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CLINICAL AND ANATOMIC RELATIONS IN CHRONIC NEPHRITIS *

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The pathologist who is also a clinician finds himself constantly in a state of disillusionment. He finds that many conventions of clinical medicine and anatomic facts do not always coincide, not in the broader sense of diagnosis, but in the finer interpretation of clinical data by pathologic diagnosis and vice versa. After years of such attempts at interpretation he becomes painfully aware that pathology, after all, does not explain everything in clinical medicine, and that in order to bring current medical lore and pathology into closer relationships, many readjustments are necessary. There can be only two such reasons why this should be: either clinical medicine is wrong insofar as clinical data have not been sufficiently "checked up" with anatomic facts in the past; or our pathology is wrong insofar as these facts have been falsely interpreted in terms of clinical medicine. Both these factors are at fault, but the clinician is more to blame because he shifts the entire burden of responsibility for the interpretation of clinical data on the shoulders of the pathologist, who is obviously in no position to interpret them. The pathologist, too, is at fault, not so much because he knows little of clinical medicine, but because in his enthusiasm for pure morphology he is apt to relegate pathogenesis and pathologic physiology into the background of his consciousness. No one who has pondered over these things can fail to realize that a large field for investigation lies in the closer correlation between clinical medicine and pathology. Tradition must be tested by the touchstone of critical observation.

These reflections are the result of studies on nephritis¹ recently published by the writer. In attempting to reconcile traditional clinical medicine with the material obtained at the autopsy table he found that, except with limitations, certain supposed varieties of clinical

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1. Moschowitz, E.: Hypertension; its Relation to Arteriosclerosis and Nephritis and Etiology, *Am. J. M. S.* **158**:668 (Nov.) 1919.

nephritis did not correspond with findings at necropsy; and, on the other hand, certain pathologic lesions afforded little more than a pure guess in attempting to predict clinical phenomena. In attempting to interpret these discrepancies the writer drew the following deductions: (1) That in the majority of instances what the clinician means is not "nephritis" but renal insufficiency. In other words, the diagnosis must be couched in terms of function rather than in those of anatomy. (2) That the large group of the so-called "clinical varieties" of chronic nephritis are remarkably indefinite things and have no precise morphological substratum. (3) That so-called various types of chronic nephritis are not end products but stages in a well defined pathogenesis.

1. *Chronic Nephritis Versus Renal Insufficiency*.—Before discussing the nature of these terms certain definitions are in order. The conception that chronic nephritis is a reaction to an injury has not been superseded. This is represented by more or less permanent changes in the organ in which the development of new connective tissue is the predominant lesion. All of the various components of the kidney structure partake in this change. There is no need to describe here in detail the histological characters of chronic nephritis. Briefly, the changes are the following:

(a) The glomeruli: These show a connective tissue change beginning with an increase in the intravascular and the extravascular endothelium² of the Bowman capsule, progressing to a connective tissue transformation of these cells, a thickening of the walls of the capillaries, and eventually partial or complete hyaline degeneration of the entire glomerulus, sometimes with calcification. Here I wish especially to emphasize that the process I have briefly described is wholly a vascular change and represents in miniature the same process as that termed "arteriosclerosis" affecting the larger vessels. The significance of this conception will be dwelt on later.

(b) The Epithelium: The epithelium may show no changes whatever. In the more advanced stages, it reveals degenerative changes, often fatty. In advanced nephritides much of the epithelial structure is deformed and destroyed by the encroaching widespread new connective tissue formation. With the destruction of some of the tubules compensatory changes occur in those that remain. There is an apparent proliferation with the formation of adenoma-like masses that

2. Speculation has been abundant as to whether the lining cells of the Bowman capsule are endothelium or epithelium. Certainly these cells possess all the potentialities of endothelial cells and none of epithelium. In studies upon "Angiogenesis and Ossification (Bull. Johns Hopkins Hosp. 27:71 (March) 1916). I arrived at the conclusion that the function of endothelium was not specific, but that it could assume all the characters of any cells of mesothelial origin.

contribute greatly to the glandular appearance so often present in advanced nephritides.

