THE RELATION BETWEEN RENAL DISEASE AND DISEASE OF THE CIRCULATORY SYSTEM.

CLINICAL LECTURE DELIVERED AT THE HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA.

BY JAMES TYSON, M.D.,

Professor of Clinical Medicine, University of Pennsylvania, Philadelphia.

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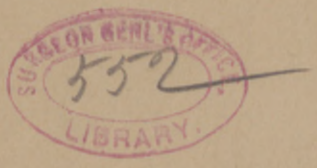

Medicine.

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THE patient I now show you is introduced more especially to illustrate the relation between kidney-disease and heart-disease, a relation not always easily made out. I desire first, however, to contrast the form of disease presented with another variety of kidney-affection, of which we have had some examples before us. I allude to parenchymatous or tubal nephritis, while this is a case of chronic interstitial nephritis, of which the final result is the chronically contracted kidney, the essential anatomical alteration in which is an overgrowth of interstitial tissue. In the parenchymatous disease, you will remember, the lesion begins in the tubules. The cells swell, proliferate, distend and enlarge the tubules, whence results enlargement of the whole organ. The man before you presents no evident symptoms. He has no general dropsy. There is, however, a little swelling below the eyes, to which I am glad to be able to call your attention, as it is a symptom the importance of which is often exaggerated. Such swellings occur quite independently of Bright's disease, and some persons are particularly prone to them. Much more serious is a swelling of the upper eyelid, although this also occasionally occurs irrespective of disease.

Notwithstanding the fact that there are no evident objective signs of illness in this case, one may still be led to suspect it by an examination of the heart, even before examining the urine. No murmur is heard, but on placing the stethoscope on the aortic cartilage we note easily a sharp accentuation of the aortic second sound, whence at once hypertrophy of the left ventricle may be suspected. That such hypertrophy is present is proven if an enlarged percussion-area of the heart

downward and to the left can be demonstrated, or if there is displacement of the apex below and to the outside of its normal situation between the fifth and sixth ribs within the nipple-line. Such a state of affairs exists in this case. I will only add that it is not always discoverable, because a coexisting pulmonary emphysema may obscure it. Such a state of affairs always demands an examination of the urine, which one is almost sure to find albuminous, although the quantity of albumin will probably be small. Rarely also albumin will be found altogether absent. As in this case, too, you will most likely find a few small hyaline or slightly granular casts, or casts containing one or two small oil-drops; casts also may be wanting, but careful searching will seldom fail to find them. Finally, the twenty-four-hours' urine will be found increased to fifty, to sixty, and even to seventy ounces, and the specific gravity will be lowered, 1005 to 1012. Such a combination of symptoms—hypertrophy of the left ventricle, no valvular disease, small albuminuria, a few hyaline or pale granular casts, no dropsy—admits of but one interpretation,—chronic interstitial nephritis. Such a state of affairs may continue for a long time and the patient may be but slightly ill. Or there may be headache, throbbing in the head, morning sickness, and symptoms of indigestion.

I.

We have, then, in this case an association of kidney-disease with heart-disease. The former is interstitial nephritis, the latter hypertrophy of the left ventricle without valvular disease. Now, what is the order of these events? Without attempting to decide the question in the case before us, I may say that modern studies have made it pretty certain that this form of combined heart-disease and kidney-disease may occur in two ways: first, both conditions may result from one and the same cause; or, secondly, the heart-affection may be secondary to the kidney-disease and its direct consequence.

Whichever may be the more common,—and I do not think this is certainly determined,—the first is the easier of explanation. For this combined kidney-affection and heart-disease, a thickened state of the blood-vessel wall, known as arterio-sclerosis or arterio-capillary fibrosis, is held responsible. The thickening is more or less general, or diffused throughout the arterial system, but is more marked in the smaller vessels, and it is not confined to any one of the three coats. Usually it begins as an endarteritis, and the intima is therefore thickened, particularly as to its subendothelial connective tissue, but the muscular coat is also the seat of morbid changes not always the same.

Gull and Sutton, in a paper which has become historic, announced in 1872[1] that the changes in the muscular coat were chiefly of an atrophic character, and, although the methods of these observers have been much criticised, the most recent studies on this subject by Councilman and Arthur V. Meigs go to confirm their conclusions both as to the seat and the nature of the changes. Councilman[2] finds atrophic changes in the muscular coat, including greater or less destruction of the muscular fibre-cells, and the formation of a homogeneous hyaline tissue invading both coats, but especially the intima, where it produces decided thickening, and encroachment to a varied extent upon the lumen, sometimes amounting to occlusion. The capillary walls are likewise thickened, and sometimes, especially in the glomerule of the kidney, obliterated. Meigs's[3] studies also find these changes for the most part confined to the intima, which is decidedly thickened. To a less extent the intima of the veins is similarly involved. The picture of the changes thus briefly described may be obtained from a small artery taken almost indifferently from any tissue or organ of the body, —for example, from the muscular substance of the heart, the kidney, or the liver.

