Symptomatology of nephritis from the view point of a clinical classification

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THE SYMPTOMATOLOGY OF NEPHRITIS
FROM THE VIEW POINT OF A CLINICAL CLASSIFICATION

Senior Thesis
1935

Donald C. Campbell
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>History of Nephritis</td>
<td>25</td>
</tr>
<tr>
<td>General Considerations</td>
<td>5</td>
</tr>
<tr>
<td>Types of Nephritis</td>
<td>25</td>
</tr>
<tr>
<td>Acute Nephritis</td>
<td>25</td>
</tr>
<tr>
<td>Subacute Nephritis with Edema</td>
<td>40</td>
</tr>
<tr>
<td>Hemorrhagic Nephritis</td>
<td>52</td>
</tr>
<tr>
<td>Chronic Nephritis</td>
<td>58</td>
</tr>
<tr>
<td>Chronic Nephritis with Edema</td>
<td>65</td>
</tr>
<tr>
<td>Chronic Nephritis without Edema</td>
<td>70</td>
</tr>
<tr>
<td>Essential Vascular Hypertension</td>
<td>83</td>
</tr>
<tr>
<td>Renal Arteriosclerosis</td>
<td>95</td>
</tr>
<tr>
<td>Conclusion</td>
<td>96</td>
</tr>
<tr>
<td>Literature Cited</td>
<td>99</td>
</tr>
</tbody>
</table>
INTRODUCTION
In this paper the attempt has been made to compare the terminology of the most used clinical classifications of nephritis, and to correlate these various terms with the symptomatology involved.

Many of the classifications that have been formulated throughout the history of nephritis have been discarded by most present day authors, so that Major (1) states a great truth when he says that the history of nephritis is strewn with the wreckage of shattered classifications. Most authors now use one of four classifications when they write in clinical terms; these four classifications being those of Volhard and Fahr, Christian, Addis, and VanSlyke. One of these must necessarily be followed to give a systematic discussion of the symptomatology, and Christian's classification has been chosen as a plan of discussion in this paper. This classification is based upon two factors. The first is Christian's definition of nephritis which is "a diffuse, progressive, degenerative or proliferative lesion involving the renal parenchyma, the interstitial tissue, or the renal vascular system."

The second factor is edema, which he has used as a basis for his classification because it is easy to observe, it is common to many cases of nephritis, and its presence and type is significant in that it frequently accompanies certain pathological conditions.

In this paper some material with reference to the etiology, pathology, diagnosis, and prognosis has been in-
cluded, as it has a bearing on the symptomatology and on the correlation of these various classifications.
HISTORY OF NEPHRITIS
Najor (1) believes that the first clinical description of nephritis was that of Guglielmo Salicetti, who was professor of Bologna about 1268. He described hardened kidneys associated with scanty urine and dropsy. Other writers whom I have read, as Monro (2) and Fishberg (3), do not mention Salicetti, but quote Cotugno, 1764, and Cruickshank, 1798, as making the first real steps in the study of pathological state later described by Bright. Both of these men noted that in certain cases of dropsy the urine is coagulable by heat. Fishberg (3) also quotes the work of Wells and Blackall who followed Cruickshank. They observed lesions in the kidney in some cases of dropsy and albuminous urine, but in other cases with the same physical findings, they were unable to find these renal changes, so were unable to state whether the albuminuria and dropsy were actually the effects of renal disease.

Bright's publication of 1827 was entitled "Reports of Medical Cases Selected with a View of Illustrating the Symptoms and Cure of Disease by a Reference to Morbid Anatomy". Christian (4) stated that he was especially interested in the subhead: "Cases illustrative of some of the Appearances observable in the examination of Diseases terminating in Dropsical Effusion and first of the Kidney". Here he reported 24 cases, 18 fatal, with description of post-mortem findings. Christian (4) says that the study of these patients with Bright's deductions as published in this volume, forms the basis of forever linking the name of
Bright with nephritis in the sense of having proved the relationship between dropsy, albuminuria, and the renal lesion, a relationship but vaguely surmised by those who did work prior to Richard Bright.