(c) *The Interstitial Tissue:* The changes in the interstitial tissue begin with a slight infiltration of round cells in the cortex, usually in the neighborhood of diseased glomeruli. This is, in all probability, the result of multiple minute infarcts, both of the glomeruli, the arteriae rectae and the larger vessels. In the more advanced stages the round-celled infiltration is more diffusely distributed between the tubules, producing a swollen and whitish appearance of the cortex. In the advanced stages this infiltration has been converted into frank fibrillar connective tissue of varying density. With the scar-like contraction of this tissue and the corresponding atrophy of the intervening parenchyma, there result a thinning and irregularity of the cortex, pitting and indentations on the surface, and, finally, when this scarring involves the organ diffusely, we find the so-called "contracted" kidney. This is the only true end result.

(d) *The Blood Vessels:* This obviously excludes the glomeruli. In the early stages, the changes may be few or none. In the later stages, the changes correspond to those ordinarily seen in arteriosclerosis of the larger vessels. These changes are too familiar to be described here. In addition to these changes, a passive congestion is an exceedingly common accompaniment, even without a frank valvular lesion of the heart. The significance of this lesion I shall also dwell upon in a subsequent portion of this paper.

Renal insufficiency is an exceedingly complex thing and is consequently not easy to define. The function of the kidneys as a whole, to say nothing of its separate components, is by no means a settled subject: nor are we quite sure to what extent some of the functions that have been attributed to the kidney are purely renal or of extra-renal origin. These are the reasons why it has been difficult to gauge the value of certain functional tests currently employed to test renal insufficiency, so that one must approach the study of renal insufficiency in an extremely critical frame of mind. At all events, some of these tests have proven beyond doubt, by the results of operation, by anatomical findings and otherwise, that they are of value in prognostically estimating renal insufficiency.

I shall not enter at present into a discussion of the relative values of any of these tests. This subject is still in the formative stage and is rich in speculation. In reviewing this work, however, certain facts stand out prominently. 1. That no single test is an adequate guide to renal function, but that a larger number in various combinations must be performed in order to gain an even fair perspective of the renal function. In other words, it is not function but functions that must

be determined. 2. That a single determination of one or various tests gives little prognostic information and indicates only an approximate determination of renal insufficiency at the time at which the tests are performed. To be of any constructive value these tests must be repeated during the entire course of the illness. 3. A corollary of the previous observation: That these tests are profoundly influenced by extrarenal factors. Among the most important of these factors are the following: (a) diet, especially fluid intake; (b) the condition of the patient; whether he is afflicted with a coexisting disease, etc.; (c) changes in the function of some of the other organs, the liver for instance, due either to the direct result of the kidney disease or to circulatory changes consequent upon the renal malady; (d) circulatory insufficiency. This is, in my estimation, the most important factor.

These observations lead one to suspect, what, indeed, proves to be true, that renal insufficiency cannot be estimated, except to a limited extent in terms of the amount or degree of anatomic injury to the kidney. I have for years attempted to correlate the extent and variety of damage of either of the glomeruli and tubules with the clinical findings expressive of disordered renal function, and have thus far failed to determine any precise relationship. In the vast majority of instances, it is true, a lesion of the kidney was found, but one could rarely predict clinically, except within certain limitations, what the extent and variety of the lesion would prove to be. Indeed, it is perfectly possible to find kidneys with little or no injury to the parenchyma, although all the evidence during life indicated impairment, even severe, of the renal function. On the other hand, badly damaged kidneys are often found at autopsy, although the clinical findings during life were normal or nearly normal. This is especially evidenced in the so-called "secondarily contracted kidney" or the "arteriosclerotic kidney" of Sutton and Gull. During life patients who harbor such kidneys reveal little in their urine, except occasionally traces of albumin and a low specific gravity. In such patients Larkin and Levy³ found normal nitrogen figures in the blood, except just before death. Nevertheless, such kidneys are frequently present as accidental findings; the patient does not die in uremia, as we should expect, but from an intercurrent infection, cardiac failure, arteriosclerosis, etc. These facts explain the futility of all attempts to explain symptoms, urinary findings and other tests of renal insufficiency, including hypertension, etc., on a mechanistic basis. The most recent attempt has been that of Elwyn,⁴ but Christian⁵ in an admirable critique reveals the fallacies of Elwyn's assumptions.