It is to be remembered, also, that there are at least two other forms of endarteritis, the first the nodular, where the changes are limited to small areas in the aorta and large arteries,—atheromatous patches, sometimes calcareous and sometimes fatty; the second the so called senile endarteritis, in typical instances of which the aorta and all its larger branches are converted into rigid inelastic tubes. It is doubtful whether the latter should be called endarteritis, it being rather an infiltration of lime-salts as the result of impaired nutrition. It begins in the muscular coat, and the vessel-walls are thinned rather than thickened, their inner surfaces roughened, and their lumina irregularly dilated, while the vessels themselves are elongated, producing abnormal tortuosities. Far from being enlarged in this form, the heart is often smaller, the seat of brown atrophy. Similar atrophic processes affect the liver as well as the kidney, and the result in the latter organ is often a typical contracted kidney. The rationale of the renal changes in senile endarteritis is similar to that in the diffuse form. The cardiac hypertrophy is, however, absent, because the nutrition of the heart is so seriously interfered with that it cannot exert its usual reactive influ-

[1] Arterio-Capillary Fibrosis, Medico-Chirurgical Transactions, London, 1872.

[2] On the Relations between Arterial Disease and Tissue Change, Trans. Assoc. Amer. Phys., vol. vi., 1891.

[3] New York Medical Record, July 7, 1888.

ence. Hence it undergoes atrophy at the same time with the liver and kidney.

It cannot be said that these three varieties of endarteritis are always sharply separable one from the other, but it is the diffuse form which is the link between the hypertrophy of the left ventricle and the contracted kidney present in the case before us. Of its consequent changes the hypertrophy of the ventricle is most easily explained. The resistance in the blood-vessels stimulates the ventricle to increased effort, and there result increased arterial tension and hypertrophy. The degree of cardiac hypertrophy is sometimes enormous, the organ weighing as much as eight hundred and fifty grams, or twenty-eight ounces, and the average in twenty-seven cases studied by Councilman being over four hundred grams, or thirteen ounces.

The alterations in the kidney, which vary greatly in degree, being sometimes scarcely noticeable and sometimes extreme, are the direct result of an interference with its nutrition. The blood-supply to the renal elements being cut off, these gradually waste and ultimately disappear. The cells and tubules thus destroyed are gradually but irresistibly replaced by fibrous connective tissue, in obedience to the pathological law elaborated by Weigert, that parts destroyed are partially replaced by cicatricial connective tissue. This contracts and reduces the size of the kidney, and perhaps, also, in this contraction further destroys the proper kidney structure and thus augments the atrophy.

It has been said that in this form of combined kidney- and heart-disease there is no cardiac murmur. Nor is there, as a rule. It is not impossible, however, for the endarteritis of which we are speaking to creep along the walls of the aorta until it reaches the aortic valves and so structurally changes them as to make them rough or incompetent and give rise to murmurs.

The causes of this form of Bright's disease are, therefore, the causes of the endarteritis, and these are various. Among the most numerous are habitual excess in eating and drinking, the poison of gout, whether uric acid or something else, lead-poisoning, and syphilis. All of these conditions introduce an irritant substance into the blood which in the course of its circulation excites an inflammation of the inner membrane of the vessel. To a less degree probably the specific causes of all the infectious diseases must be included in this category,—possibly, even, malaria. The subjects are usually middle-aged men, between the ages of forty and fifty-five, but they may be younger. Councilman has found these changes more common in the negro than in the white race.

I am, however, one of those who do not believe that every instance of renal disease associated with cardiac hypertrophy is the result of an intermediate endarteritis. Interstitial nephritis is not the only form of renal disease which is associated with cardiac hypertrophy, although it is the variety most frequently thus associated. Any case of chronic nephritis is liable sooner or later to become associated with hypertrophy of the left ventricle, while pronounced contraction of the kidney may occur without general vascular change sufficient to explain the contraction.

