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INTRODUCTION

Richard Bright in 1827 first noted coagulation of protein on heating urine(16). This became and still is the chief criterion of kidney disease. Thomas Addis(5) states that an individual who excretes more than thirty mg. of protein per twelve hour specimen and in whose urine five thousand casts per twelve hour specimen are found should be classed as having nephritis. Henry A. Christian(13) defines nephritis as a,"diffuse, more or less progressive, degenerative or proliferative lesion involving in varying proportion the renal parenchyma, the interstitial tissue and the renal vascular system."

The purpose of this paper is to give the physician who meets these cases of nephritis in his general practice a better understanding of the lesion in the kidney he is dealing with as a disease entity.

As one begins to read the literature on this subject he is appalled by the apparent confusion that exhists concerning nephritis. The problem of classification tends to confuse one, there appears to be no general agreement and no sure ground on which to stand. This is largely due to the rapid accumulation of new knowledge concerning the function of the kidney and the pathology as well, both of which I shall attempt to present, and also the failure to correlate.

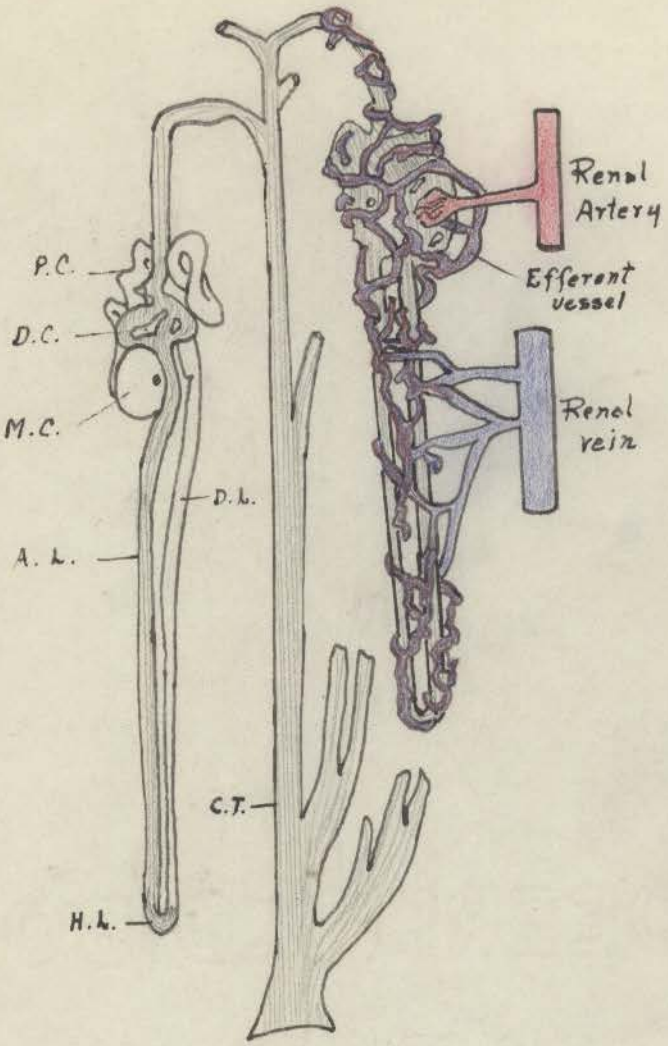
The terminology itself is often perplexing for

a wide variety of terms are often used by different investigators to describe the same disease process. In fact it often seems that the name of the disease has seemed paramount in the mind of the worker.

Therefore I shall try to present a simple approach to what is happening in the kidney during nephritis. To this end the following subjects have been dealt with in the order named: 1. Anatomy and histolgy of the kidney. 2. The physiology of the kidney function. 3. The problem of correlating pathological and clinical findings. 4. The problem of classification. 5. A classification of nephritis into two pathological groups. 6. The pathology of nephritis in which the lesion is confined to (a) the secretory part of the nephron and (b) the vascular part, with cases to illustrate each.

Embryonically the kidney is mainly derived from the surface of the coelom and is thus a mesodermal structure. It is built up of a large number of units, each of which is formed by a long unbranched tube, closed at one end and running a somewhat devious route through the cortex and medulla, to terminate with other tubes like it in a collecting tubule which opens into the pelvis of the kidney. This collecting tubule carries the fluid from the secretory cells to the pelvis and hence out the ureter. It apparently has nothing to do with the formation of the urine. Due to this tubular system, Howell suggests that the kidney may be spoken of as a compound tubular gland (14).

The constituents of the urine that is secreted by the kidney is determined by the tubules of the "gland". The tubule begins in what is known as Bowmans capsule. Bowmans capsule has the appearance of a hollow sphere and is made up of a delicate epithelium. One side of this capsule is invaginated by a twining mass of capillaries and arterioles. This vascular nodule nearly fills the invaginated cavity. The capsule, together with the vascular nodule or tuft it surrounds, is designated as the Malpighian body. The capsule opens into or is continuous with the tubule proper, which doubles and twists



On the left, the tubule is drawn after a diagram of G. C. Huber's. The tubule is outlined from the capsule to the loop of Henle and is shaded from that point to the end of the collecting tubule. On the right, a diagram of the circulation is added. M.C. Malpighian corpuscle. P.C. Proximal convoluted tubule. D.L. Descending loop. H.L. Henles loop. A.K. Ascending loop. D.C. Distal convoluted tubule. C.T.Collecting tubule. (Taken from Cushny"The Secretion of Urine")

in the region of the capsule and then straightens out toward the capsule, forming a loop differentiated as the Loop of Henle. Now from the capsule, the tubule again makes a second but shorter series of convolutions known as the distal convoluted tubule to end in the collecting tubule (14). The collecting tubules empty into the final common pathway, the ureter which passes on down to the bladder. It is estimated that the kidney is made up of 2,000,000 such units as have just been described(3) and (13).

Histologically the tubule proper is composed of epithelial cells of three different types. The proximal convoluted tubule and the upper part of the descending limb of Henles loop are lined with high cells standing on a basement membrane and showing striations in the outer zone. These striations are rows of granules running toward the lumen and terminating in fine granules which appear to stand in close relation to the prominent striated border which forms the internal border of the cell. The narrow portion of of the descending loop or limb of Henle is lined with epithelium of a thin p pavement type with large nuclei making this part very thin walled. The lowest part of the descending limb and the loop itself are lined by a short columnar type

of cell with an outer finely striated dark zone and an inner lighter one without the striated free border. This type continues with little further variation until the collecting tubule is reached. The second tubule resembles the proximal one in character, except in possessing no striated border, and perhaps failing to stain so readily. The epithelium throughout the tubule and capsule rests on a fine basement membrane and is supported by reticular tissue in which lie the abundant blood, lymph, and nervous supply(13).

The blood supply of each secretory unit consists of arteries that extend through the medulla to the cortex and give off a series of side branches(13). These are the afferent vessels each of which breaks up into a small capillary tuft or nodule already spoken of and referred to as the glomerulus which is enclosed by the invaginated Bowmans capsule. The epithelium of the capsule is reflected over the glomerulus. The capillaries collect into an efferent vessel which is slightly narrower than the afferent artery. This again breaks into a series of capillaries on the wall of the tubules and forms their only blood supply(13). This second set of capillaries ends in veins which collect to form the renal vein.

Thus the blood flows first through the glomerulus

supplying Bowmans capsule and then is distributed to the tubules including the loop of Henle. It may then be noted (6) that practically the whole of the blood supplied to the tubules first passes through the capillaries of the glomerulus.

The lymph vessels of the kidney (25) form a meshwork round the tubules and collect into larger trunks which issue from the hilus. Lymph also escapes through a number of vessels which accompany the veins comming from the convex surface of the kidney.

The nerves of the kidney although small are about fifteen (7) in number. They have small ganglia developed upon them and are derived from the renal plexus, which is formed by branches from the celiac plexus, the lower and outer part of the celiac ganglion and aortic plexus, and from the lesser and lowest splanchnic nerves (25) and (14). They accompany the renal artery and its beanches and are distributed to the bloodvessels and to their cells of the urinary tubules.