3. Larkin and Levy: *International Clinics*, 1918, ii, 26.

4. Elwyn: *Am. J. Urol.* **3**:47, 1919.

5. Christian: *Progressive Med.* **24**:119, 1919.

To discuss all the possible relationships of each of the numerous clinical findings and tests for renal function at present at our command would be futile in the light of the inadequacy of our present knowledge of the significance of these tests. I shall, in this place, merely discuss three of the most important, viz., albuminuria, hypertension and albuminuric retinitis.

Albuminuria.—In a previous paper I have already discussed the significance of this symptom and its relation to anatomic damage to the kidney. I tried to show that neither its presence nor its quantity is at all commensurate with the variety and degree of damage to the kidney. Albumin may be present in considerable quantities even when the kidneys are entirely normal, as in orthostatic albuminuria, or in cases of circulatory insufficiency due to valvular heart disease, disappearing when sufficiency has been restored. In both instances, especially the latter, the presence and disappearance of the albumin cannot be explained on other than purely physiologic grounds. On the other hand, albumin may be absent or practically absent, even when the kidney has suffered extensive damage, as in the so-called "contracted" kidney. It apparently makes little difference whether the glomeruli or the tubular portions are involved or both; the presence or quantity of albumin bears little relationship to the amount or degree of damage to the kidney.

I am willing to concede, indeed, I have demonstrated this to my own satisfaction, that albumin is usually proportional to the extent and degree of the tubular degeneration associated with many infections, (e. g., typhoid fever, pneumonia, subacute bacterial endocarditis) the albumin resulting from cell autolysis or increased filterability, but I do not believe that the changes in the tubular epithelium are to any great extent a determining factor in causing albuminuria in the other nephritides, especially of the chronic variety.

These observations leave us no ground for assuming that the kidney is merely a filtering organ, an assumption that physiologists have already amply disproven. The presence of albumin is determined by other factors than mere damage to the glomeruli or the tubular cells. Pressure and volume changes within the blood vessels, the composition of the blood, especially of the threshold bodies⁶ and as yet little understood colloid changes in the plasma are equally, if not more, important factors in causing albuminuria, as are pathologic changes within the kidney.

I am fully aware that albumin is probably not the main or even the earliest evidence of renal insufficiency. As Myers and Kilian⁷

6. Cushny: *The Secretion of Urine*, London, 1917.

7. Myers and Kilian: *Am. J. M. Sc.* **157**:674, 1919.

have shown, diminished phthalein and increased blood urea and creatinin figures may be found even when albumin is absent from the urine. I simply mean to convey that albuminuria bears no consistent relation to the amount or degree of pathological changes within the kidney, that is, so far as our microchemical methods permit us to determine.

Hypertension.—In the paper already mentioned I submitted the thesis that hypertension was not a consequence of nephritis or arteriosclerosis, but that it was a primary compensatory phenomenon due to unknown causes, and that the nephritis and arteriosclerosis represented secondary changes due either to the hypertension itself or to the cause or causes of the hypertension. I shall not here detail the lines of reasoning that led me to this conclusion; I shall simply say that subsequent observation and reflection have confirmed me in this belief. My conception expressed in terms of clinical medicine is the following: The vast majority of the nephritides or cardionephritides began clinically as cases of so-called "essential" hypertension; i. e., the patient reveals on physical examination a greater or lesser degree of hypertension, greater on the diastolic scale, with or without cardiac hypertrophy, but without evidence of renal insufficiency as apparently evidenced by the absence of albumin or casts. I am not aware at this time of studies that show the status of other tests of renal insufficiency in clinical cases of essential hypertension, but I would not be surprised if such tests showed evidences of renal insufficiency, even though albumin were absent. In any event, if one follows such cases, as I have done, one finds generalized changes occurring in the tissues of the body, especially in the arteries, notably the retinal, the coronaries, the cerebral and the renal.

If arteriosclerosis, the albuminuric retinitis and nephritis are analyzed in their morphologic and genetic aspects, no one, I believe, can escape the conclusion that they are all manifestations of one and the same lesion, a primary vascular productive inflammation affecting all the blood vessels from the capillaries to the aorta. In the kidney, as I have described, and as all authorities are agreed, the primary change is in the glomeruli. This represents the type known as "glomerulonephritis." As the process advances, the larger vessels become affected. All subsequent lesions in the kidney may be traced morphologically from these primary changes in the blood vessels of the organ. Owing to the destruction or impoverishment of the blood supply of focal areas in the kidney, smaller or larger infarcts occur which in turn produce new connective tissue, first in the form of round cell infiltration, and later in the form of fibrillar and hyaline connective tissue. Much of the degeneration of the epithelium can be explained

by the same pathogenesis, although some of it is probably due to waste products from the altered metabolism. The disappearance and malformation of the tubules are accounted for in large measure by the destructive effects of the new connective tissue transformation.

