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THE DIAGNOSIS OF CHRONIC INDURATIVE OR INTERSTITIAL NEPHRITIS.*

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Discussing so trite a subject as the diagnosis of chronic indurative or interstitial nephritis, one can scarcely do more than emphasize the importance of certain pathologic and clinical features of the disease—features that have significant diagnostic, prognostic and therapeutic bearings. It is impossible to add anything new to our knowledge of the subject. Indeed, as a matter of fact, we at this day are scarcely better informed on the subject than was Bright himself. It is true that Aetius (died 367 A. D.), Avicenna (980-1036), and Van Helmont (1577-1644) attributed certain cases of dropsy to disease of the kidneys, and that Cotunnus (1736-1822), in 1770, discovered that the urine of dropsical patients is coagulable by heating, but our first insight into the true nature of the nonsuppurative diseases of the kidneys was furnished by Richard Bright (1789-1858) in his memorable publications in 1827 and subsequently. It is also true that Wells (1757-1817), in 1806, Blackall (1771-1860), in 1813, and Alison (1790-1859), in 1820, anticipated somewhat the observations of Bright, but the reports of these writers were fragmentary and their reasoning in large part erroneous. Bright, however, recognized the dependence of the symptoms, dropsy and albuminuria, on the lesions in the kidneys, which he described accurately; further, he recognized that although albuminuria and dropsy are the characteristic symptoms of certain diseases of the kidneys, in some cases the amount of albumin may be small and the dropsy slight or altogether absent, and he described many of the associated phenomena, such as uremia and the cardiovascular changes, and many of the complications, such as blindness, apoplexy, inflammation of the serous membranes, etc. Indeed, to those interested in the subject the original papers of Bright are a constant source of delight.

In view of the dependence of the diagnosis of chronic indurative or interstitial nephritis on changes in the urine and in the cardiovascular apparatus, preliminary reference may be made to the differential diagnosis of albuminuria, especially to the disorders associated with slight amounts of albumin in the urine, and to the cardiovascular alterations.

THE DIFFERENTIAL DIAGNOSIS OF ALBUMINURIA.

Albuminuria is a term used to denote the presence in the urine of different proteid substances—serum albumin, serum globulin, nucleo-albumin, albumose, peptone, fibrin and hemoglobin. Formerly regarded as diagnostic of Bright's disease, it is now generally known that albuminuria may be due to a wide variety of diseased conditions. We know, however, that large amounts of albumin in the urine almost always indicate serious kidney disease, but that, on the contrary, serious disease of the kidneys may exist for a long time with little or no albumin in the urine. In the great majority of cases of albuminuria the albumin is moderate in amount, and one generally has to determine whether the albumin is due to disease of the kidneys, to disease of some other organ, or to both. The importance and significance of albuminuria are always much enhanced by the associated presence of casts, but still we have to bear in mind that both albumin and casts may be present without serious disease of the kidneys, and that serious forms of Bright's disease may exist without either albumin or casts in the urine. The differential diagnosis of albuminuria, therefore, is of considerable importance. For purposes of study we may distinguish the following forms of albuminuria: 1, Extrarenal, spurious, accidental or factitious albuminuria; 2, so-called functional, physiologic or cyclic albuminuria; 3, albuminuria without noteworthy alterations in the kidneys, and 4, albuminuria with noteworthy alterations in the kidneys.

EXTRARENAL, SPURIOUS, ACCIDENTAL OR FACTITIOUS ALBUMINURIA.

These are the cases in which the albuminuria is but a subsidiary factor and entirely dependent on the admixture with the urine of different albuminous fluids—blood, pus, chyle and seminal discharges. Chyle is a very rare constituent of the urine, and when present will scarcely fail of recognition. Seminal discharges in the urine are of more common occurrence; the varietal tyro will scarcely fail to detect them. The greatest interest attaches to the cases of albuminuria associated with blood and pus in the urine—the result of inflammation and ulceration of, and of hemorrhage from, any part of the genito-urinary tract. In these cases the amount of albumin is small—not more 1/10 by bulk (after the heat and acid test), and it is proportionate to the amount of blood and pus. A disproportionate amount of albumin should always excite a suspicion of the coexistence of nephritis. The presence of casts in the urinary sediment is of the greatest importance—their persistence being clear evidence of nephritis, and indicating that at least a part of the albumin in the urine is due to circulatory and tissue alterations in the kidneys. One must avoid error in presuming the non-existence of nephritis in