With these salient points regarding the anatomy and histology of the kidney in mind let us undertake to briefly point out the normal functioning and physiology of the kidney. First, what is the function of the kidney as a vital organ in the body? The purpose of the kidney is to secrete the urine which is formed by the glandular

and tubular structures of the organ made up of the glomerulus, proximal and distal convoluted tubules and the loop of Henle and in turn excreted by the straight connecting tubules. In the excretion of this waste product urine, the kidney accomplishes a threefold (7) function: first, the elimination of the end products of protein metabolism such as urea, uric acid, creatinine, sulphates, and phosphates.. These substances exist in the blood in small quamities and in the urine in large quanities. They have been called non-threshold substances by Cushny (13) because they are excreted accorrding to their entire amount in the blood and not because of an increase in their threshold value. Second, to help maintain a normal blood volume and composition. Thus the kidney assists in the conservation of these substances of metabolism and of water in constant amounts, sufficient for the needs of the body. They hold back entirely the substances which the organism needs in its economy and discharges the remainder through the act of excretion. Third, to assist in the regulation of the acid-base balance of the body. Basic and acid radicals are ingested with the food. Phosphorous and sulphur are also taken in with foods and are oxidized in the body to form phosphates and sulphates. Non-volatile acids in combination with bases are eliminated through the kidney

while volatile acids are eliminated through the lungs. These factors are significant in maintaining the acid-base balance of the blood.

There have been many answers through the years to the question of how the kidney functions and accomplishes those tasks pointed out in the foregoing paragraph. The work published by Bowman in 1842 accorrding to A.M.Richards (23)furnished no evidence that any connection exhisted between the Malpighian body and the uriniferous tubules. Bowman did proove that the capsule of the Malpighian body is the expanded extension of the membrane of the tubule. His first identification of the complete unit of structure by which urine is formed must therefore be regarded as the beginning of the modern study of renal function. Bowman also gave one of the earliest theories as to the part played by the tubule and glomerulus in the formation of urine. Richards records (23)Bowmans own statement as follows: "Thus the Malpighian bodies are as unlike as the tubules passing from them are like the membrane, which, in other glands, screens its several characteristic products from the blood. To these bodies therefore, some other and distinct function is with the highest probability to be attributed. The peculiar arrangement of the vessels in the Malpighian tufts is clearly desiigned to produce a retardation in flow of blood through them. It would indeed

be difficult to conceive a disposition of parts more calculated to form the escape of water from the blood than that of the Malpighian body. A large artery breaks up in a very direct manner into a number of minute branches, each of whichnsuddenly opens into an assemblage of vessels of far greater aggregate capacity than itself, and from which is but one narrow exit. Hence must arise a very abrupt retardation in the velocity of the current of blood. The vessels in which this delay occurs are uncovered by any structure. They lie bare in a cell from which there is but one outlet, the orifice of the tubule. This orifice is encircled by cilia in active motion directing a current toward the tubule. These exquisite organs must not only serve to carry forward the fluid already in the cell, but must tend to removepressure from the free surface of the vessels, and so to encourage the escape of their more fluid contents. Why is so wonderful an apparatus placed at the extremity of each uriniferous tubule if not to furnish water to aid in the separation and solution of the urinous products from the epith lium of the tubule?"

This suggestion that the glomerulus is the chief site of fluid elimination in the kidney developed into universal belief. However Bowman had not given any clear idea of the nature in which the glomerulus separates water from the blood.

Carl Ludwig in 1884 offered a conception of the process by which fluid is separated from the blood in the glomerulus (14) and (13). Using anatomical facts demonstrated by Bowman and confirmed by himself and applying the principles of hydraulics, he stated that a significant pressure must be exerted by the blood within the glomerular capillaries upon their walls, and that this pressure must result in the filtration of a certain amount of fluid through them. He assumed that the membrane through which the fluid passed was normally impermeable to proteins to fats, and to salts which might be combined with these, and hence that the urine as formed in the glomerulus is a protein free filtrate containing blood crystalloids in the proportion in which they exist in the blood. There would thus be formed at the beginning of the uriniferous tubules, a complete but diluted urine which became concentrated by diffussion as it passed along the tubules. This is the inevitable corallary, for no other process could account for the differences in composition between a blood filtrate and the urine as it leaves the kidney. Three types of experiment were carried out to proove this (23):

(1) Proof of parallelism between urine elimination and blood pressure.

(2) Application of physics principle: in order to separate dissolved substance from its solvent by filtration through a membrane, permeable by the solvent but not by the dissolved substance, filtration pressure must be greater than the osmotic pressure of the dissolves substance. This

was worked out to proove that the only substance of plasma which could physically be held back in the glomerulus are the proteins; hence the fluids separated in the glomerulus must be the water of the blood containing all dissolved substances except proteins.

(3) It was alsomprooven that physical factors ratherothan "vital" or "secretory" were at work by noting diuresis following ingestion of sodium chloride and unaccompanied by increase in oxygen utilization or carbon dioxide formatiân .

These facts led Baylis(48) to sav, "The evidence for this theory of glomerular filtration is overwhelming".

Cushny has brought forward thetheory known as the Modern Theory of renal secretion. It varies little from the theory advanced by Ludwig which it accepts but also develops and makes an added contribution. In this theory (13) he states that the secretion of urine consists of two distinct processes differing not only in site but in nature, The first of these, the filtration occurrs in the glomerulus and is purely a physical phenomena as Ludwig held. The second, the reabsorption occurrs in the tubules and depends on the vital activity of the epithelium which Cushny accounts for in the following manner: "The energy supplied by the blood pressure , that is indirectly by the heart, is insufficient to perform the whole

work of secretion, and the kidney must itself furnish the greater proportion of the energy required. The blood pressure in the glomerular capillaries suffices for filtration, however, and the capsule filters off the colloid substance of the blood plasma by which it is impermeable, while allowing the rest of the constituents to pass through without alteration in their relative concentrations; the glomerular filtrate is thus practically deproteinized plasma. In its passage through the tubules this fluid is altered by the absorption of certain constituents by the epithelium; the passage of the absorbed water and solids of the glomerular filtrate through the epithelial layer entails the expenditure of energy by the cells; it is an active absorption, not the passive diffussion which was believed by Ludwig to be sufficient."

It is now obvious from the foregoing discussion of kidney function that any discussion of renal pathology, i.e. the renal lesion in Brights disease, must be based on a consideration of changes that take place in the nephron or kidney unit (6). The glomerulus, tubule, and blood vessels going to make up this unit are histologically and physiologically related. In nephritis the pathology focusses on these elements and their essential relationship.

It must be understood that since the elements of the unit are so closely related functionally, it is impossible to have injury to one part without injury ultimately resulting in the other two if the process is not checked rather promptly (3). If the glomerulus is injured the corresponding tubule suffers as it receives its blood supply from the afferent arteriole as it leaves the glomerulus (45). Also a narrowing as from sclerosis of the afferent arteriole will result in a decreased blood supply to both glomerulus and tubule (31). Damage from one part means damage to another part.