The kidney in chronic nephritis may, therefore, be conceived as a tissue filling the interstices of a framework of blood vessels, depending on the integrity of these blood vessels for its preservation and function. When this framework is injured, the organ, like a house, will fall to pieces. This is the reason why I agree with those who hold that chronic nephritis is a primary vascular disease, e. g., Jores. *Chronic nephritis and arteriosclerosis, therefore, are, to my mind, one and the same lesion.* I believe it is incorrect to view arteriosclerosis, either clinically or pathologically as a disease affecting the larger vessels only. It affects the entire arterial system, from the capillaries to the aorta.

The lesions in chronic nephritis, as a result of this local arteriosclerosis, may be viewed as representing a continuous series of granulomatous changes, and all phases of the morphology may be explained in the light of such changes. The various lesions encountered in chronic nephritis are subject to the identical laws of morphology as apply to granulomatous changes in other tissues from whatever causes. Thus the changes in the kidney are entirely analogous to those witnessed in the various stages of cirrhosis of the liver, or of chronic oöphoritis or in an ordinary granulating wound.

Retinitis.—A more readily grasped analogue, which few appreciate, is the complete identity even down to the minutest details between the lesion of chronic nephritis and those of albuminuric retinitis. Accept any description of the pathological lesion in retinitis, that of Collins and Mayou⁸ for instance, and the lesions in both nephritis and retinitis are paralleled in every detail, both in morphology and in the order of their appearance. Indeed, these authors admit that the lesions "are in reality degenerative processes secondary to changes in the retinal vessels." This analogue is, I believe, a strong support for the thesis that the nephritis is not primary but a result of the hypertension: for this type of retinitis as far as my observation leads me to believe, is never present unless hypertension is or has been present, and if the retinitis is sequential to the hypertension or to the cause or causes of the hypertension, it seems to be a logical deduction that the nephritis; which is the identical lesion, cannot but be a consequence as well. It would be an interesting study to see how far the nephritis and the retinitis parallel each other in gravity.

8. Collins and Mayou: *Pathology and Bacteriology of the Eye*, Philadelphia, 1911.

Depending, therefore, on which organ is most affected a certain clinical picture is developed, which may be that of generalized arteriosclerosis, a localized arteriosclerosis (cerebral arteriosclerosis) apoplexy, aortitis, coronary sclerosis (resulting in chronic myocarditis), and finally chronic nephritis. The patient usually presents himself at a time when the more advanced stages are manifest, but if we observed the real beginnings of the disease, a circumstance, as Mackenzie emphasizes, of fundamental importance in the biological study of disease, I believe that practically all such cases would have revealed the clinical syndrome of "essential hypertension." Certain it is, that the presence or degree of hypertension bears little or no relation to the presence or degree of damage done either upon the arteries or the kidney. Just as we see hypertension often associated with little or no disease of the arteries and profound disease of the arteries (decrecent type of Allbutt) associated with no elevation of blood pressure, so we see increased blood pressure where the kidneys are normal or practically normal⁹ (Hirschfelder,¹⁰ Mosenthal¹¹) while, on the other hand, normal blood pressure may be present in patients whose kidneys are profoundly diseased. The latter phenomenon is seen not uncommonly in association with the senile or "arteriosclerotic" kidney, a form which corresponds, in my belief, to the decrecent type of arteriosclerosis and is, moreover, indistinguishable morphologically from the contracted kidney resulting from a progressive glomerulonephritis.¹² Indeed, all attempts to correlate these two phenomena have thus far failed, either when we conceive of the destructive process within the organ as a whole, or analyze it in terms of the different components of the kidney structure. This is one of the main arguments I have adduced to support the belief that the hypertension is the primary and the arterial and kidney lesion the secondary phenomenon. Genetically, the hypertension certainly preceded the signs of nephritis in a very large percentage of all cases, as any clinician with experience can testify. Moreover, this belief is supported by the fact that all other chronic nephropathies, morphologically easily definable

9. I have recently acquired two such kidneys in patients in whom the systolic blood pressure was over 200. These will be reported later.