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cases in which a small amount of albumin and casts are associated with a few leucocytes or pus corpuscles. In most of these cases the albuminuria is due in great part to nephritis—a few leucocytes or pus corpuscles being regular constituents of the urine in Bright's disease. The means of determining the situation and nature of the lesion causing the pus and blood in cases of spurious albuminuria scarcely falls within the scope of this communication.

SO-CALLED FUNCTIONAL, PHYSIOLOGIC, CYCLIC, INTERMITTENT, PAROXYSMAL, DIETETIC, POSTURAL AND ADOLESCENT ALBUMINURIA.

The occurrence of a "physiologic" albuminuria is now generally conceded. It is found especially in young subjects, especially in male subjects under 25 years of age. It is usually detected accidentally, as, for instance, at examinations for life insurance, or for other certificates of health. In some cases it appears to be constant and it lasts for a relatively long time; in other cases it is intermittent—occurring at stated or indeterminate periods. In many of the cases the presence and the amount of the albumin are much influenced by certain circumstances—posture (whence it is sometimes absent on arising in the morning and present later in the day), exercise, emotional and other excitement, cold baths, certain articles of diet (especially proteids, but also large amounts of ordinary mixed foods), prolonged anxiety, college and university examinations, etc. In diagnosing this form of albuminuria considerable circumspection must be exercised. The patient should be a young subject; the urine should be normal in amount (certainly not increased), normal in color, and normal in specific gravity (certainly not of lessened specific gravity); the amount of albumin must be small—never more than 0.1 per cent.; the urine must contain no other abnormal constituent; there must be no local disease of the genito-urinary tract, such as gleet, spermatorrhea, leucorrhea, etc., that might give rise to spurious albuminuria; every bodily organ must be examined and found to be in perfect health—in particular there must be no hypertrophy of the left ventricle of the heart, no accentuation of the aortic second sound, and no increased arterial tension; nor may there be any evidence of disorder of the heart, lungs or liver that might occasion congestion of the kidneys; there must have been no past, nor may there be any present, edema, uremic manifestations or retinal changes; and at the most there must not be more than an occasional hyaline cast. Even in cases that meet these requirements, much caution must be observed, and the diagnosis must not be made until the patient has been long under observation, until both the morning and the evening urines have been repeatedly examined, and until the albumin is found to vary with the influences under which it develops. And when the diagnosis has been made one should stand willing to renounce it immediately on the development of signs of disease likely to be attended by albuminuria. Caution is always necessary inasmuch as albumin may be temporarily absent even for long periods in certain cases and at certain stages of chronic indurative (or interstitial) nephritis, whereas, in other cases it may be present in such small amounts as to require delicate tests for its detection. More than a small amount of albumin always suggests a latent nephritis that for the time being may reveal itself by no sign other than the albuminuria. The caution necessary in the diagnosis of these cases is evident from the statement of Senator, who believes that most cases of so-called cyclic or functional albuminuria are

really cases of latent nephritis, and that no case of albuminuria may be regarded as functional or physiologic if the albumin exceeds 0.4 or 0.5 parts in 1,000. The diagnosis of functional albuminuria in late adult life had best be dispensed with entirely, as practically without exception small amounts of albumin in the urine of such subjects means chronic nephritis (excluding cases of extrarenal albuminuria).

The cause of this functional or cyclic albuminuria is not well understood. It has been attributed to vascular alterations (congestion) of the kidneys, and to disturbances in metabolism, in consequence of which albumoses, excessive in quantity or abnormal in quality, are formed. That many of these cases are really cases of physiologic albuminuria may well be doubted. Some of them are certainly cases of spurious albuminuria. In most cases it is likely that the glomerular epithelium suffers some nutritional disturbance; that it is the seat of at least slight irritation in some cases may be inferred from the associated presence of oxalates in considerable numbers. In some cases the renal epithelium is probably unduly sensitive. Inasmuch, however, as most cases recover entirely after a time, the kidney alterations—still within the range of the normal—are more or less persistent; in other cases they are intermittent or paroxysmal. These cases may be confounded with the rather unusual cases in which following an acute nephritis in early childhood a trace of albumin persists throughout life, but the patient lives to a good old age without other manifestations of nephritis developing. Such persistent albuminuria, of course, indicates slight alterations in the renal epithelium, and in case careful inquiry is not made into the antecedent history of the patient, the condition may be regarded as "physiologic" albuminuria.