From an anatomical standpoint alone, it would seem apparent then that there could be three types of nephritis corresponding to the three divisions of the nephron (3). The disease process could affect the glomerulus, tubules, or blood vessels. But here is introduced one of the most illusive problems of medicine, one that has baffled pathologists and clinicians alike since 1827 when Richard Bright a physician in Guys Hospital in London first published, "Reports of Medical cases Selcted with a View of Illustrating the Symptoms and Cure of Disease by a Reference to Morbid Anatomy", with the sub-head, "cases illustrative of some of the appearances observable in the examination of diseases terminating in Dropsical Effusion and first of the Kidney" (16). Twenty-four cases eighteen of which were fatal were reported with a de-

scriptionof the post-mortem findings. The studies of these patients with the deductions will link forever the name of Richard Bright to nephritis in the sense of having prooved the relationship between dropsy, albuminuria, and a renal lesion. Bright heated urine in a spoon over a candle and noted coagulation in these patients. This became and still is the criterion of a renal lesion (16). Bright opened the problem then of trying to establish a consistent correlation of symptoms and findings physi cal to those noted on post-mortem. Bright wrote, "Four observations I have made, I have been led to believe that the e may be several forms of the disease to which the kidney becomes liable in the progress of dropsical affection. In the first, a state of degeneracy seems to exist which from its appearance might be retarded as marking little more than simple debility of the organ. The size of the kidney is not materially altered, nor is there any obvious morbid deposit to be discovered. The second form of the disease of the kidney is one in which the whole cortical part is converted into a granular texture, and where there appears to be a copious morbid interstitial deposit of an opaque white substance. The kidney is generally rather larger than natural, sometimes it is increased very much, but at other times it is little above the natural dimensions. The third form of the disease is where the kidney is quite rough to the touch

externally, the feel is hard. The tubular portions are observed to be drawn near the surface of the kidney; it appears in short like a contraction of every part of the organ." (16) Bright suepected that all these might be stages in the same disease. Not only wa this the first attempt at a correlation of symptoms clinically with post-mortem findings but also the first attempt at classifying the lesions found in the kidney. Now more than one hundred years later this illusive problem is still not satisfactorly solved. This has led Addis to say (17), "Any clinical study of Brights disease leads always to an accumulation of facts all interesting in themselves, but for the most part disconnected and inexplicable-----there are more facts to fit together than ever before, or at least we are able to define them more exactly". The old problems of the relationship between the renal, vascular, venous, and general tissue changes still remains. There is no general agreement in regard to classification.

There are godd reasons why a satisfactory classification of nephritis is difficult to attain(12). First, we are dealing with a very complex organ. This is evident by simply being reminded again of the functional parts of the kidney, the renal arteries, arterioles, including the afferent vessels; the glomeruli with their tufts of capillaries lined with endothelium and covered with flat

epithelium ; Bowmans capsule; the tubules with their four parts, proximal convoluted tubule, Henles loop, and the distal convoluted tubule and collecting tubule; interstitial tissue; the veins; the lymphatics. The functional unit of the kidney is a complicated sequence of structure amd each part of the unit is a compex structure. Secondly, as previously pointed out the various parts of the kidney are so interrelated and interdependent that changes in any one part results in structural or functional changes in one or more other parts. For example, diseases of the arteries and arterioles affects the function of the glomerulus and even brings about changes in the tubules and vice versa. Certain changes in the glomeruli and tubules, especially atrophy leads to an increase of connective tissue giving rise to replacement fibrosis and scar formation. Swelling of the epithelium in certain forms of degeneration especially cloudy swelling, and the appearance of an abundant exhudate in the interstitial tissue, can interfere seriously with the blood supply of the organ by increased internal pressure and thus disturb normal function. Slowly developing reduction of arteriole blood supply by disease of the arteries and arterioles and chronic venous hyperemia results in disturbed nutrition of the glomeruli and tubular epithelium resulting in all grades of atrophy even to complete disappearance of these structures and repacement fibrosis.

A third factor is that known and unknowm causes that can damage the kidney may be more or less specific for one or another of these various elements. Individual elements of any one type may not be equally susceptible to the action of the injurious agents, so that at no time are all the glomeruli or all of the tubules affected to the same extent. The causes, toxic or otherwise, may act continuously or remitantly or only intermittently over varying periods of time. Variations in the nature, severity, and mode of action of the agents capable of injuring the renal elements thus furnish a great number of variables which increase the difficulties of a classification of nephritis, especially a pathological one.

One becomes even more conscious of the problem involved if a consideration ismgiven to all of the pathological processes that can occurr in each of the renal elements. Following are a few of those to be found: 1. In the arteries and arterioles; embolism and thrombosis, arteriosclerosis, obliterating endarteritis, intimal thickening . 2. Glomeruli: thrombosis, accumulation of leucocytes , proliferation of lining endothelium within the cappillaries , proliferation of covering epithelium, hyalin and amyloid degeneration, fibrosis. All of which changes alter the permeability of the glomeruli. 3. Bowmans capsule: pre-

cipitation of substances that have escaped through the glomerular walls, especially fibrin, proliferation and desquamation of the lining epithelium, all of which may block the outlet. In addition pericapsular fibrosis will interfere with the expansibility of the capsule. 4. Tubules: regressive changes from milder degeneration to complete necrosis, partial or complete plugging of the lumen of tubules with accumulated debris. 5. Interstitial tissue: accumulation of exhudates of all kinds from the serous exhudate of simple edema to the purulent exhudate of suppurative nephritis, proliferative changes leading to focal or diffuse fibrosis. 6. Veins: thrombosis and passive hyperemia.

Nephritis, like other diseases, is not a static condition. The pathological processes occurring in the kidneys are continually undergoing quanitative and qualitative changes (8). This may lead to a marked alteration in the clinical picture. The tissue element is therefore another compicating factor in the classification of nephritis. For example because of the intimate interdependence of the different parts of the functional unit, destruction of a tubule is followed by destruction of a corresponding glomerulus and vice versa. Hence a renal disease as nephrosis that begins primarily in the tubules or glomerular nephritis

beginning in the glomerulus, may, if the patient lives long enough assume most of the clinical and many of the pathological characteristics of that form of renal disease that begins primarily in the arterioles.

Thus when all of these factors are considered, the number of mathematical possible combinations becomes so great that one is led to suggest that perhaps there are almost as many types of nephritis as there are patients with the disease(12). This contributes to the difficulty of classifying satisfactorly and consistently, nephritis.

Richard Brights attempts at drawing the known loose ends together into a feasible classification have beenn already mentioned. Others through the years have likewise tried but each succeeding generation has brought a mass of new knowledge that revealed the inadequacy of the classific ations of this disease. The accompanying diagram taken in part from Cecil's Text Book of Medicine and prepared by H.A. Christian shows some of the attempts that have been made and that are at the present time the most generally accepted classifications(49)

It seems apparent that in the study of nephritis by these various workers there is a general recognition of

A COMPARATIVE SCHEMA OF VARIOUS CLASSIFICATIONS OF NEPHRITIS

	CHRISTIAN:	VAN SLYKE and ASSOCIATES (1930):	ADDIS (1931):
ACUTE	Acute and subacute nephritis With renal edema (nephrosis syndrome) Hemorrhagic nephritis	Hemorrhagic nephritis (glomerulonephritis) Acute Nonhemorrhagic nephritis; degenerative (nephrosis, lipoid or amyloid) Acute	Degenerative Bright's disease Acute Hemorrhagic Bright's disease Acute
CHRONIC	Chronic nephritis With renal edema Without renal edema	Hemorrhagic nephritis (glomerulonephritis) Chronic Nonhemorrhagic nephritis; degenerative (nephrosis, lipoid or amyloid) Chronic	Degenerative Bright's disease Chronic Hemorrhagic Bright's disease Chronic
CHRONIC	Essential hypertension progressing into chronic nephritis Renal arteriosclerosis progressing into chronic nephritis	Arteriosclerotic nephritis (nephrosclerosis)	Arteriosclerotic Bright's disease
	FISHBERG (1931):	**MOSENTHAL (1931):**	**O'HARE (1931):**
ACUTE	Benign albuminuria including orthostatic Nephrosis Larval Necrotizing Multiple glomerular embolism Nephritis Focal glomerular Acute interstitial	Tubular nephritis Albuminuric Anuric Edematous Hypertensive and convulsive Glomerular nephritis Focal Focal infectious Focal embolic Diffuse Acute	Nephrosis Simple Of pregnancy Necrotizing Lipoid Nephritis Acute Hemorrhagic Essentially edematous
CHRONIC	Diffuse glomerular Nephrosis Chronic Amyloid	Diffuse Subacute Chronic	Chronic Hemorrhagic Essentially edematous Nephrosis Amyloid Lipoid (?)
CHRONIC	Essential hypertension including malignant phase Senile arteriosclerotic Kidney	Essential hypertension Arterial nephritis Sclerosis of arteries and arterioles (benign nephrosclerosis) Arteriolar necrosis (malignant sclerosis)	Arteriosclerotic Kidney (a) Hypertensive 1. Prerenal stage (vascular hypertension) 2. Renal stage (chronic hypertensive nephritis) (b) Nonhypertensive decrescent arteriosclerotic Kidney.