How is the cardiac hypertrophy to be accounted for in this second set of cases? It must be admitted that the explanation is not so easy as in that where chronic endarteritis is present. I will first review the theories which have been from time to time given, for theories alone they must be acknowledged to be. The oldest, which may be termed the "chemical theory," was advanced in its cruder form by Bright himself, whose acute observation had not failed to notice the association of cardiac hypertrophy with the disease so deservedly coupled with his name since 1827. According to this hypothesis, the retention of excrementitious substances in the blood is responsible for the increased arterial tension and the hypertrophy of the left ventricle. At the present day George Johnson in England and Senator in Germany still hold this view. At one time Johnson held that the hypertrophied state of the muscular coat was the effect of its resistance to the onward movement of the noxious blood, while the coat thus thickened further reacted upon the effort of the heart to overcome it. More recently he ascribes this hypertrophy of the middle coat in the vessels of the kidney to an effort to cut down the supply of blood in accordance with the reduced demands of the small kidney. Recent studies by modern methods do not find the changes in the middle coat early described by Johnson, while experiments which have for their object charging the blood with urea and allied excrementitious substances have also failed to excite hypertrophy. It should be added, however, that it is not possible by experiment to produce precisely the conditions furnished by diseased kidneys, especially in the matter of duration. It is very generally conceded that uræmia is due to retained excrementitious substances which are in health eliminated by the kidney; while the experimental introduction of these same materials has as yet failed to produce uræmia. Here, too, it is to be remembered that sound kidneys are encountered, which by copious diuresis promptly eliminate the substances introduced.

The so-called "mechanical theory" of cardiac hypertrophy was

advanced by Traube, whose researches in 1856 gave a decided impulse to clinical study of the subject. According to Traube, the increased arterial resistance was caused by two supposed states: the first being an over-fulness of the vessel because of the diminished withdrawal from the blood of water for the formation of the renal secretion; and the second, that the movement of arterial blood into the kidney was hindered by the renal contraction itself. The first hypothesis was erroneous in the case of contracted kidney, where the urinary secretion is really increased, and the second is opposed by the fact that even ligature of the renal arteries fails to increase arterial pressure, because of the ample space elsewhere to take up the blood thus diverted. Nor did Cohnheim's further elaboration of the mechanical theory, which located the increased resistance more precisely behind the wasted glomerule, give any more permanent life to it.

I incline to the belief that the difficulties are best met by supposing the primary changes in the heart to be *compensatory* in their nature, set up with a view to making up for the gradual loss of renal substance. Such an action is paralleled everywhere in the physiological economy. Nowhere do we meet with loss of function which is not at once met by an attempt of nature to supplement it. The dependence of the urinary secretion upon cardiac pressure is well understood, and an increase of cardiac power is the most reliable means available for stimulating the action of the kidneys, when desired, in therapeutics. The diuresis which is so constant a symptom of the contracted kidney is certainly the direct result of a supplemental contraction of the left ventricle, which it is reasonable to suppose is induced for the purpose named, and results in hypertrophy.

This view receives confirmation in the subsequent course of the disease. So long as the free secretion which is the result of the compensatory action of the heart is kept up, so long the patient remains tolerably comfortable, and perhaps even for a time unconscious of the presence of disease. But an organ thus overgrown is apt sooner or later to suffer in its nutrition, and especially is this the case if its arteries be the seat of an endarteritis which interferes with the free movement of the blood and produces also fibro-myocarditis. And what are the further consequences? The strong propulsive power of the heart declines, the pulse falls away in tension and power and becomes more frequent and sometimes irregular. The urine secreted diminishes in quantity and assumes a darker hue. Fortunate is the patient if the specific gravity of the urine rises *pari passu* with its reduced quantity, as it indicates that the normal quantity of solids is kept up. Too fre-

quently, however, this is not the case, and excrementitious substances accumulate in the blood, laying the foundation for uræmia. Headache, nausea, a foul and even urinous breath, may be superadded, and uræmia set in, preceded by drowsiness, or it may be ushered in suddenly with convulsions. Or another set of symptoms may supervene. The patient becomes short of breath, first on slight exertion, and later this very distressing symptom occurs without such exciting cause. This sort of asthma is often spoken of as uræmic asthma, as if due to the same causes as uræmia, and this may sometimes be the case. More frequently the failing heart is responsible. The organ is no longer able to move the blood onward, the lungs become engorged, aëration becomes imperfect, and hence the dyspnœa. For a time this symptom may be averted by whipping up the heart by cardiac stimulants, and the right ventricle even comes to the rescue for a time, and hypertrophies in its effort to overcome the now disturbed compensation. Subsequently this as well as the left ventricle may become dilated, and œdema of the lungs set in, with annoying cough and serous frothy expectoration, sometimes blood-tinged. Nor does general dropsy continue absent, but ensues sooner or later with the growing heart-failure. Our resources are now almost at an end, but are not exhausted, as even these symptoms sometimes subside.