ALBUMINURIA WITHOUT NOTEWORTHY ALTERATIONS IN THE KIDNEYS.

A slight amount of albumin may be found in the urine in a great variety of morbid conditions without noteworthy alterations in the kidneys. Thus it may be found in different blood conditions, such as the anemias, leukemia, purpura, scurvy, etc.; in certain forms of intoxication, such as lead poisoning, mercurial poisoning, etc.; in conditions associated with the presence of substances such as sugar and bile-pigments in the blood; after the administration of anesthetics; in fever conditions, and in certain nervous disorders—epilepsy, apoplexy, meningitis, tetanus, exophthalmic goiter, injuries to the head, etc. In most of these cases the albuminuria is attributable to nutritional disturbances in the glomeruli and renal epithelium induced by defective blood supply; in some cases the result of nervous influences. The true nature of these cases is usually readily recognized. The albuminuria is slight and temporary, as a rule; the primary disorder is sufficiently obvious, and there is no other manifestation of Bright's disease. It is important, however, to point out that the conditions in the kidneys found in some of the intoxications and in fever states merge gradually into the well-defined lesions of nephritis—that there is no sharp dividing line between them.

ALBUMINURIA WITH NOTEWORTHY ALTERATIONS IN THE KIDNEYS.

In this group are included the cases of active and passive congestion of the kidneys, cases of toxic degeneration of the kidneys (most of the cases of febrile albuminuria), the kidney of pregnancy, amyloid degeneration of the kidney, the acute and chronic suppurative

and non-suppurative inflammations of the kidneys, and the tumors of the kidneys. In all of these cases the albuminuria is due to some more or less severe temporary or permanent damage to the kidneys, and the albuminuria acquires its clinical significance and diagnostic importance from the attendant phenomena. In acute congestion of the kidneys the albumin is small in amount, the urine is decreased in quantity and frequently more or less hemorrhagic, and the causative factor usually can be determined. In most cases, however, acute congestion of the kidneys represents but the early stage of acute nephritis from which it is scarcely to be differentiated. In chronic congestion the albumin varies in amount in different cases. In chronic heart and lung diseases it is usually small in amount, but in cases of chronic congestion due to obstruction of the renal veins by a tumor or ascites, etc., the amount may be large. The diagnosis of chronic congestion is to be based on the attendant phenomena and not on the amount of albumin. Toxic or febrile albuminuria is an interesting condition that merits much attention. The albumin in these cases is due to the direct action of some toxin on the renal epithelium rather than to the fever, though this may be a contributing factor; in the one case the toxin induces marked degeneration of the renal epithelium, in another case it leads to severer lesions—to an acute nephritis. In toxic albuminuria the albumin is slight or moderate in amount and transitorily disappearing with the intoxication or infection that gives rise to it. A detailed discussion of the albuminuria of the different forms of Bright's disease scarcely falls within the scope of this communication.

THE CARDIOVASCULAR CHANGES IN CHRONIC NEPHRITIS.