Christian (4) quotes Bright's, "Reports of Medical Cases" in which Bright discusses his belief that there may be several different forms of kidney disease. "...In the first, a state of degeneracy seems to exist, which from its appearance would be regarded as making a simple debility of the organ. The size of the kidney is not altered, nor is there any obvious morbid deposit to be discovered. The second form of the diseased 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 larger than natural; sometimes it is increased very markedly, but at other times it is little above the natural dimensions. The third form of the disease is where the kidney is quite rough and scabrous to the touch externally. The feel is hard. The tubular portions are observed to be drawn near to the surface of the kidney; it appears in short, like a contraction of every part of the organ."

Bright is not sure of the existence of these three forms, for he goes on "...On the contrary it may be such that the first form never goes much beyond the first stage; and that all the other cases are to be considered as
more or less modifications, and more or less advanced stages of one and the same disease." The question as to whether nephritis is a single disease with different stages, or several entirely independent conditions, is still being debated.

Christian (4) believes that Bright's first and second group are now scarcely divisible but include cases of acute, subacute, and chronic glomerulonephritis, while the third group includes an end stage of glomerulonephritis or vascular nephritis. This seems true if we use a clinical classification, but if we use Bell's (5) pathological classification, the first group could well come under infectious nephrosis.

Monro (2), quotes Sir Thomas Watson, 1871, that "so-called Bright's disease has by common consent been resolved into two if not more distinct forms of disease". The two forms correspond to the large white and small red kidney. These were the chronic forms, and besides there was acute Bright's disease.

Monro states that this classification into one acute and two chronic, represented the best teaching in Britain in the 'seventies and 'eighties of the last century. He says that later Roberts pointed out that the change in the large white kidney to the atrophic form was often accompanied by a similar change in the clinical features. He then recognized this fourth variety of Bright's disease with features both anatomically and clinically intermed-
ately between, or a combination of, the large white and the small red kidney. This he states, is often spoken of as the small white kidney, but it may be neither small nor white as size and color are both variable.

Fishberg (3) credits Wilks and Bartels for the fact that during the third quarter of the past century it was customary to consider chronic Bright's disease as consisting of two varieties, chronic parenchymatous and chronic interstitial nephritis. Weigert, cited by Fishberg (3), showed the untenability of this separation, because he pointed out that in all instances of parenchymatous nephritis, interstitial changes are also present, and in the so-called interstitial nephritis, the connective tissue proliferation is undoubtedly secondary to changes in the renal parenchyma. While these objections were recognized as valid, this division of chronic nephritis became standard teaching and remained so until recent years.
GENERAL CONSIDERATIONS
There are certain general considerations which should be understood before discussing the classification and the symptomatology of the various disease processes. An understanding of these considerations is fundamental and essential, if we are to understand the pathologic processes back of the various nephritides.

**Normal Renal Function:**

The human kidney is almost solely an excretory organ. As an excretory organ it must work in a complex balanced way, for its elimination activity must be so balanced that the body tissues are maintained in equilibrium at certain levels, which can vary, at least for certain substances, within only narrow limits, in order that body cells function in a normal way. The maintenance of equilibrium in body fluid constitutes the most important activity of the kidney in its excretory function.

Just how the kidney does its work has long been a topic of discussion, and various theories have been suggested in explanation. Cushing (6) has advanced what he calls the "modern theory" of renal activity, which seems best to meet the known conditions of renal functions. According to this theory, blood pressure in the glomerulus with its structure providing a filtration membrane, causes filtration from the plasma of the constituents of the urine, while active absorption in the tubules determines the final composition of the urine. Filtration in the glomerulus is purely physical; absorption in the tubules depends on vital
activity of the epithelium. The critical demonstration of the correctness of this theory was supplied by the experimental work of Wearne and Richards (7). By means of an extremely fine glass cannula they succeeded in piercing the glomerulus capsule in the frog's kidney, and collected, under observation with a microscope, actual glomerulus fluid from a single glomerulus. This they analyzed qualitatively and quantitatively and compared the several constituents with those found in the circulating blood and with bladder urine. Their findings are quite in accord with the theory of glomerular filtration and tubular absorption and add great probability to this theory of renal activity.