10. Hirschfelder: *Diseases of the Heart and Aorta*, Philadelphia and London, 1918.

11. Mosenthal: *Medical Clin. N. America*, July, 1917, p. 101.

12. Vide MacCallum (*Textbook of Pathology*, 1917): "The gross appearance of such a kidney (arteriosclerotic) differs in no way, therefore, from the end result in a protracted glomerulonephritis (the so-called secondarily contracted kidney), and in all probability something similar may result if the destruction be severe enough and time be given in the case of the tubular and interstitial forms. As a matter of fact, except perhaps through the presence of the strikingly thickened blood-vessels, it is difficult if not impossible to distinguish microscopically the types of ultimately contracted kidney."

from that which I have described, amyloid, subacute bacterial endocarditis, chronic surgical lesions, experimental destructions, congenital cystic kidneys, parenchymatous nephritis,¹³ etc., are never associated with hypertension.

The reason why we cannot predict the variety or degree of changes, in other words, the "type" of kidney that we shall find from clinical findings alone, lies, I believe, in the fact, that these changes or "types" do not represent end products, but only phases of a definite progressive morphologic pathogenesis, so that the "type" of kidney found at autopsy does not represent in any sense the final result, transcribed in reports as the "cause of death", but rather, that particular stage of the disease in which the patient happened to die, whether from an apoplexy or coronary thrombosis or uremia. The nephritis is therefore a glomerular nephritis in the beginning; a diffuse or granular nephritis, which may be white or red or mixed, large or small, in the next stage; and a contracted kidney in the final stage. The only stage that can on morphological grounds be consistently defined as an "end product" is the final stage of such a pathologic process, the so-called "contracted" kidney. Genetically, therefore, it is reasonable to suppose that in the so-called "essential" hypertension the kidneys present little damage, limited to the glomeruli where the early changes in chronic nephritis originate; while in the hypertension in which renal functional tests show a profound insufficiency the damage to the kidney is diffuse and extreme. I cannot state this with any reasonable degree of exactitude, because both my experience and the reported observation are inadequate. The difficulty is that patients with "essential" hypertension do not often die in that stage.

The evidence which I have presented is sufficient, I believe, to demonstrate that it is extremely hazardous to predict the amount and degree of damage in the kidney by clinical findings alone. It now remains to determine, if possible, the factor or factors that cause this discrepancy. Not being anatomic, the factors must be physiologic. This is necessarily so, because productive inflammations never completely disappear.

I am convinced that by far the largest factor or rather the largest common denominator of the entire problem is circulatory insufficiency. No one who has seen anything of the clinical phases of "chronic nephritis" can fail to be impressed by the dominating rôle of circulatory insufficiency from the very beginning of the malady to the end. In the earlier stages, whether we view it in the light of a compensatory mechanism or not, this insufficiency is manifest in a more or less persistent hypertension, with a resulting hypertrophy of the left ven-

13. Epstein: J. A. M. A. **69**:444 (Aug. 11) 1917.

tricle. In the further course of the disease, other evidences of a progressive circulatory failure arise. These are increased rapidity of the heart action, disturbances in rhythm (gallop rhythm, extrasystoles, auricular fibrillation) and signs of stasis (enlarged liver, hypostasis, edema of the ankles, etc.). If coronary sclerosis occurs, with resulting fibrotic changes in the myocardium due to the blocking of the terminal branches of the coronary vessels, all signs of a real anatomical myocarditis become manifest. In addition to those already mentioned, two very important signs now appear. The first is a lowering of the blood pressure; the second is a change in the electrocardiographic tracing, described by Oppenheimer and Rothschild¹⁴ as "arborization block." During this stage of the illness, which may be described as the middle phase, the patient is responsive to digitalis, and this, despite the fact that the hypertension may not be influenced to a considerable degree; so that by the continuous administration of this drug we are able to keep the subjective and objective evidences of circulatory insufficiency at a certain level; the circulation, in other words, may be said to be compensated. When the signs of circulatory insufficiency increase (decompensation) an increase in the quantity of digitalis combined with bodily rest usually suffices to restore the patient to his previous condition. Finally, it is noted that the attacks of decompensation increase in severity, frequency and duration. All the signs of a grave circulatory insufficiency ensue; the patient no longer responds to circulatory "stimulants" and unless his life is cut short by an apoplexy or an attack of angina pectoris, he dies from a pure circulatory failure or from uremia.