These changes are of extreme interest and importance; as a matter of fact, they dominate the clinical picture of the disease and they assume commanding position in the prognosis and in the treatment. The lesions are widespread, involving the heart, the large and the smaller arteries, the capillaries, sometimes even the veins. The lesions of the heart in chronic indurative nephritis involve the muscle and find their expression in hypertrophy. With this, at times, there is associated some interstitial myocarditis with increase of the intermuscular fibrous trabeculae, especially in the neighborhood of many of the smaller coronary arteries which frequently are obliterated. In some cases, especially late in the course of the disease, fatty degeneration of the heart muscle also may supervene. Valvular lesions are extremely uncommon. Those that are found in cases of renal disease are either an antecedent condition, or they result from mechanical causes, from dilatation of the cavities of the heart. The lesion in these cases is one of relative insufficiency—the valve leaflets, in themselves normal, being incapable of closing the abnormally enlarged orifices. The hypertrophy of the heart is predominately a lesion of the left ventricle. In the majority of cases the left ventricle alone is affected; in the remainder of the cases both ventricles are affected. The right ventricle is never affected alone. Simple hypertrophy of the left ventricle is the first event; later this is associated with some dilatation—eccentric hypertrophy. The longer the nephritis continues (the longer the patient lives) the more certain the development of consecutive enlargement of the right ventricle the increased pressure in the left ventricle coupled with degenerative alterations in the heart muscle, leading to increased pressure in the right ventricle. Here also the hypertrophy is of the eccentric

variety. Predominating dilatation of either or both ventricles is an unusual event until toward the termination of life; its development is of ominous moment—it usually presages an early fatal termination. It has been stated by Senator and others that the hypertrophy of the primarily contracted kidney is of the simple variety, whereas that associated with the secondarily contracted kidney and with the arteriosclerotic kidney is of the eccentric variety—hypertrophy with dilatation. But this statement scarcely permits of general application.

This hypertrophy of the heart occurs in all forms of nephritis, but not in all cases. In none of the varieties, however, does it so dominate the clinical picture as it does in chronic indurative or interstitial nephritis. It may be expected from the time of the contraction or atrophy of the kidney, be it of the primary or the secondary variety. Thus it occurs early in the primary form, but its occurrence may be (but usually is not) much delayed in the secondary form. It may, however, occur in chronic diffuse non-indurative (or parenchymatous) nephritis, and it is observed in some cases of acute nephritis, particularly in some of the cases of acute nephritis following the infections. In some of the chronic cases in which it should be expected, for some more or less inexplicable reason it may not occur. These, however, are the unusual cases. The absence of the hypertrophy may be due to faulty nutrition—the heart not being sufficiently well nourished to enable it to hypertrophy; to sclerosis of the coronary arteries; to the vicarious action of one of the other emunctories removing those excrementitious products ordinarily eliminated by the healthy kidneys, etc.

The changes in the arteries are more complex than are those in the heart, and the exact mode of their causation is still debated. In many cases the larger arteries show a loss of elasticity, in other cases more or less arteriosclerosis and atheroma; but neither the one nor the other is a constant feature. The medium-sized and the smaller arteries almost invariably have thickened walls—the lesions being conspicuous in the middle and in the innermost coats. Presumably the first alteration consists of a hyperplasia of the muscular coat—an alteration effected in response to increased functional demands, the result of an effort on the part of the arteries to control the circulation. After a while, or in some cases possibly from the beginning of the disease, fibroid or hyaline degeneration supervenes. In some cases both the muscular hypertrophy and the fibroid alteration may be observed side by side. The changes in the innermost coat consists especially of thickening of the subendothelial layer, and in many cases of some thickening also of the endothelium itself. In the early stages of the disease the arterial lumen is diminished from contraction of the muscular coat. Later, on account of the increased arterial pressure, the overaction of the heart and degeneration of the walls of the arteries, the result of defective nutritive supply, in part, at least, attributable to obstruction or compression of the vasa vasorum, the arterial lumen becomes increased. The increase, however, is in part counteracted by the thickening of the endothelium. The changes in the arteries though widespread are not distributed uniformly throughout the body. In many cases they are most marked in the kidneys; in a few cases they appear to be almost confined to them. A noteworthy arterial condition consists of the development of miliary aneurisms that in many cases are numerous and implicate especially the arteries of the

brain, and rupture of which frequently leads to the fatal termination.