Filtration through the glomerulus, like filtration through filter paper, necessarily depends upon several factors; on difference in pressure on the two sides of the membrane, on the character of the membrane, and in the nature of the fluid to be filtered. The influence of variations in the character of the membrane is often underestimated. For instance, variations in oxygen supply may cause marked changes. Variations in the fluid are important. The renal membrane holds back the large molecules of the colloids of the blood serum. These in turn exert a considerable osmotic pressure and may thus retard filtration.

In absorption in the tubules there are, according to Cushny, two groups of substances, "threshold bodies" useful to the body, which are in part taken up by the tubules and
returned to the blood, and "no threshold bodies" of no further service to the body, which are not reabsorbed. Substances in the tubules which are not reabsorbed exert osmotic pressure and so influence reabsorption. These two differently acting groups have a large influence on the composition of the urine and what is far more important, on the resultant composition of the blood and body fluids. Absorption is an active vital process, though, of course, greatly influenced by the physical and chemical properties and rate of flow of the fluid in the tubules.

Blood supply to the kidney is a very great factor in determining renal function. The blood supply to the kidney is remarkably abundant. Christian (8) states that experiments indicate that the kidney is irrigated with nearly twice its weight of blood per minute and possibly in man as much as 1000 to 1500 liters of blood flow through the kidney in twenty-four hours. The great importance of renal circulation to renal function is apparent. It is at once obvious that vascular sclerosis must make a great difference in renal function, by decreasing the caliber of blood vessels, changing their distensibility under pressure, influencing response to vaso-motor stimulation, by reason of changes in vessel wall, or increasing resistance to flow in various ways. These changes must effect the glomerular membrane and the tubular epithelium by changing the oxygen and nutrition supply, and actually influence the amount of substances brought to the kidney and the filtration process
that is going on in the glomeruli, as well as the reabsorption from the tubule; all of which must act to very profoundly influence renal function.

Although the blood supply is a very important factor in renal function, the paramount influence in determining the amount and composition of the urine is the chemical composition of the blood plasma. Tubular absorption returns to the plasma needed substances (threshold substances). There is an optimal condition of solution for these, and until this is reached, absorption from the tubules takes place. According to Cushny (6), this is an important determining factor in the final constitution of the urine. As already pointed out, colloid concentration in the glomerular capillaries exerts an osmotic tension which, as colloids increase or decrease, reversely affects filtration. Many of these effects are dependent on physical conditions, but in addition vital cell activity must play a part in the tubules.

Christian (8) says that under constant conditions of food and fluid intake, hourly urine excretion is far from constant. Both amount and concentration vary from hour to hour, so that considerable periodic change in both is the normal human condition. This variation is increased by normal human habits of eating and drinking. Normally day urine excretion considerably exceeds night excretion. Departure from these normal variations, both over short periods, and by day, as contrasted to night, are indicative of
disturbed renal function and form the basis of various concentration tests of renal efficiency which have a considerable value in clinical medicine.

A very important function of the kidney is elimination from the body of acids formed in metabolism, and thereby maintaining in equilibrium the proper reaction of the plasma. The reaction of the blood lies between limits indicated by litmus and phenolphthalein and that of the urine between phenolphthalein and methyl orange. The work of the kidney is to remove sufficient acid to maintain the constant pH of the blood. Henderson and Palmar (cited by Christian (8)) calculates that in this work, the kidney may free the body of 60 to 70 c. c. of normal acid per day, and under pathological conditions far more is removed.