different types of renal disease that are more or less common to all observers. Volhard & Fahr and Addis (38) approaching the problem of classification from different directions have come to recognize three chief types of nephritis whose characteristics are: 1. Hematuria, acute, intermittent, or chronic, usually with hypertension , and nitrogen retention. 2. Marked hypertension, preceeding any serious renal signs. 3. Edema and heavy proteinuria without hematuria or hypertension. Volhard & Fahr (50) call these three types glomerulonephritis, nephrosclerosis, and nephrosis. Addis (17) calls them hemorrhagic, arterio-sclerotic and degenerative Brights disease. Both agree on the primary histological changes common to each type as follows: 1. Inflamatory glomerular destruction. 2. Thickening of small renal arteries. 3. Degeneration affecting the tubules. Van Slyke (38) confirmed these findings. It would seem obvious then that for the most part the problem of classification is also one of terminology. Different workers use different terms to describe the same pathological alterations. Hence as Dr. G.P.Pratt stated in al lecture befor the senior class of 1936, "It doesnt make so much difference what you call the different forms of nephritis just so you know what you are talking about". However it would be well to be acquainted with the terminology used by various workers in order that one might

at least intelligently read the literature.

It would seem to be of value here to present one of the more widely accepted classifications of nephritis in some detail and have chosen for that purpose that of Addis. This should acquaint usnwith the terminology a little better and also help us to understand the pathological concepts underlying such a classification.

I HEMORRHAGIC BRIGHTS DISEASE

This is the glomerulonephritis of the pathologist but for clinical use, Hemorrhagic Brights disease is used for it emphasizes the outstanding and constant clinical features of the condition i.e. presence of blood casts and an abnormal number of red blood cells in the urine.

The initial stage is a sequel of a streptoccocal infection. It frequently escapes notice, but in its more severe form, the urine contains so many blood cells that it has a mohagany brown appearance. When the precipitate is examined it is found to consist in the main of distorted red blood cells, with considerable mixture of pus cells and epithelial cells. Among the cellular debris there are casts that vary from lemon yellow to dark brown. Red blood cells can be seen incorporated in the matrix of those of lighter color. These are the blood casts that are pathognumonic of Hemorrhagic Brights disease.

In other respects the symptomotaology is very variable, but there is usually a moderate increase in diastolic pressure a nd often a slight generalized edema. When the streptococcal infection has run its course and has disappeared as happens for instance in scarlet fever, there is rapid subsidence in the activity of the renal lesion and ultimately a healing, with a definite defect that is compensated for by hypertrophy of the kidney.

The latent stage is probably due to the continuance of focal infection streptococcal in nature. This may go unnoticed, even the urine showing no changes. This latency may continue for as long as ten years with compensatory hypertrophy continuing all of the time.

The active stage may follow the initial or it may be an exacerbation of the latent. A fatty degeneration of tubule cells may supervene. There is increase in casts and protein excretion. If untreated there is general anasarca. When the infection dissappears the disease may become latent and heal or it may on the other hand go on to the terminal stage.

As the terminal stage approaches there is a gradual but very radical alteration in the nature of urinary sediment. As one after another of the glomeruli become dis-

abled and fibrosed so that urine no longer flows fro m the tubules, fewer red blood cells and pus cells come from the shrunken kidney and blood casts are hard to find. When the amount of secreting tissue is reduced to less than one-third of the original amount, the urea concentration of the blood begins to rise and as the kidney grows smaller , the blood urea concentration rises higher and higher until under its influence the small amount of renal tissue is secreting urine that is constantly diluted. All casts are renal failure casts(51). Now weakness and lassitude set in or an unexplained vomiting or a sudden dimness of vision.

II DEGENERATIVE BRIGHTS DISEASE

This group is called Degenerative Brights Disease because of the constant and most prominent feature of the sediment is a large number of epithelial cells in various stages of granular or fatty degeneration. The chief characteristics here are edema with abundant albumén in the urine without hematuria or hypertension. In this group Addis puts the kidney lesions due to poisons of known chemical constituency such as metals, malaria, and also the lesions due to generalized toxemias as that of pregnancy and focal infections.

III ARTERIOSCLEROTIC BRIGHTS DISEASE

This is the group in which a hypertension of

unknown origin is noted before any renal injury can be determined. This group is of great importance because it occurs more frequently than any other form of Brights disease. These are the patients with hypertension who are often told they are suffering from "chronic interstitial nephritis".

The kidney is not the only organ affected here, others perhaps more serious are affected. Functional tests to measure the extent of normal functioning of the kidney are important in this group.

This classification is schematically presented by Addis as follows:

DIVISION	SUB-DIVISION	ETIOLOGY
Hemorrhagic	Initial → Latent → Healed; Initial → Active → Terminal	Streptococcus
Degenerative	Cryptic Poisoning-- known chem. const. Toxemia-- pregnancy Toxemia--generalized inf. Toxemia-- focal infection. Toxemia-- mixed infection.	Unknown Metals, Malaria etc. Toxins of Pregnancy Pneumonia, Diphtheria Staphlococcus, Sinus Inf. Tubercular Osteomyelitis.
Arterio-sclerotic		Unknown

In the last analysis the most satisfactory classification will perhaps be the most flexible and will be concerned chiefly with the bringing together into somewhat loose groups those clinical and pathological combinations that experience teaches are generally found together (12). Two chief groups of nephritis may be suggested: 1. Diseases in which secretory portions i.e. glomeruli and tubules are primarily affected. The clinical and pathlgical conditions classified as nephrosis, parenchymatous nephritis, and glomerulonephritis will be included here. Nephrosis is variously used by different men as a descriptive term. Christian (33) uses the term nephrosis as applied to any degenerative lesion in the kidney. Bell states(28) that nephrosis is a degenerative lesion, "adegenerative renal disease in which the lesions are restricted to the tubule". He goes on further to say that nephrois can not be distinguished from glomerulunephritis and that transitions are very common. Therefore it would seem not only permissible but adviseable for our purpose to put these in the same group i.e. lesions of the secretory portions, the glomeruli and tubules. The vessels are not primarily involved and the circulation through the kidneys is not impaired until late in the disease after the great number of glomeruli have been obstructed and destroyed. Increased blood pressure is therefore either absent or appears late

in the course of the disease

The changes in the parenchyma are either retrogressive or inflamatory in nature or a combination of both. As a result the permeability of the physiological unit is increased. Not only do the usual nitrogenous waste products escape from the blood through the kidneys, but albumen passes through also. There is therefore little or no retention of waste products in the blood. Phenosulphonophthalein is excreted in approximately normal amounts, and albumen is a constant finding. The loss of albumen is important for several reasons. If the albumenuria is sufficiently great and exists long enough, the protein of the blood plasma is depleted and the osmotic pressure of the blood is reduced. These two factors are important in the development of the nephritic edema.

The gross and micrscopic appearance of the kidney in this group is variable. Size and color depend on predominating tupes of change and combinations of other types of changes in the parenchyma and secondary changes in interstitial tissue. If the disease progresses long enough the clinical, gross, and microscopical appearance approaaches that of the second or vascular group i.e. increased blood pressure and retention of nitogenous waste and shrinking of the kidney.

2. This is the vascular group for the primary change occurs in the arteries and arterioles. It is characterized clinically by high blood pressure, increased retention of nitrogenous products, increased output of dilute urine, reduced excretion, and absence of edema. The kidneys are small and granular with numerous scars. There is a thickening of the walls of the arterioles and atrophy of the corresponding glomeruli and associated tubules. This type has been designated as a chronic interstitial nephritis or arteriosclerotic kidney. High blood pressure should not be the only criteria here however for as Christian states(36), "Cases of hypertension in whom tests of renal function show very little disturbance should be classed as cases of primary or essential hypertension rather than nephritis". Allen (31) is also of the same opinion.