The cause of these cardiovascular alterations has not been thoroughly worked out. Considerable discussion still obtains with reference to whether the primary alterations are in the arterioles (stop-cock action of Johnson), or in the capillaries (the arteriocapillary fibrosis of Gull and Sutton). Doubtless the conditions differ in different cases. Thus arteriosclerosis itself may be the primary event (and this seems to be especially common in this country), and it leads to both the kidney alterations and the cardiac hypertrophy. In this instance the disease is a widespread process, and its etiology is the etiology of arteriosclerosis. However, in many cases the nephritis is, the primary event and leads to the cardiovascular alterations. What seems to be true is that the cardiovascular alterations result from obstruction to the flow of the blood in the arterioles and capillaries throughout the body, and that this obstruction is provoked by the presence in the circulating blood of some irritative metabolic product or products that should be, and in health are, eliminated by the kidneys. The nature of this poisonous metabolic product, whether there be one or several poisons, and whether the same poison or poisons are operative in all cases has not yet been determined. Whether the poison or poisons exert their action on the circulation through the vasomotor system—irritation provoking contraction of the arterioles, or whether they exert a direct action on the vessels obstructing the flow of blood through them entirely independently of the nervous system, is still debated. The question is further complicated by the adherence of certain writers to the mechanical theory first proposed by Traube, later elaborated by Cohnheim, and modified by Tyson, who looks on the cardiovascular changes as compensatory in nature and set up with a view to supplement the gradual loss of renal substance. For the time being, as clinicians, therefore, we have to content ourselves with recognizing the clinical manifestations, and appreciating the importance of these cardiovascular alterations. I have already had occasion to mention these in detail.¹

SYMPTOMS OF CHRONIC INTERSTITIAL NEPHRITIS.

The first clinical manifestations of chronic interstitial nephritis differ materially in different cases. For the present, leaving out of consideration that form of chronic indurative nephritis that develops late in the course of the large white kidney, and which in many cases is scarcely to be distinguished from the large white kidney, it may be said that the early stages of chronic indurative (or interstitial) nephritis—the red granular kidney, usually escape detection, or they are discovered accidentally by the routine examination of the urine of patients ill with other diseases, or in examining applicants for life insurance or for other certificates of health. When, finally, after a number of years the disease does produce obstructive symptoms, these are usually of such a nature that they are likely, for a time at least, to be attributed to disease of some organ other than the kidneys. Thus, while the patient may present himself to his physician with the idea that he is suffering with diabetes on account of the large amount of urine that he voids, he is just as likely to complain of dimness of vision, the consequence of albuminuria neurorretinitis, or of one of the many manifestations of chronic uremia,

such as dyspnea, asthma, gastrointestinal derangements (gastric catarrh, gastric hemorrhage, diarrhea), or headache, hemicrania, tinnitus aurium, or vertigo, etc., or neurasthenia, pains in the muscles or joints, or eczema, or palpitation of the heart and precordial distress; or, the patient, in apparent good health, may suddenly develop a severe and even fatal attack of cardiac failure, pass into uremic coma or convulsions, or he may suffer an apoplexy and die.

DIAGNOSIS.

Revealing itself thus in different ways, the diagnosis of chronic interstitial nephritis depends on the results of an examination of the urine and of the cardiovascular apparatus. The characteristics of the urine are too well known to need detailed mention. Suffice it to say that the urine is increased in amount, of low specific gravity. Especial interest and importance attaches to the albuminuria. The amount of albumin is usually slight; often there is no more than a trace; at times none may be found. Importance attaches to the absence of albumin in many cases. The albumin may be absent for days or weeks at a time; it may be absent for the early morning urine and present in that passed later in the day; and it may be present only after exercise, emotional and other excitement, or after eating, especially after eating proteids. In this respect it resembles the so-called functional or cyclic or dietetic albuminuria, and especial care must be exercised in the differential diagnosis, as already pointed out. The urinary sediment usually contains a few hyaline casts, rarely a few epithelial and granular casts. Frequently the casts are very narrow.