**Albumin in Urine:**

Albumin in the urine, as determined by clinical tests, is always an abnormality. Its presence is one of the most delicate of indices of disturbed renal function. Sometimes this departure is unimportant and not a sign of kidney disease. Transitory changes in the circulation, severe exercise, slight irritants of various types, and fever will cause an albuminuria which is transient in nature. However, if it is persistantly present or is repeatedly occurring, it should be regarded as a definite sign of some disease of unknown import to the individual until its nature is thoroughly determined. It is important when albuminuria is found to consider whether its presence can be ex-
plained by some simple benign cause, or whether with albuminuria the patient shows other signs of renal disease. Persisting or recurring albuminuria, particularly with casts or blood cells in the urine, especially if the patient shows edema or circulatory disturbance, with few exceptions, means some form of nephritis whose importance to the individual depends upon its subsequent course. Such findings always merit careful study of the patient. It does not follow, however, that all individuals found to have albumin and casts in one or several examinations necessarily have nephritis, or have any greater probability of developing a subsequent nephritis than individuals never known to have such urinary changes.

Lee (10) found that nearly 5% of 6000 apparently healthy college men showed albumin in the urine as a definite ring with the nitric acid test. Following up these men, they developed no signs of nephritis. MacLean (11) got the same percentage of albuminuria in 50,000 soldiers in military training, and following these soldiers into active war service, found that of 132 that developed nephritis only 17% had shown albuminuria in earlier examination where there was no evidence of actual nephritis.

There is a fairly common, definite type of albuminuria so called orthostatic albuminuria, which does not seem to have any serious significance. The chief characteristic is the rapid appearance of albumin in considerable amount in the urine after the patient has been in an upright pos-
Ition, and its disappearance from specimens passed following a prone position.

Christian (8) states that Jehle (12) has given one of the best discussions of orthostatic albuminuria. He believes that in many of these patients it is not the upright position but an excessive lordosis that determines the albuminuria. The patient may stand with the lordosis corrected and show no albuminuria, or lie flat with a lordosis made by a firm pillow under the lumbar spine and show albuminuria. Others, while accepting Jehle's other ideas as to orthostatic albuminuria, do not concur in his belief in the importance of lordosis as the causative factor. Some think that usually there is an abnormal permeability of the kidney and so, in a sense, some underlying nephritic element.

The condition occurs in youth, most often between about nine years of age and the time of puberty, and particularly in thin types that have rapidly increased in height. In some, there are no associated symptoms, but many of these individuals are easily fatigued, often pale, neurasthenic, with frequent headache or pain in the back. Palpitation, cardiac arrhythmia, and vasomotor instability are not infrequent. These various symptoms are probably the accompaniment of the habitus rather than the result of any disturbance in renal function.
Casts and Cells in the Urine:

It seems reasonable that the urine from an inflamed kidney should carry with it formed elements which are characteristic of the process of inflammation, and that a kidney in which the lesion is in the main of a degenerative nature should yield a urine whose sediment is distinctive.

Acting upon this hypothesis, Addis (13) made a study of various physical factors on the formed elements of the urine. He found that all casts whose matrix was hyaline disappeared from neutral sodium chloride solution when the salt concentration was less than 0.5 percent. He also observed that the less the hydrogen ion concentration, the greater was the concentration of sodium chloride necessary to keep the casts from dissolving. This explains why dilute or alkaline urine has few or no casts present.

Cushny (6) says that often the protein solution after leaving the glomerulus is solidified in the tubules by absorption of water and increasing acidity and a cast of the tubule is formed which is finally driven downward by the pressure from behind and appears in the urine. The appearance of the cast varies according to the point at which the protein solidifies and the condition of the tubules through which it passes. The chief constituent is generally the protein derived from the capsule, but the most prominent features may be lent by the detritus and more or less degenerated cells from tubules. Hyaline casts point to a glomerular leakage; with evidence that the epithelium
of the tubule is degenerating slightly, there will be added fine granules; if more markedly, coarse granules usually brown in color; if very rapidly, fragments and entire cells. Of the fatty and waxy casts, Christian (8) states that the fatty casts correspond in activity to medium brown granular casts, while waxy casts, about which relatively little is known, seem to be about equal to fine brown granular casts in their indications of activity of the process.