Finally, it must be stated that not every case of interstitial nephritis is attended with hypertrophy of the left ventricle. In addition to the cases of contracted kidney from senile endarteritis already referred to, cardiac hypertrophy is apt to be absent in the interstitial nephritis of the weak and cachectic.

A pertinent question is one as to diagnosis,—as to whether it is possible to say of a given case that it is one of endarteritis with consequent renal cirrhosis and cardiac hypertrophy, or one in which the renal condition is primary. It is true that some symptoms may be referred to the vascular and others to the renal cause, and it is not unimportant to be able to recognize early the symptoms of arterial sclerosis before those of renal involvement make themselves apparent, since the latter indicate a more irremediable stage. Thus, the early head symptoms, such as headache and vertigo, are probably due to derangements in the circulation in the brain, while the apoplectic phenomena which often terminate the disease—when other symptoms would not lead us to expect the end—are directly due to defects in the vessel walls associated with the extreme intravascular pressure. A throbbing sensation in the head is included in the symptoms ascribed to intravascular pressure, and it is reasonable to suppose that when this occurs associated with

vertigo and without objective symptoms of Bright's disease, such as albuminuria and casts, it is due to primary vascular change. Late in the disease, when the objective symptoms are well defined, it may be ascribed to secondary hypertrophy. When the arcus senilis attends these two symptoms, vertigo and throbbing, there is probably endarteritis, although the arcus is more frequent with senile arteritis. There is no peculiarity in the vertigo by which it may be assigned to one or the other condition. It may be transitory, or may last long enough to force the patient to sit down, or even to cause him to fall, though even then the duration is apt to be for a few minutes only. A slow pulse is apt to be associated with these vertigoes, and sometimes an extremely hypochondriacal state, all prior to the albuminuric stage. A tendency to a mild form of epileptic seizure is described by the French authors.[1]

Epistaxis is another symptom which may be directly ascribed to the arterio-sclerosis, and it is often the first symptom to attract attention by its profuseness and frequent recurrence. On the other hand, palpable stiffening of a blood-vessel wall attainable by the finger is more apt to indicate senile endarteritis. High arterial tension as detected by the sphygmograph before it is noticeable by the finger, and before any signs of cardiac or renal disease present themselves, points to endarteritis.

There seems every reason to believe that the prognosis of arterio-sclerosis is more favorable before the renal and cardiac changes manifest themselves. It is desirable, therefore, that it should be discovered as early as possible; and attention to the facts named may lead to this.

The treatment of the combined kidney- and heart-disease is not different from that of interstitial nephritis. Even greater rigidity is necessary in eliminating nitrogenous food, and all food should be reduced to a minimum. A diet of milk diluted with water is the safest of all. Bread and butter may, however, be allowed, and even succulent vegetables easy of digestion, such as potatoes, peas, and string beans, while simple fruit-juices, as those of oranges and lemons, are allowable. Mental excitement and immoderate muscular exertion must be avoided, and the heart should not be overworked in any way.

The medicinal treatment especially directed to the arterio-sclerosis may be divided into that intended for the cure of the endarteritis and that directed to the relief of symptoms. The only drug from which results may be expected for the former purpose is the iodide of potas-

[1] Grasset, Du Vertige Cardio-vasculaire, Paris, 1890.

sium, which should be given a fair trial in doses as large as can be borne without deranging the stomach. For the relief of the symptoms more especially due to the sclerosis—viz., headache, throbbing, and vertigo—the nitrites are often useful, and this in my experience is their sole use in Bright's disease. Nitro-glycerin should be given in doses of one-hundredth of a grain every four hours, rapidly increased to one-fiftieth, as the smaller dose is often without effect. The aim should be to produce the physiological effect, which is a sense of fulness or a flushing. The sodium nitrite may be substituted in three-grain doses. It has the advantage of being more permanent in its effect, although it is slower in its action.

II.

The second form of combined heart- and kidney-disease to which I wish to call your attention is that wherein the heart-disease is primary. It is commonly disease of the mitral valve. The kidney-disease does not occur in connection with aortic valvular disease until mitral disease is superadded. It is well known that in mitral regurgitation, as soon as compensation ceases the blood accumulates first in the lungs, then in the right side of the heart, and finally in the venous system, engorging especially the liver, the stomach, and the kidneys. With the effects upon the first two I have nothing to do at present, although they are of a very positive character and generally manifest themselves sooner than the renal symptoms.