In view of the oftentimes slight evidence of renal disease on the part of the urine the cardiovascular lesions assume considerable, even dominant, importance. The clinical evidence of the cardiovascular lesions consists of hypertrophy of the heart, especially of the left ventricle, accentuation of the aortic second sound, and of increased arterial tension. The signs of the cardiac hypertrophy are sometimes obscured by coexisting emphysema of the lungs, but usually one may make out displacement downward and outward of the apex, increased force and vigor of the apex beat, which though usually slightly broader than normally is still well circumscribed, and the percussion evidences of enlargement of the left ventricle. Concurrently with increase in the muscular volume of the heart the first sound becomes more prolonged, duller and lower pitched than in health. The second aortic sound becomes markedly accentuated—a very important sign, and a sign that frequently may be made out when enlargement of the heart is as yet problematic. The changes in the pulse are of great diagnostic value. In the early stages of the disease, the arteries being contracted, the pulse is small; the internal pressure being increased, the artery resists compression and flattening; on account of the increased internal pressure and the contraction of the vessels, the pulse waves are small. The pulse, therefore, is hard and resisting to the palpating fingers, the pulse waves are small, the artery remains persistently full between beats (and this is the characteristic feature), and considerable pressure is required to obliterate the pulse wave. Later to these there is added the evidence of arteriosclerosis, and later still the more characteristic changes of atheroma. As I have said elsewhere,² the existence of these cardiovascular changes, as also of the kidney lesions, may for a long

1. The Interrelationship Between Cardiovascular Disease and Renal Disease, Philadelphia Medical Journal, Oct. 27, 1900. Diseases of the Kidneys, Nephritis, Bright's Disease, Wood's Reference Handbook of the Medical Sciences, revised edition, vol. v, 1902.

2. What follows is a reiteration of what the author has already said in the Philadelphia Medical Journal and in Wood's Reference Handbook of the Medical Sciences, l. c., which may be consulted for a fuller discussion of the questions concerned.

time remain entirely unknown to the patient and be entirely unsuspected by the physician. So long as the heart continues to perform its increased work well no symptoms occur. Should, however, the increased quantity of the urine or the development of slight swelling about the eyes or the ankles attract the patient's attention, or should he suffer from epistaxis (usually of serious moment), or from dimness of vision (due to neuroretinitis), or from severe muscular cramps in the calves of the legs (which are quite common), or from any of the symptoms of chronic uremia, inquiry on the part of the physician may elicit the information that for months, possibly years, excitement and exertion have been provocative of breathlessness and palpitation of the heart, but having an obvious cause they were regarded as of no particular significance. As the disease advances, however, the nutrition of the heart no longer keeps pace with its enlargement, degenerations ensue, and evidences of embarrassed circulation result. It is now that symptoms referable to the cardiovascular system dominate the clinical picture. To the hypertrophy of the heart, if it were simple, there supervenes dilatation, and to disease of the left ventricle is added disease of the right. There result cardiac asthma, congestion and edema of the lungs, bronchitis, gastrointestinal disturbances, generalized edema and effusions within the serous cavities and alterations in the urine. The urine lessens considerably in amount, and it becomes of high color and increased specific gravity; albumin increases in amount and casts become more numerous, and dark granular, epithelial, and even blood casts and free erythrocytes may be encountered. The symptoms referable to the heart and lungs, at first transitory and nocturnal, become permanent, the other symptoms mentioned are added, and if relief is not afforded, death ensues with cardiac failure or uremia or both dominating the final scene. Toward the end of life concurrently with the cardiac failure, the pulse which had been of high tension may become of lessened tension; the second aortic sound becomes less accentuated; with embarrassment of the right heart the second pulmonary sound becomes accentuated; signs of dilatation, and galop rhythm, always of serious moment, supervene.

So long as cardiac compensation is maintained the diagnosis of chronic indurative or interstitial nephritis is evident from the results of an inquiry into the antecedents of the patient, the special etiologic factors in the case, the different clinical manifestations, and an examination of the urine and of the cardiovascular apparatus. Indeed, a diagnosis based on increased arterial tension, accentuated second aortic sound and the physical signs of hypertrophy of the left ventricle will rarely be wrong. The diagnostic importance of these cardiovascular alterations can not be overestimated. They are among the earliest clinical manifestations of the disease, and they may be detected even in the absence of positive signs of kidney disease in the urine. Such is their double import that, in the event of suspicion of chronic indurative nephritis, they should be diligently sought, and in the event of their accidental detection in the course of the routine examination of a patient, the presence of an unsuspected or latent chronic indurative nephritis must be persistently borne in mind until these cardiovascular signs are otherwise adequately accounted for.