The study of the urinary sediment in a systematic way has been well worked out by Addis (13). The patient is allowed to eat breakfast, but after that all fluids are withheld. The urine is collected between 6 p.m. and 6 a.m. and this quantity measured. The ten cubic centimeters are centrifuged for five minutes at 1,800 revolutions per minute in a special graduated centrifuge tube with a diameter so narrow towards the tip that an accurate reading of small volumes may be made. Grossly the sediment is significant. In normal persons there will be about 0.2 c.c. of what seems to be mucus. In the initial stage of hemorrhagic Bright's disease, if the renal lesion is pronounced, there is a large amount of brown precipitate. In the active stages there are diminishing degrees of the brown color until in some cases it is imperceptible. In the latent stage there is often no appreciable deviation from what is observed in the normal. In the terminal stage there is no mucus, so the cells and casts form a closely packed white deposit at the extreme tip. In the degenerative Bright's diseases, no
brown color is ever seen and the amount of cloudy white deposit varies with the number of casts and epithelial cells. In arteriosclerotic Bright's disease there is simply the colorless mucus that is obtained from the urine of normal people.

To do the microscopic examination, the supernatant fluid is decanted off and a part of the remainder removed with a pipette. A drop is then introduced into each side of a blood counting chamber, and the number of casts is counted under low power over the ruled areas. The cells are counted under a high dry lens and usually over unit areas of one sq. mm. From this work a differential cast count is made for the total volume of the urine, since this sediment represents the number of casts and cells in ten cubic centimeters. Addis (14) gives the following figures for such a twelve hour specimen voided by a normal man following a dry day.

<table>
<thead>
<tr>
<th>Composition</th>
<th>Range</th>
<th>Average</th>
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<tbody>
<tr>
<td>Red blood cells</td>
<td>0-425,000</td>
<td>65,750</td>
</tr>
<tr>
<td>Casts</td>
<td>0-4,270</td>
<td>1,040</td>
</tr>
<tr>
<td>White blood cells</td>
<td>322,400-1,000,000</td>
<td>322,500</td>
</tr>
<tr>
<td>and Epithelial cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>10-30 mgm.</td>
<td></td>
</tr>
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Blood Chemistry:

It is to be remembered that nephritis is not a disease of the kidneys alone but a generalized process with, as a rule, definite disturbances in the circulatory mechanism
and changes in body metabolism. All of these contribute to changes found in the blood. There may be an accumulation of substances, the result of katabolism and of retention. Some of these may be substances that are normally being excreted, but during normal renal function they are present in the blood in smaller quantities. Slight changes may seriously disturb that normal equilibrium of substances in the body fluids, which is so essential for the function of body tissues. Changes in equilibrium may lead to acidosis and become a complication in terminal stages of renal lesions.

So far, we have learned more about the changes in the non-protein nitrogen elements of the blood than of any of the other substances. The total non-protein nitrogen in the blood is made up of several end products or stages in the metabolism of exogenous or endogenous protein. These substances are urea, uric acid, creatine, creatinine, and the "rest nitrogen" fraction left after the other fractions have been determined.

Mosenthal (15) has shown that the urea nitrogen determination yields the most information with regard to the retention of waste products in the blood. This is partly because the micro-methods for determining the urea nitrogen are easier to carry out than are the methods for determining the non-protein nitrogen. Lewis and Rivers working in Mosenthal's laboratory showed that when protein is metabolized normally, approximately 80 percent is set free in the
form of urea. The selective action of the kidney maintains the urea nitrogen at a level of 50 percent or less of the total non-protein nitrogen of the blood. An impairment of renal function, even of very slight degree, may result in an increase of the percentage of urea nitrogen. It was also shown that an increased percentage of urea nitrogen may occur, whether the total non-protein nitrogen is high or low. This is important in early diagnosis of renal impairment, as the increase in the percentage of urea takes place before the increase in the total non-protein nitrogen.