I have used the term "circulatory insufficiency" in a rather broad sense, for I am fully aware that this term comprises many elements aside from blood pressure, changes in rhythm, etc., such as myocardial tonus, blood velocity, volume flow and the viscosity of the blood, but until further investigation enlightens us on the relative importance of these elements in bringing about circulatory insufficiency, we must depend on a clinical concept of this phenomenon.

At all events, the similarity of the circulatory insufficiency noted in the nephritides associated with hypertension and that witnessed in frank valvular disease of the heart is striking. They parallel each other closely not only in signs and symptoms but also in the sequence of clinical events and their response to treatment. The same laws of cardiodynamics apply to both. Furthermore, there is one lesion representing circulatory insufficiency common to both, namely, congestion (*Stauung*) of the internal viscera. This is shown in brown induration of the lungs, nutmeg liver, chronic congestion of the spleen and

14. Oppenheimer and Rothschild: J. A. M. A. **69**:429 (Aug. 11) 1917.

cyanotic kidneys. These lesion I have found exceedingly common in autopsies upon cases of "chronic nephritis." The point I wish to bring out is that clinically tests for renal insufficiency are usually coordinate with evidences of circulatory insufficiency, and that the functional state of the circulation has a greater effect in increasing or decreasing the evidences of renal insufficiency than perhaps any other factor.

Not all the conventional functional tests are affected in this manner; I refer especially to quantity of urine, albumin, phthalein, urea and nonprotein nitrogen. Creatinin, uric acid and salt are not so readily affected. The figures rise and fall depending on the condition of the circulation. When the heart action is good, the figures approach normal, and conversely, when it is bad; just before death the figures show the widest variation from the normal.

These observations, it seems to me, receive a strong corroboration from what we find in cases of circulatory insufficiency due to pure valvular disease in which a genuine anatomic nephritis can definitely be excluded. We all know that in mild compensated valvular lesion of the heart, tests for renal insufficiency usually reveal normal findings. We also know that when signs of myocardial or, perhaps, better said, circulatory insufficiency develop, signs of renal insufficiency manifest themselves. There is oliguria; albumin and casts appear, phthalein excretion is reduced, and the blood urea nitrogen figures are above normal. When compensation is restored by rest and digitalis, these promptly disappear. Very often patients exhibit evidences indicating a combination of cardiac and renal disease so that there may be doubt as to how far the malady is cardiac or renal. With the improvement in the condition of the circulation, all signs of renal impairment disappear. If they do not completely disappear we may accept this as evidence that either complete compensation is no longer possible, or, less likely, that an associated productive renal lesion is present.

Observations of Rowntree, Geraghty and Fitz¹⁵ are extremely important as confirming this view. They found in moderate experimental congestion of the kidney, that the excretion of salt, iodid and lactose may be interfered with. The excretion of the phthalein may be normal, but if the congestion is extreme, it may be decreased. "Therefore, in experimental congestion, functional pictures indistinguishable from those of mild or advanced nephritis without cardiac decompensation have been found. The gradual amelioration of experimental congestion is accompanied earliest by an increased phthalein output, later by improvement in salt and iodid excretion, and lastly by a slight amelioration of the delayed lactose excretion." Rowntree

15. Rowntree, Geraghty and Fitz: *Arch. Int. Med.* **2**:258 (Aug.) 1911.

and Fitz¹⁶ found that clinically cases of passive congestion behaved in a similar way.

These observations, it seems to me, render the examination for renal insufficiency of little value when made during the attacks of decompensation. For purposes of prognosis such tests, as Christian insists, should be made in the interval.