When, however, failure of cardiac compensation occurs, diagnostic difficulties arise. The clinical picture in these cases much resembles that of an affection primarily cardiac and secondarily renal. Given a patient with evident lack of cardiac compensation, with signs of

hypertrophy and dilatation of the heart, but with such dilatation that it may be well-nigh impossible to determine accurately which side of the organ is especially involved; with or without murmurs; with albumin and casts in his urine—does he suffer from a condition primarily cardiac and secondarily renal, or vice versa? Is the affection one of a primary heart lesion with secondary congestion or cyanotic induration of the kidneys, or is it one of a primary kidney lesion with secondary hypertrophy and dilatation of the heart? The question is extremely difficult to settle offhand in many cases. The presence or absence of murmurs is not definitely diagnostic unless it is possible to accurately localize them and refer them to positive valvular defects. We bear in mind that if there be marked cardiac debility, a murmur of some valvular defect may be temporarily absent; on the other hand, in chronic indurative nephritis, if the cardiac dilatation be sufficient a relative mitral insufficiency may arise and a murmur not present previously becomes audible. Thus murmurs complicate the situation. However, a diastolic murmur is usually suggestive of valvular disease, since the murmurs of dilatation and consequent relative valvular incompetency are systolic. In the majority of cases the diagnosis can be made by bearing in mind that in congestion of the kidneys the casts are usually hyaline only, and that the amount of albumin, which may be considerable, varies from time to time with the state of the heart—increasing or decreasing with impairment or improvement in the cardiac activity. Again, in renal congestion we endeavor to ascertain the cause by reference to the past history of the patient and by noting that the kidney lesion is but part of a general condition that finds its expression also in congestion of the liver and spleen, effusions within the serous cavities, anasarca, etc. If, however, the urine remains albuminous despite the subsidence of signs of congestion in other parts of the body; if the specific gravity of the urine lessens, and if in addition to hyaline even a few epithelial casts are discovered, possibly also some erythrocytes, it is evident that in addition to the congestion of the kidneys there exists a nephritis. Whether or not this is a condition of long standing or the final result of long-continued congestion remains to be decided by reference to the past history of the patient. It is in these cases that the therapeutic test is of the greatest diagnostic value. It is in these cases that digitalis is urgently indicated. If, as sometimes happens, the exhibition of digitalis is followed by marked improvement in the condition of the patient, with final absence of casts and albumin from the urine, the condition is definitely determined to have been one of renal congestion. If, however, with improvement in the cardiac condition, albumin and casts do not disappear from the urine, we are then confident of the existence of nephritis—a conviction that may be confirmed by an examination of the cardiovascular apparatus now that compensation has been restored.

In many cases eye manifestations are of great diagnostic importance. Thus the first manifestations of the disease may be edema of the eyelids—especially the lower lids. This may be moderate, sometimes transitory; at times the first, and rarely the only manifestation of the disease for some time. I have known it to develop and persist for seven years before any albumin or casts could be detected in the urine and before any certain evidences of cardiovascular alterations could be elicited. Especial interest, however, attaches to the albuminuric neuroretinitis and to uremic amaurosis. Albuminuric neuroretinitis occurs most frequently in

chronic indurative or interstitial nephritis, but also in chronic nonindurative (or parenchymatous) nephritis; it is therefore more common in subjects over 40 years of age, though it has also been observed in children. Though in a few cases unilateral it is usually bilateral. Often the dimness of vision that it occasions may be the first symptom of the disease, though it is not likely that this comes on before the albuminuria. In many cases the vision is but little impaired; in the absence of involvement of the macula lutea, of extensive hemorrhages and of optic neuritis, no complaint may be made. Thus these important and serious lesions may go unsuspected and undetected unless examination of the eyegrounds be undertaken. These retinal changes bear no relationship to the severity of the renal lesions nor to the amount of the albuminuria; in some cases they even appear to improve despite the progress of the kidney lesions, though this is the reverse of the rule. Hemorrhages are common; in other cases retinal effusions and detachment, vascular alterations or a papillitis is to be observed—so that the ophthalmoscopic picture varies considerably in different cases. Though the retinal lesions may be extensive, vision is rarely lost except in cases of what is called uremic amaurosis. This is an extremely interesting condition, the nature of which is not understood. While it may occur independently of uremic convulsions, it usually follows the convulsions. The blindness is sudden in onset, usually complete, short in duration (two or three days), and usually very rapid in recovery. The ophthalmoscopic picture is usually quite normal; in other cases the lesions of neuroretinitis are detected. At times the blindness is not complete; in rare cases hemianopsia has been observed.