One may justify such a classification by a recognition of two factors(15); 1. The basic pathological changes are distinctly different in the two types. 2. These structural alterations have fundamentally different effects on renal function. Cases in the first group may be either acute, subacute, or chronic and have fundamentally been termed by others parenchymatous nephritis, glomerulonephritis, and nephrosis. The basic pathological process common to all these forms is degeneration with inflamation of varying degrees of intensity. The fundamental functional change

change is an increased permeability of the renal filter. The second group is essentially chronic and included cases generally classed as chronic nephritis interstitial and primary, genuine or arteriosclerotic contracted kidney. The underlying pathological process is is a diffuse hyperplastic sclerosis of the smaller branches of the renal arteries, especially the afferent vessels to the glomeruli. The effect of this change is a reduction in blood flow and blood pressure, and therefore of effective filtration pressure in the glomeruli, with resultant inadequate excretion of waste products.

In the FIRST of these two main groups, the s secretory apparatus of the kidney is damaged. The kidneys themselves are swollen and larger than normal and, in the acute and subacute forms, the surface after the capsule is stripped off is realatively smoothe, the cortex is increased in thickness, and the normal cortical markings are indistinct and irregular(15). Microscopically, there are various types of alterations in the glomeruli(40) and retrogressive changes in the tubular epithelium. As the disease progresses and becomes chronic, more and more physiologic units are destroyed and are eplaced by fibrous tissue, the surface becomes pitted with small scars, and the cortex shows irregular thickness. The glomeruli suffer serious changes

even in nephrosis(20). The blood flow through the glomerular capillaries may or may not be interfered with as a result of thrombosis or of swelling or of proliferation of the lining endothelium. When, as in lipoid nephrosis, the cappilaries are only partially obstructed so that they continue to function, atrophy of the tubules does not occurr. The most important functional alteration in this type of nephritis is an increased permeability of the glomeruli due to alterations in the endothelium, damage to the basement membrane and retrogressive changes in the covering epithelium. This explains the of retention of waste products and the presence of albumen and even blood in the urine. In spite of the partial disturbance in the glomerular blood flow the increased permeability permits the adequate elimination of waste products. The available filtration pressure within the hyperpermeable glomeruli is adequate for proper functioning of the mechanism.

The increased permeability of the glomeruli in the first type of nephritis permits the escape of albumen in the urine (15). The lymph which escapes through the cappillary walls of all organs contains albumen. There There are only three locations in the body in which albumen does not normally escape through the cappillary wall, namely; in the glomeruli of the kidneys, in the

alveolar walls of the lung and in the choroid plexus of the brain. In each of these locations the cappillary endothelium is covered on its outer surface by a layer of adherent flat epithelium. In the glomeruli at least these are separated by a thin hyaline basement membrane(39). Epithelium is normally impermeable to colloidal solution. It appears probable therefore that the presence of albumenuria in the first type of nephritis is due to alterations in the basement membrane and retrogressive changes in the epithelium of the glomeruli rather than to changes in the endothelium.

The edema which is so characteristic of this type depends on(15) two things: 1. the depletion of the serum albumen of the blood by its loss in the urine and 2. retention of crystalloids in tissues. The retention of crystalloids in the tissues is apparently not due to the inability of the kidneys to excrete them but to some other mechanism possibly concerned with an effort to maintain the concentration of the protein of the blood at their normal level(35). The accumualtion of chlorides in the tissues increases the osmotic pressure of the tissue fluids, and this, in turn leads to withdrawl of water from the blood, causing concentrarioon of serum albumen in the blood and increasing the fluid content of the tissues, including edema(26) (35).

The presence of large amounts of albumen in the urine together with the products of disintergration of tubular epithelium, which is the seat of various retrogressive changes, furnishes material for the formation of the casts which are characteristic of this type of nephritis. Casts are more important than albumin and may be gound when the albumin test is negative(1). They aowavs indicate renal damage. The presence of albumin is a factor in the increased specific gravity of the urine in this disease.

All forms of this type of nephritis, whether they are c lled nephrosis, glomerular nephritis, or parenchymatous nephritis, show the aforementioned characterisitics i.e exhudation, degeneration, and increased glomerular permeability in varying degrees throughout the course of the disease (15). The progressive destruction of physiologic units in very chronic cases may finally result in such reduction of available glomerular filtration surface that an increase in systemic blood pressure becomes necessary in order to supply a filtration pressure adequate for proper elimination of waste products. Thus, increased blood pressure, not a part of the disease itself, may appear late in the course of this type of nephritis, perhaps as a compensatory mechanism.

It would be well here to present some cases that would illustrate the typical features of the lesion in this first division of nephritis, cases in which the lesion has been found to be confined to the secretory portion of the nephron. I will present cases taken from those as presented by Addis(5). Though Addis presents these cases according to his own classification as given earliere in this paper, yet they will illustrate adequately the lesions as found according to the simpler classification used in this paper.

Case I Marian B. Aged 40.

CLINICAL DIAGNOSIS: Hemorrhagic Brights disease, active stage.

ETIOLOGY: Wound infection.

DURATION: Thirty-one days.

COURSE: On the tenth day after a pelvic operation evidence of a septic condition appeared, and a few days later the urine was found to contain much blood and many casts. It seems probable that the infection was streptococcal in origin for shortly afterwards erysipelas developed. The blood urea concentration rose to very high levels, only renal failure casts were found in the urinary sediment and after thirty-one days the patient died of uremia.

PATHOLOGICAL OBSERVATIONS: At autopsy a suppurative metritis and local pelvic peritonitis were found and a bronchopneumonia. The heart was not enlarged. Smears of pus in the pelvis

showed many gram positive cocci. The kidneys were slightly enlarged, measuring 12.5by 7 by 5 cm. Their capsules stripped easily leaving a pale smooth surface on which were a few very small hemorrhages. The cut surface showed some swelling of the cortex but was otherwise normal. The renal arteries were normal .

MICROSCOPIC EXAMINATION: GLOMERULI. Practically every glome ulus is involved. Some of them show a typical early extracapillary glomerulitis with typical glomerular "crescents" but in the majority the lesion is of the intracapillary type, consisting of swelling and leucocytic infiltration of the glome ular tuft. In none of them is there any considerable development of connective tissue.

TUBULES. The general appearance of the convoluted tubule is normal as is the ascending limb of Henle's loop. The epithelium in some of the former divisions shows a slight swelling and granular degeneration and in an occasional group of tubules the epithelium is filled with fat droplets of irregular size. In some areas the cells of the lining of the tubules are very irregular in shape and arrangement and have the appearance of a regenerated epithelium. The lumen of the tubules of the cortex contains granular material mixed with a few leucocytes, and in many are well formed granular and hyaline casts. In the large collecting tubules are masses of granular material , desquamated epithelial

cells and definitely formed large renal failure casts.
INTERSTITIAL TISSUE. Thenonly lesions in the interstitial tissue are scattered small areas of beginning connective tissue formation and slight round cell infilt ration. Even in the most advanced of these there is no significant compression of the tubules as the lesion is only incipient.
ARTERIES. The arteries throughout are normal.

Case II. Patrick F. Aged 66.