Anatomic Varieties of Chronic Nephritis.—From the foregoing discussion it may be gathered that clinical findings offer little or no basis for furnishing a classification of the forms of chronic nephritis that I have described. This form has received a host of names in textbooks; glomerulonephritis, productive nephritis, diffuse nephritis, interstitial nephritis, arteriosclerotic disease of the kidney, arteriocapillary fibrosis, primary and secondary contracted kidney, etc. Each of these names conveys some aspect of the pathology, but in order to obtain an adequate concept, which must include the origin, spread and progress of the disease, the structures involved and the physical characters of the diseased organ, all of these adjectives would be necessary as prefixes. No single name or group of names can suffice. It seems to me that the term "arteriocapillary fibrosis," devised by Gull and Sutton, is the most applicable. However, it may be taken for granted that none of the methods of clinical examination at our command can enable us to foretell whether we shall find such a kidney in the stage of a glomerulonephritis or that of the large or small red kidney, or the granular kidney or the contracted kidney. All that we have the right to say is that we shall find a kidney of this particular type. It has seemed to me from the few observations I have made, that the longer the duration of the disease, the more progressive the lesion. This is certainly a reasonable expectation.

The one unfailing clinical finding associated with this form of nephritis is hypertension. No other nephropathy is associated with this phenomenon. There are two exceptions to this rule. (1) Cases that have developed coronary sclerosis with symptoms of angina pectoris. The resulting fibrous myocarditis causes such an insufficiency of the heart muscle as to apparently neutralize the increased peripheral resistance. Anamnesis of such patients reveals the interesting fact that previously, perhaps a year or two ago, the blood pressure had been considerably elevated. I have a number of records of such cases. I have seen one case of angina pectoris in which this decrease occurred under my observation. In another, the associated interstitial myocarditis was proved by autopsy. (2) Cases of "decreascent" nephritis. I call this variety decreascent because it clinically corresponds to the decreascent arteriosclerosis of Allbutt. These patients reveal at

16. Rowntree and Fitz: Arch. Int. Med. 2:258 (Aug.) 1911.

necropsy extensive general arteriosclerosis and the so-called "arteriosclerotic" or "senile kidney" or the "arteriocalillary nephritis" of Sutton and Gull. As Allbutt has pointed out in connection with the decrescent arteriosclerosis, so in this form of nephritis there is no hypertrophy of the left ventricle, and it is the exception rather than the rule for these patients to die from the causes common in the diseases of the hypertensive type.

The other sign characteristic of the hypertensive type of nephritis is an albuminuric retinitis. As far as I am aware, this type of retinitis is practically always associated with hypertension either present or past.

There are, however, other chronic nephropathies with different genetic and morphologic characters of their own, which while offering many of the signs and symptoms of the hypertensive type, yet possess certain symptoms and findings sufficiently characteristic to render them clinical entities as well. Most of the tests for renal insufficiency are common to both.

I shall exclude for obvious reasons the chronic surgical and specific nephropathies.

There remain for discussion the following varieties of chronic nephritis:

1. *Parenchymatous nephritis or nephrosis (Epstein)*.—Although pathologic studies of this variety of nephritis are still lacking, it seems necessary, because of its clear cut clinical characteristics, to recognize this malady as of an entirely different type from the foregoing. This type of nephritis is a disease of youth or middle age. The urine is usually diminished in amount, rich in normal solid constituents and in albumin and casts. Edema and anasarca are early and prominent symptoms. But the most characteristic findings, according to Epstein, are the impoverishment of protein in the blood plasma, with an increase in the globulins, and a relative or absolute increase in the lipoid and cholesterol bodies. Epstein has obtained excellent results in this variety of nephritis by a diet high in protein and low in fats.

2. *Chronic glomerulonephritis associated with subacute bacterial endocarditis (Streptococcus viridans)*.—While in the literal sense this lesion is not a chronic one, except in the healed stage, it is included in this discussion. This variety was first described by Löhlein¹⁷ and more recently by Baehr.¹⁸ The lesion according to Baehr is characteristic of subacute bacterial endocarditis and occurs in no other hematogenous bacterial infection. The lesion is a progressive one, is limited strictly to the glomeruli, and consists in swelling, degeneration and desquamation of the cells of Bowman's capsule, later followed

17. Löhlein: Ueber die entzündlichen Veränderungen der Glomeruli bei menschlichen Nieren und ihre Bedeutung für die Nephritis, Leipzig, 1906.

18. Baehr: Proc. New York Path. Soc., December, 1911.

by fibroblastic changes in the capsule and eventually (in the healed stages) by hyalinization of this mass. The new connective tissue formation never proceeds beyond the confines of the glomerulus. This lesion affords to my mind a convincing refutation of the argument of those who regard a glomerulonephritis as the primary cause of a hypertension.

