright, R., *Reports of Medical Cases*, London, 1827, p. 76.

6 Bright, R., *Guy's Hospital Reports*, 1836, vol. i, pp. 368, 371, 397.

7 Watson, T., *Lectures on the Principles and Practice of Physic*, 1871, vol. ii, fifth edition, pp. 744-745.

8 Roberts, W., *A Practical Treatise on Urinary and Renal Diseases*, London, 1865 (also fourth edition, 1885).

9 Roberts, W., *op. cit.*, p. 322.

10 Roberts, W., *op. cit.*, p. 322.

11 Barker, L. F., *Clinical Medicine*, 1922, p. 310.

12 Dunn, J. S., *Glasg. M. Journ.*, February, 1924, pp. 68-69.

13 Elwyn, H., *Archives of Internal Medicine*, 1926, vol. xxxviii, No. 3, p. 346 f.

14 Christian, H. A., *Journal of the American Medical Association*, 1929, vol. xciii, pp. 23-25.

15 Barker, L. F., *Clinical Diagnosis of Internal Diseases*, 1916, vol. ii, p. 845.

16 Barker, L. F., *Clinical Medicine*, 1922, p. 309.

17 Bain, W., *Lancet*, 25th February, 1928, p. 389.

18 Shaw, H. B., *Hyperpiesia and Hyperpiesis*, London, 1922, pp. 103, 167.

19 Allbutt, T. C., *Arteriosclerosis*, 1925, p. 64.