CLINICAL DIAGNOSIS: Hemorrhagic Brights Disease, latent stage.
DURATION: Less than one year.
ETIOLOGY: Not known.
COURSE: On October 19, 1921, evidences of the latent stage of glomerular nephritis were found by examination of the urine. A year before the routine examination of urine had failed to disclose any abnormality. During November 1921 the patient died in another hospital.
PATHOLOGICAL OBSERVATIONS: Autopsy showed syphylis of the aorta, an aneurysm of its arch and a general arteriosclerosis. There was also present a chronic ulcerative endocarditis with embolic destruction of arteries to the skin of the hand and of the superior mesenteric artery. The kidneys were normal in size. Their capsules stripped easily, leaving a smooth surface of greyish pink color. An occassional petechial hemorrhage was present. The cut surface showed indistinct markings. The renal arteries were normal

MICROSCOPICAL EXAMINATION: GLOMERULI. Practically all of the glomeruli appear normal to low magnification. There is no definite increase in the nuclei of the tufts, no fibrosis and Bowmans capsule is free of exhudate or red blood cells. Xareful search with higher magnification, however, shows an infiltration of the tuft with polymorphonuclear leucocytes, these cells being few in number and scattered diffusely through the intracapillary tissue. No focal capillary emboli are present, either recent or old.TUBULES. The epithelium of the convoluted tubules of the cortex shows a mild recent cloudy swelling and theri lumens contain granular material. There are also present red blood cells and blood casts. Occasionlly a tubule is found which contains polymorph-onuclear leucocytes embedded in the granular material which fills its lumen , and a moderate number of hyaline and granular casts are present in the straight tubules of the medulla. In the smaller cellualr scars scattered irregularly throughout the cortex the tubules are irregular in shape and their epithel-ium is of the atypical regenerated type. INTERSTITIAL TISSUE. Throughout the cortex there is a moderate slightly irregular proliferation of the intertubular connective tissue. The new formed tissue is quite cellular, being made up of fibro-blasts with a few collagen fibrils and a diffuse scattering of leucocytes. The majority of these cells are lymphocytes,

but polymorphonuclears may also be found in considerable numbers. ARTERIES. The larger arteries show a moderate fibrous thickening of their intima. The medium sized interlob ular arteries and smaller branches are normal

SUMMARY: The re is a low grade, but still active inflamatory processm in the glomeruli and interstitial tissue, as evidenced by the polymorphonuclear infiltration and the escape of red blood cells from the capillaries. The tubular epithelium shows a mild parenchymatous degeneration. The arteries are essentially normal.

Case III. Richard B. Age 17.

CLINICAL DIAGNOSIS: Glomerular nephritis, terminal stage.

DURATION: Two years and five months.

ETIOLOGY: Scarlatinal streptococcus.

COURSE: On March 21, 1924, the urine was seen to be dark red in color. A week later there was a pronounced generalized edema. Evidences of a recent undiagnosed scarlet fever and of an acute hemorrhagic nephritis were found. The edema and hypertension persisted until June 1924 and for a short time during that month there was blurring of vision with edema of the discs and retinal hemorrhages, but for the next two years all these symptoms dissappeared. A gradually increasing anemia remained. During the last year the blood urea nitogen concentration slowly rose, the proportion of

renal failure casts increased and in June 1926 symptoms of uremia became evident. He died of uremia on July 18, 1926.

PATHOLOGICAL OBSERVATIONS: Only the kidneys were obtained after death. They were of normal size , but the capsules were somewhat adherent. They stripped fairly easily, leaving a purplish red fine granular surface and an occasional petechial hemorrhage. The cut surface showed indistinct markings. The arteries were normal.

MICROSCOPICAL EXAMINATION: GLOMERULI. Every glomerulus is affected by a rather old inflamatory process. The majority are enlarged and their tufts show a marked increase in nuclei. These excess cells are fibroblasts, mononuclear leucocytes and a moderate number of polymorphonuclears and there is also a development of connective tissue fibrils. Bowmans space is filled with exhudate and crescents which show a more or less organization with the development of capsular adhesions. The fibrosis both in and around the tufts has trabsformed about one-third of the glomeruli into fibrous nodules. TUBULES. Throughout the large areas of the cortex the convoluted tubules have ceased to exhist as such and are represented by irregular clumps and masses of atrophic epithelial cells with no lumen. In other places they still maintain their lumens but are markedly distorted in their shape , and occasionaly areas are found where they are greatly dilated and contain hyaline material. Other tubules contain granular material or hyaline

and granular casts and a few groups may be found which contain red blood cells and blood casts. There are many large renal failure casts in the collecting tubules. There is only a moderate amount of cloudy swelling in the epithelium of the convoluted tubules. In the most of the tubules the epithelium though atypical in structure is well preserved. INTERSTITIAL TISSUE. Throughout the cortex there is an extensive and diffuse fibrous proliferation of the interstitial connective tissue. This, by the atrophy and dilatation of the tubules and glomeruli previously described, has produced an extreme alteration in the architecture of the kidney. In the developing inflamatory tissue is a heavy infiltration with leucocytes of both the mononuclear and polymorphonuclear type. These areas are not confined entirely to the cortex but are found extending down through the medulla. ARTERIES. Both the larger arcuate arteries and the smaller interlobular branches show a moderate sclerosis.

SUMMARY: The kidney shows a diffuse inflamatory process which is quite old as judged by the proliferative changes in the interstitial tissue but still active as evidenced by the red blood cells and polymorphonuclear leucocytes in the tubules and tissues. The arteries are sclerotic.

Case IV . Benjamin C. Aged 10.

CLINICAL DIAGNOSIS: Degenerative Brights Disease.

DURATION: Unknown, but more than one year. Observed during last three months.

ETIOLOGY: Tuberculsis osteomyelitis of the spine with secondary infection and continuous suppuration.

COURSE: In 1926 the patient was under treatment for t.b. of the spine . He entered the hospital in September 1927 with a draining sinus, markedly emaciated and eith ascites . Edema became pronounced . The blood pressure was very low. During October and December the urinary sediment showed evidences of degeneration without any marked increase in red blood cell excretion. The boy became more edematous and died on December 8, 1927 after a severe diarrhea had commenced.

PATHOLOGICAL OBSERVATIONS: At autopsy there was found an active chronic pulmonary tuberculosis with secondary involvement of the intestines, mesenteric lymph glands and the cervical and thoracic vertebrae. Amyloid disease involved the liver, kidneys, spleen, and intestinal and gastric mucosa. The kidneys were of normal size. Their capsules stripped easily, leaving a smooth grevish pink surface. The cut surface showed an opacity of the cortex. The pelvis of the kidneys and the arteries are normal.

MICROSCOPICAL EXAMINATION: GLOMERULI. Every glomerulus examined shows a deposit of amyloid in the tuft. In the majority of them the masses are quite small and limited

to two or three clumps. In others about a third of the tuft is obliterated, and very rarely does the amyloid occupy more than half of the glomerulus. The deposit may be followed from the afferent vessel , which stands out prominently because of the infiltration about its walls, along and into the capillaries of the tuft. The uninvolved portions of the tuft are essentially normal. The capillaries are patent and there is no leucocytic infiltration nor fibrosis. Bowmans space is free of exhudate and granular material. TUBULES. The convoluted tubules of the cortex and broad ascending limbs of Henle's loop show extreme degenerative processes. Fatty degener ation is seen in scattered small focal areas, but cloudy swelling is the process most frequently observed. The cells of the tubules are greatly swollen and filled with large deep granules of eosinophils. As a rule the nuclei are intact in these walls of the cells; occasionally there is necrosis and desquamation. The lumens are filled with coagulated hyaline and granular material which in the straight tubules is organized as definite casts. No renal failure casts are present. INTERSTITIAL TISSUE. The interstitial tissue is esentially normal. An occasional small group of round cells can be found around some of the larger arteries. ARTERIES. The larger arteries are normal. Around the arterioles to the glomeruli and the capillaries of the vasta recta is a thin deposit of amyloid.

SUMMARY: The kidney shows a moderate deposit of amyloid around the capillaries and arterioles of the glomeruli and medulla. There are severe degenerative changes in the ep epithelial cells of the cortical tubules. The interstitial tissue and large arteries are normal.

Case V. Alonzo P. Aged 35.

CLINICAL DIAGNOSIS: Degenerative Brights Disease, non-bacterial toxins, malaria.

ETIOLGY: Malaria.

COURSE: An intense malarial infection was followed by anuria for four days. During the next three days small amounts of urine were excreted but the blood urea concentration rose to high levels and the patient died seven days after the onset.

PATHOLOGICAL OBSERVATIONS: Only the kidneys were obtained at autopsy. They were found of normal size. Their capsules stripped easily, leaving a smooth greyish pink surface in which no hemorrhages could be seen. The cut surfaces showed a marked opacity and widening of the cortex. The renal arteries show no definite thickening.