In some cases skin symptoms are suggestive, though their nature is frequently overlooked. Thus there may be intolerable itching, formication, numbness of the extremities or urticaria. In the late stages more or less widespread erythematous, or bullous, or desquamative skin lesions may occur.

THE EARLY CIRCULATORY INDICATIONS OF CHRONIC BRIGHT'S DISEASE.*

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By chronic Bright's disease we mean that familiar form of degeneration involving the blood vessels, the kidneys and the heart that in its regular course leads to the death of so large a proportion of the human race who have otherwise been healthy and able to enjoy active and useful careers.

PRIMARILY A DISEASE OF THE CIRCULATION.

I have long since ceased to regard this condition as essentially a disease of the kidneys, though in the final catastrophe these organs are more often chiefly at fault. Primarily, it is a disease of the circulation in which the brain and the kidneys, being as it were end-organs, first manifest symptoms.

A case that has been under observation for five years has just ended fatally by the involvement of the circulation of the brain, producing progressive stupor and finally coma, paralysis and death. The kidneys at the time of death were apparently in good enough order to have maintained life for a long time. In this case the greatest care had been exercised in protecting the kid-

neys by diet, an even temperature and every other possible means, thus allowing the arterial disease an opportunity for its complete development. The same case, if less carefully guarded, would have progressed by repeated attacks of uremia to a death by the development of anasarca and exhaustion.

So the paradox appears that a person may die from Bright's disease with fairly good kidneys, proving that in this disease the brain and the kidneys are both end-organs, and that in particular cases the brain may suffer more than the kidneys.

KIDNEY SYMPTOMS LATE TO APPEAR.

This point is important in considering the early indications of chronic Bright's disease. The kidneys are insensitive organs, rarely giving rise to pain, intermittent in their action and entirely removed from direct observation. For that reason disorder of the kidneys must have reached a grave stage before it becomes a matter of consciousness. On the other hand, the brain, as the seat of consciousness, is highly sensitive to any interference of its functions. It is capable also of examination and observation by the observation of the fundus of the eye which is in close relationship to the brain.

So the brain records at all times in a more or less distinct manner the condition of the circulation and a careful study of the symptom-complex soon reveals which disturbances of the circulation indicate organic disease of the vessels and early Bright's disease. Attention and observation soon make this symptom-complex of extreme significance.

Even in cases in which chronic Bright's disease follows acute nephritis the establishment of the chronic condition is characterized by certain detectable vascular changes. In cases of acute nephritis one watches the circulatory system with anxiety because when changes are established the chance of complete recovery is diminished.

CIRCULATION SYMPTOMS.

There are, of course, disturbances of circulation connected with acute Bright's disease. The heart is temporarily debilitated so that there is often established a blowing systolic murmur at the apex. With the profound anemia and the nervous phenomena that accompany the disease this may lead to functional disturbances of the circulation. These must, however, be distinguished from the changes that take place in the arteries and indicate the transition from subacute nephritis to the chronic general condition. The same change often indicates the establishment of a chronic nephritis in cases of valvular disease of the heart that have been accompanied by prolonged congestion of the kidneys.

The contracted kidney develops gradually and only after a very long time gives symptoms referable to it.

Though we can hardly suppose that cardiac hypertrophy can be established except by some cause acting for a considerable period of time, still it is often the earliest detectable symptom of chronic nephritis. Abnormal arterial tension for the moment may be absent either on account of treatment or some other cause. A physical examination shows distinct cardiac hypertrophy, and we suspect at once the existence of a contracted kidney.

SOME EARLY SYMPTOMS.

A striking point in Bright's disease that first comes to our notice as a circulatory disturbance is the way in which it progresses. Ordinarily, a patient comes under observation, and as the result of treatment the symptoms entirely disappear and he considers himself well. Later,

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