Let us first study the condition of the kidney itself. As stated, it is engorged with blood from the venous side. The renal vein and its branches are filled with blood as far back perhaps as the Malpighian body. This backward pressure resists the onward flow of the arterial blood, and the congestion is thereby further augmented. The effect is to swell the kidney somewhat and to darken its hue, which on section will be found more intense in the pyramids. A slight hardness also results, and the combination of these two conditions, color and density, has suggested the term *cyanotic induration* for such kidneys. Further changes are not marked or constant. There is sometimes a slight overgrowth of the interstitial connective tissue, and a slight tendency to degeneration in the cells.

Much more decided are the clinical phenomena resulting from such congestion. It is a well-recognized condition of copious secretion of urine that the blood should move freely through the kidney. A stasis is followed immediately by diminished filtration of water, the twenty-four-hours' quantity being reduced to from thirty to twenty ounces, and

even to less. As the solids at first at least remain the same, the urine is dark-hued, the specific gravity is high, the reaction is markedly acid, and a copious sediment of urates and uric acid makes its appearance as soon as the urine cools off. There is almost always a small amount of albumin found. Casts are sparsely, if at all, present, and are of the hyaline and faintly granular variety. Both red and white blood-corpuscles are also sometimes detected, as might be expected. This condition of the kidney and the symptoms are the direct results of the cardiac valvular disease. They may also be produced by any cause producing venous stasis, as pulmonary emphysema, chronic pleurisy, and thrombosis of large veins. Their effect is further to augment the symptoms of the cardiac disease. The circulation, already everywhere obstructed, is further impeded, there is dyspnœa, dropsy increases, the appetite fails, there are nausea and constipation. Sleep, already disturbed by dreams, becomes more so, and a more distressing picture than is presented by such a case is rarely met.

Yet these symptoms are often easily amenable to treatment so long as the heart-muscle remains capable of being influenced by digitalis. I have seen many a patient, apparently *in extremis*, gasping in orthopnœa and with legs heavy and almost bursting with dropsical effusion, completely relieved by a few large doses of this drug. But they must be large doses, not less than eight to ten minims or fifteen to twenty drops every three hours until an effect is produced. If digitalis fails, the tincture of strophanthus may be given in the same doses, or caffeine citrate in three-grain doses, each every four hours, or sparteine sulphate in doses of one-quarter to one-half grain. Purgation should not be omitted, but should rather be pushed to the production of watery catharsis. The ingestion of fluids should be restricted, and the Hay's treatment of dry diet with purgatives is sometimes useful. But I have found a restricted milk diet, limited to two ounces every two hours, associated with the drugs above named, more efficient.[1]

Diuretin is a remedy from which good results may be expected in these cases. My own experience with it has not been large, but I shall use it more in the future. The dose is from seventy-five to one hundred grains daily in solution, about fifteen grains being administered at a time in a tablespoonful of water. The rapid increase of the twenty-four-hours' urine from five hundred cubic centimetres to three thousand three hundred cubic centimetres is reported from its use.

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[1] See some cases reported by the writer in a paper "On the Management of Obstinate Dropsies," Medical News, June 21, 1890.

Such a kidney is of course liable to become the seat of an acute or a chronic nephritis.

III.

The next form of kidney-involvement to which I call your attention as being secondary to disease of the vascular apparatus, commonly heart-disease, is more frequently seen on the post-mortem table than recognized in the living subject. It is *embolic infarction*, produced by the lodgement in some branch of the renal artery of an embolus derived from the heart or a blood-vessel. Its most frequent source is a fragment of vegetation or clot from a diseased heart-valve. An embolus may also arise from a thrombus in an artery, but more frequently it is caused by one in a vein. If from the latter, it must be carried first to the right heart and thence through the lungs into the left heart, and thence by the aorta to the kidney, and must of course be small.

The effect of the lodgement of an embolus in the kidney is a wedge-shaped hemorrhagic infarct, which in time whitens, contracts, and is ultimately absorbed, leaving a mere cicatricial mark.

Most frequently a renal infarct occurs without noticeable symptoms. Its occurrence, if looked for by reason of the presence of valvular heart-disease, might be ushered in by the sudden appearance of a small amount of blood in the urine. A sudden pain in the region of the kidney simultaneously occurring would go to confirm the diagnosis. No treatment is indicated, even if the event is recognized.

IV.

Finally, kidney-disease and disease of the vascular apparatus, and especially cardiac disease, may coincide accidentally, each the result of its own cause, and reacting the one upon the other in various degrees and variously aggravating the symptoms of each, so that it often becomes a very nice question to settle which is the preponderating disease. Fortunately, this difficulty does not always extend to therapeutics, the same remedies which are useful to one affection being commonly indicated for the other. A careful study of each case should, however, be made on its own merits, and due weight assigned to each factor of the disease.