MICROSCOPICAL EXAMINATION: GLOMERULI. In all of the glomeruli the tufts are well preserved and show no definite abnormalities. Bowman's space is free of fibrinous exhudate but in the majority precipitated granular material can be seen. TUBULES. All of the convoluted tubules throughout the cortex and their

spiral terminal portions which extend into the outer zone of the medulla are the seat of active degenerative processes. Their epithelial cells are swollen. The protoplasm is granular and though the nuclei are preserved in most instances in some cells pycnosis of these structures with necrosis and desquamation has occurred. The same lesions are found in the broad ascending limb of Henle's loop. In the lumen of the tubules in the cortex is a large amount of granular debris which has the same appearance as the granular material which is seen in Bowman's capsule. In some of the tubules recently shed red blood cells are found. Very few definitely formed casts are present in the tubules of the cortex but in many of the large collecting tubules and ducts of Bellini are broad renal failure casts. There are many desquamated cells included in these formations. INTERSTITIAL TISSUE. The interstitial tissue throughout the cortex is normal except that there are a few small scattered rather cellular scars. ARTERIES. There is a moderate fibrous thickening of the intima of the arcuate arteries and the same lesion may be found in a few of the smaller interlobular branches. SUMMARY: The kidney shows marked degenerative lesions in the epithelium of the tubules and evidence of simple glomerular damage in the leakage of protein through its membrane. There is also present a slight arteriosclerosis with some small scars in the interstitial tissue. Renal failure casts are present.

These cases as presented show the patholgy of that type of nephritis in which the lesion is confined to the secretory part of the kidney unit i.e. the glomeruli and the tubules. We see that in no one of these cases is the patholgical process confined to the glomerulus or the tubule alone but though one may be predominantly involved yet both show patholgical changes. This bears out the contention held by many observers already referred to, that damage to one part of the secretory unit usually means damage to the other part. This further justifies the pathological classification used in this paper, that of grouping together lesions of the glomeruli and tubules. This leaves the second group of patholgical lesions yet tombe discussed in detail, those in which the lesion is confined to the arteries and arterioles. This is the arteriosclerotic group so designated by most workers.

In the SECOND or VASCULAR GROUP, conditions are quite different. The glomeruli are not primarily injured, and the filtration apparatus is not rendered more permeable. So far as the glomeruli are concerned, the function of filtering the urine from the blood proceeds more or less normaly until the secondary changes occur in the glomeruli. The primary change in this type is in the smaller arteies and arterioles, especially the afferent vessels to the glomeruli, and consists of a narrowing of their lumens, as a result of either arteriospasm or, more commonly, of a diffuse hyperplastic sclerosis. This change is quite different from the

ordinary type of arteriosclerosis. The latter is nodular in distribution, involving only a sctor of the circumference of the vascular lumen(15), and consists of a form of connective tissue hyperplasia, with fatty degeneration and deposit of lipoids, in the intima. This change may materially interfere with the circulation in small arteries and, as a result a terminal thrombosis, may entirely occlude the vessel, such as a branch of the coronary or renal artery. Such a result is focal rather than diffuse(52). In the hyperplastic type fibrosis without noticeable fatty degeneration occurs throughout the entire circumference of the intima. The lumen is gradually narrowed and is ultimately obliterated and replaced by a core of connective tissue(15). This change is not limited to the renal arterioles. In cases of this type of nephritis it has been seen in the smaller arteries and arterioles of the spleen, pancreas, and liver. The second type of nephritis is therefore essentially a generalized disease of the arteries of the body and is not a primary disease of the kidneys. The occurence of this change in the arteries of the kidneys affects renal function and ultimately causes death from uremia.

The secretion of urine depends on two factors, blood pressure and rate and volume of blood flow in the capillaries. In order to maintain a pressure and flow adequate to the normal secretion of urine in the presence of this

diffuse hyperplastic arteriosclerosis, an increae in systemic blood pressure is necessary. This is characteristicaly the first symptom to manifest itself in this form of disease(19). However Christian states(37), "cases of hypertension in whom tests of renal function show very little disturbance should be classed as cases of primary or essential hypertension rather than nephritis", Alvarez(32) also points out that ,"Hypertension cannot be ascribed regularly to infection or streneous life". Increase in systemic bleod pressure at first compensated for the narrowing of the arterioles, and the glomeruli receive enough blood under sufficient pressure to excrete normal waste products of the body. Later, the glomeruli are progressively destroyed or rendered incapable of functioning as a result of either extension of sclerosis into the glomerular capillaries or complete occlusion of afferent vessels by thrombosis or obliterating endarteritis.

The factor of safety of the kidney is high since there is four or five times as much kidney substance as is actually necessary to perform adequately the function of these organs. Hence three-forths of the normal kidney substance may be removed eithout the animal showing any sign of insufficency. Therefore a very extensive destruction of glomeruli and their tubules may occur without evidence of renal insufficency, provided an adequate blood pressure and blood flow are maintained in the remaining intact glomeruli. In this type of

nephritis, retention of waste products is not due to primary deficiency in function of the glomeruli but to theri failure to receive sufficient blood under adequate pressure to enable them to act as efficient filters. The increased systemic blood pressure is a compensatory mechanism which may for a time enable the kidneys to perform their function in a satisfactory manner but at the same time endanger life by its effect on other organs , especially the brain(15).

It has been shown by injecting the kidneys which were the seat of this type of disease, that only a part of the capillary loops were open in a glomerulus whose afferent vessels were markedly narrowed. This may be a further compensatory mechanism. If the narrowed artery cannot deliver enough blood to maintain the necessary blood pressure and blood flow in its whole glomerulus, it may be able to maintain these necessary conditions in a part of the glomerulus, so that this structure is not rendered entirely functionless(42).

Proof has been furnished by experimentation that the glomeruli are merely filters through which passes a fluid containing urea, chlorides, and other waste products in the same concentration as that in which thery are present in the blood and that the urine is concentrated in the tubules as a result of action in the tubular epithelium by the absorption of water(10) and (23). In this vascular type of nephritis the

kidneys are unable to concentrate the urine in thenormal manner. The urine is increased in quanity and its specific gravity becomes fixed at a low level(26). The quanity of voided urine is not as great as the estimated amount usually thought to be about the normal i.e. 100 liters in twenty-four hours that passes through the glomeruli of the normal kidney(13). It also contains urea and other waste products in greater concentration than thery are present in the blood but not in as great concentration as they occur in the normal urine(24). Hence some ability to concentrate is still possesed by the kidneys in this type of nephritis.

There are probably two factors to be con sidered in accounting for the increased quanity and lowered specific gravity of urine in this disease: 1. Atrophy of the tubular epithelium and 2.diminished blood flow through the plexus of capillaries which surround the tubules and receive theri blood supplu from the efferent blood vessels of the glomeruli(15). In this type of nephritis the function of the glomeruli is interfered with not by primary disease of their structure but as a result of changes in the vessels which supply them with blood. Destruction or partial or complete loss ofmfunction of a glomerulus from this cause is followed by atrophy of the tubule, that receives its secretion, and atrophic epithelium cannot function normally.

Perhaps of greater importance is the inadequacy of the supply to the tubules as brought about by these pathological changes. The efferent vessels leave the glomerulus and break up into a plexus of capillaries which surrounds the first and functionally most important part of the renal tubules connected with that glomerulus. A glomerulus supplied by a sclerosed vessel or one that is stenosed receives a diminished quanity of blood, perhaps only enough to fill a part of the capillary loop. The amount of blood which reaches the peritubular plexus is therefore below normal. This diminished blood supply results in inadequate nutrition of the tubular epithelium which is concerned with the concentration of urine. Insufficient nutrition leads to atrophy and to diminished function i.e. incomplete concentration of the urine.

Therefore in a case of this vascular type of nephritis of moserate or great severity, two things occur (15): 1. The glomeruli do not filter off from the blood the total enormous amount of dilute solution of waste products furnished by the glomeruli of the normal kidney. This is due to reduced cirulation of blood in the glomerular capillaries because of the narrowed lumen of the arteries and afferent vessels. The amount of urine separated in the glomeruli, however, proboably greatly exceeds the quanity passed from the bladder. Diminished glomerular filtration must be present to account for the accumulation of waste products in the blood. 2. As a result

of atrophy of the tubular epithelium due to diminished glomerular function and the reduced blood supply to the tubule, the normal concentration of the urine filtered through the the glomeruli does not take place.