Viewing the renal lesion separately, aside from the associated cardiac lesion, the one clinical finding characteristic of this lesion is hematuria which is fairly constant. If the bleeding is not macroscopic it is microscopic.

3. *Amyloid kidney*.—An amyloid kidney is a manifestation of general amyloid disease. The amyloid, greater or lesser in amount is deposited almost entirely in the blood vessels, in the glomeruli, the arteriae rectae and the larger vessels. Usually, there is a profound fatty or lipid degeneration of the tubular cells; occasionally the amyloid is deposited in a kidney the seat of a widespread connective tissue change.

Hypertension, hypertrophy of the left ventricle and retinitis are absent in amyloid disease of the kidneys. As a rule, the urinary findings are fairly characteristic. The urine is light in color and of a low gravity; albumin is plentiful, and casts especially of the waxy variety are fairly abundant. The nephritic signs are usually so overshadowed by the underlying general condition, usually tuberculosis, that they play a small rôle in causing the death of the patient. Such patients die, as a rule, from cachexia.

CONCLUSIONS

1. Clinical findings in nephritis cannot be interpreted in terms of morphologic pathology, except to only a very limited degree. This is due to (a) various extrarenal factors; (b) to the fact that the "type" of the kidney as found at necropsy does not represent an end product but a stage in a fairly well defined pathogenesis. The lesion begins as a glomerulonephritis and all subsequent stages down to the contracted kidney can be traced and are explainable, according to established genetic and morphologic criteria, from this lesion.

2. Thus the conception is set forth that chronic nephritis is essentially a vascular disease, beginning in the capillaries (glomeruli) and extending therefrom to the larger blood vessels. The term "arterio-capillary fibrosis" devised by Sutton and Gull, appears to fit the nature of the malady better than any in current use. In this light chronic nephritis and arteriosclerosis are one and the same lesion. Arteriosclerosis is conceived not as a disease affecting only the larger vessels, but of the entire arterial system from the capillaries to the aorta.

3. The lesions in albuminuric retinitis are analogous morphologically with those of chronic nephritis. This analogy and the sequential relation of albuminuric retinitis to hypertension is a strong argument in favor of the previously submitted thesis that nephritis is not the primary cause of hypertension but is a secondary consequence to the hypertension itself or of the cause or causes (unknown) of the hypertension.

4. The presence or extent of albuminuria bears no consistent relationship to the degree or variety of anatomic destruction of the kidney. Physiologic conditions are more important factors in causing albuminuria than anatomic disturbances in the kidney.

5. The presence or degree of hypertension bears no consistent relationship to the degree or variety of anatomic destruction of the kidney. The probability is very strong that *clinically* cases of chronic nephritis begin as cases of "essential hypertension." If patients with essential hypertension are followed over a long period of time there progressively develop the clinical evidences of either a generalized arteriosclerosis, a localized arteriosclerosis (cerebral endarteritis, coronary sclerosis, albuminuric retinitis) or a renal arteriocapillary fibrosis (chronic nephritis) or a combination of these.

6. The only variety of chronic nephritis that can be reasonably termed an end result is the so-called "contracted" kidney. The contracted kidney arising from a chronic glomerulonephritis (secondary contracted kidney) is morphologically indistinguishable from the "primary contracted" kidney. A "contracted" kidney may be unassociated with hypertension, left ventricular hypertrophy or evidences of renal insufficiency. In such instances, the patient does not die a "renal" death. This kidney is termed the "decreased" kidney since it corresponds clinically to the "decreased" variety of arteriosclerosis described by Allbutt.

7. The most important extrarenal factor in modifying renal insufficiency in "arteriocapillary fibrosis" is circulatory insufficiency. Other things being equal, improvement in circulatory insufficiency is coordinate with improvement in renal insufficiency, and vice versa.

8. There is a striking parallelism between the signs of renal insufficiency in arteriocapillary fibrosis associated with hypertension and those noted in frank valvular lesions of the heart. Decompensated phases of valvular heart disease may show evidences of renal insufficiency indistinguishable from those witnessed in chronic nephritis.

9. As a consequence of these studies the following clinical pathologic classification of chronic nephritis is submitted: 1. Arteriocapillary fibrosis. 2. Chronic glomerulonephritis of subacute bacterial endocarditis. 3. Amyloid kidney. 4. "Chronic parenchymatous nephritis" or nephrosis (Epstein).