In this form of nephritis therefore, increased quanity of urine voided of low specific gravity actually means both decreased glomerular filtration and incomplete concentration of the urine in the tubules.

- Fixation of specific gravity is a characteristic clinical manifestation of this type of nephritis. It is probably the result of four factors: 1. As a result of vascular changes and the structural and functional alterations which they entail, the factor of safety of the kidneys is reduced to or below the critical point. 2. As a consequence these organs are continually functioning at the maximum capacity. 3. They cannot respond to normal diurnal changes in blood pressure and blood flow which are responsible for the differences in specific gravity of day and night urines of normal persons.

Cases illustrating the lesion in the vascular type of nephritis will now be prsented. Once more the cases will be chosen from the series presented by Addis(17) and designated by him as Arteriosclerotic Brights disease.

Case I . Leonard C. Aged 35.

CLINICAL DIAGNOSIS: Arteriosclerotic Brights disease.

DURATION: Observed during the last six days.

ETIOLGY: Unknown.

COURSE: Hypertension had been noted five months before death but for how long a period it had previously exhisted is not k known. The patient died of cardiac decompensation with acute suppurative parotits as a complication. On the day before his death the blood urea concentration had risen to 278 mg. per 100 c.c. but the urinary examination suggested that the lesion in the kidney was arteriosclerotic and did not represent the terminal stage of glomerular nephritis.

PATHOLOGICAL OBSERVATIONS: Only the kidneys were available for post-mortem examination. They were of normal size measuring 12 by 6 by 4 cm. Their capsules stripped fairly easily, leaving a reddish purple surface in which were a few retracted scars. The cut surface showed no very apparent abnormalities. The renal arteries were definitely thickened.

MICROSCOPIC EXAMINATION: GLOMERULI. Most of the glomeruli are normal. The tufts are not fibrous, the capillaries are patent, and Bowmans space is empty. Those glomeruli which enclosed in scar tissue are compressed however, and in some there is a development of fibrous connective tissue which more or less obliterates the tuft. The number of glomeruli

so involved as compared to the normal ones is small. TUBULES. All of the convoluted tubules and broad ascending limbs of Henle's loop show a marked parenchymatous degeneration. There is a cloudy swelling of the epithelial cells of the milder type. Their nuclei are well preserved but the protoplasm is swollen and of a ground glass appearance without the accumulation of definite granules. The lumen of these tubules contains large amounts of granular material, while in the straight tubules definite hyaline and granular casts are found. No red blood cells or leucocytes are found. INTERSTITIAL TISSUE. Throughout the greater part of the cortex the interstitial tissue is normal. There are however scattered areas where scars are found formed by a fibrous proliferation of tissue which is still cellular and which contains a few round cells. Where these reach the free surface of the kidney is seen superficial retracted scars formed. ARTERIES. There is a moderate fibrous thickening of the intima of the arcuate and larger arteries. The smaller branches of thearteries to the cortex are somewhat more pronounced than normal due to thickening of their walls, but the arterioles to the flomeruli are in most cases normal.

SUMMARY: The kidney shows a moderate arteriosclerosis which has not involved many of the glomerular arterioles. There are a few fibrous scars in the interstitial tissue, and a widespread recent cloudy swelling of the epithelium.

Case II. Jane M. Aged 45.

CLINICAL DIAGNOSIS: Arteriosclerotic Brights Disease.

ETIOLGY: Pregnancy toxemia?

DURATION: Unknown. Observed for three years.

COURSE: In 1902 during pregnancy there was a long continued toxemia which terminated with convulsions. In 1915 a routine examination showed a blood pressure within the limits of normal variation. No examinations were made thereafter until May 1921 when the blood pressure was found to be 210 systolic and 140 diastolic. The urine contained almost no protein, 15,200 hyaline casts, no red blood cells and 350,000 white blood cells and epithelial cells per twelve hours. She was in fairly good health thereafter until May 1924 when she became first mentally confused, then stuporous and finally deeply unconscious. She died three days later. The blood urea concentration on the day before she died was 98 mg. per 100c.c.

PATHOLGICAL OBSERVATION: Autopsy showed a general arteriosclerosis, the cerebral vessels being particularly involved. The heart was about one-hlf normal size and the valves were normal. In the right hemisphere of the cerebellum was a recent hemorrhage 5 cm. in diameter which extended 1.5 cm. into the left hemisphere. The kidneys were somewhat small, measuring 12 by 4;5 by 3 cm. The capsules stripped easily leaving a fairly smooth surface and the markings on the cut surface were normal. The left renal artery was distinctly thickened.

The left renal artery was distinctly thickened. Otherwise except for a beginning bronchopneumonia the organs showed no significant gross lesions.

MICROSCOPICAL EXAMINATION: GLOMERULI. The great majority of the glomeruli are practically normal. A few show a slight or moderate increase in intracapillary connective tissue and occasionally a complete hyaline tuft is seen. There is no significant decrease in their number, however, nor any hypertrophy or dilatation of them. TUBULES. The convoluted tubules of the cortex are also essentially normal, except in the regions of scarring described later. Here there is more or less atrophy of the tubules and their cells depending on the amount of increase in the interstitial connective tissue. These are not extensive. The straight tubules of the medulla are also normal. A few contain granular material and after considerable search a few hyaline casts can be found. INTERSTITIAL TISSUE. Scattered through the cortex are small scars, consisting of fibrous connective tissue. These are not extensive and only a few tubules or a single glomerulus are surrounded by each so that no appreciable amount of the cortical tissue is involved. There is only a moderate round cell infiltration in these scars. ARTERIES. All of the arteries show a moderate sclerosis. There is a definite fibrous thickening of the intima of all of them, even the finer branches to the periphery of the cortex. About the larger arcuate branches in the

deeper portions of the cortex there is considerable perivascular connective tissue formation and some round cell infiltration.

SUMMARY: The arteries of the kidney show a moderately severe arteriosclerosis, a part of the general arterial disease, but there is only a moderate associated damage to the renal tissue. Only a slight evidence of active inflamatory or degenerative processes are seen.

These cases illustrate the essential features of this vascular type of nephritis, nephritis in which hypertension preceeds any signs of renal disease. The hepertension being due to a hyperplastic sclerosis of the smaller renal arteries and arterioles, may be a part of a general arteriosclerosis. In the kidney the narrowing of the lumen leads to a defect in the nutrition of the tubules resulting in injury to the secretory part of the kidney unit. Consequently there is a nitrogen retention and shows a similar terminal picture to other forms of neohritis with the exception that in the vascular type, hemorrhage is always absent until wide destruction has taken place. Failure in concentration of urine is also a conspicuous feature. A viscious cycle is set up as increased blood pressuretends to compensate for the narrowed lumen giving the clinical picture often described as cardiovascular renal disease.

CONCLUSIONS

1. Kidney function is the secretion of urine which consists of two distinct processes, filtration occuring in the glomerulus, a purely physical phenomena, and the second, reabsorption which occurs in the tubules the energy for which being supplied by blood pressure.
2. Any discussion of renal lesion in nephritis must be based on a consideration of changes that take place in the kidney i.e. the glomerulus, tubule, and blood vessels supplying the tubules.
3. The elements of the kidney unit or nephron are so closely related functionally that injury to one part ultimately results in injury to other parts if not checked.
4. Anatomically three types of nephritis are possible according to whether the disease process effects the glomerulus, tubules, or blood vessels.
5. Reasons why a satisfactory classification of nephritis is difficult to obtain: (a) Compexity of the organ (b) Interdependence of various parts of theunit--disease process does not stay confined to just one part as for example the glomerulus. (c) Variations in etiolgy give variations ism disease processes.
6. Division of nephritis into two main groups (a) the pathology is primarily in the secretory part of the nephron i.e. glomerulus or tubule, and (b) primary changes occuring in the arteries and arterioles.

7. The basic changes in the first type of nephritis are degeneration and inflamation resulting in increased permeability of the renal filter without retention of nitrogenous products but loss of albumin in the urine retention of crystalloids and edema. In the second type the pathological change is a hyperplastic sclerosis resulting in nutritional disturbance to the tubules and nitrogenous retention. Hypertension is the first clinical evidence of the disease.

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