Myers and Killian (16) have shown the prognostic value of creatinine determination. Theoretically, the amount of increase in the creatinine of the blood should be a safer index of the decrease in the permeability than should the increase in urea, for the reason that creatinine on a meat-free diet is entirely endogenous in origin, and its formation and elimination are normally very constant. Urea on the other hand is largely exogenous and a lowered nitrogen intake may reduce the work of the kidney in eliminating urea. It would seem that creatinine being almost exclusively of endogenous origin, furnishes a most satisfactory criterion as to the deficiency in the excretory power of the kidneys and a most reliable means of following the terminal cause of the disease.

Myers and Killian (16) report observations recorded on 100 cases of nephritis observed between 1914 and 1918, showing creatinine retention. Of these 100 cases, 85 had a
creatinine of over 5 mgm. percent, the figures ranging from 5.1 to 33.3 mgm; 80 of these 85 cases had died by 1919. Of the 5 remaining, the condition of 3 was essentially unchanged, while two had recovered. These two cases showed only temporary elevation of the blood creatinine.

While the non-protein nitrogenous substances are probably the best understood, much work has been done on other blood chemistry. Working with blood proteins in nephritis, Epstein (17) found a disturbance of the albumin-globulin ratio in chronic nephrosis. More recently, the work of Barker and Kirk (18) on plasmaphoresis has confirmed this and has helped to relate a definite syndrome to protein deficiency. Epstein (19) has also shown a hypercholesteremina and a lipoidemia in cases of chronic nephrosis. These will be discussed in connection with the subject of subacute nephritis with edema.

Christian (8) discusses the increase in blood chlorides in acute nephritis during the edema and in subacute and chronic nephritis, and the low blood chlorides in the terminal stages of chronic hypertensive nephritis. He ascribes these variations to a disturbance in the renal threshold which normally maintains the constancy of these chlorides.

Anemia:

Brown and Roth (20) have reviewed 187 cases of chronic nephritis, diagnosed as such at the Mayo Clinic. Cases of macroscopic hematuria were thrown out and it was found
that there was no relationship between microscopic amounts of blood in the urine and the anemia. They have also done experimental and laboratory procedures to show that the anemia is not on a hemolytic basis, and that in chronic nephritis, there is no lack of the protective power of the serum. They believe that the important factor is defective blood formation, and they showed evidence that the bone marrow suffers damage concomitantly with renal, retinal, and cardiac tissues. Their conclusion is that chronic nephritis is a constitutional disease in which renal injury is only one phase of a widespread toxic damage that involves the renal, cardiac and retinal tissues.

The fact that anemia is of definite prognostic importance in chronic nephritis, has also been shown by Brown and Roth (21). They have studied 139 cases with this in mind and have found that the percentage of hemoglobin and the concentration of creatinine in the blood in chronic glomerular nephritis shows a close inverse relationship. They found that a hemoglobin of 60 percent or less has approximately the same serious prognostic significance within the two and one-half year period as have blood creatinine values of about 5 mgm. for each 100 c.c. That is, a mortality rate of 85 and 86 percent respectively.

Hypertension:

"Hypertension", says VanSlyke (22), "is the quantitative measurable effect of circulatory change in nephritis." In his discussion of the subject, he agrees with the observ-
ations of Janeway. Janeway (23) believed that hypertension in renal disease could arise in three ways.

One type is that which can arise through simple quantitative reduction of kidney substance below the factor of safety. This he believes is due to a vascular hypertonus from retained poisons of some kind.

The second type arises in connection with the unknown intoxication which causes disturbances of the central nervous system and which we call uremia. Clinically, this is associated with acute nephritis, sometimes at its very onset, besides the subacute and chronic inflammatory affections of the kidney.

The third type may arise in primary irritability of the vasoconstricting mechanism, probably extra-renal causes, which lead eventually to arteriolarsclerosis. Here the kidney disease is the result and not the cause of the generalized vascular lesion. If this vascular lesion goes on to result in an atrophic kidney, then a renal element may be added to the hypertension that is already present. In these primary vascular diseases it is probable that the widespread narrowing of the vascular bed produces an organic influence in peripheral resistance.

**Edema of Nephritis:**

The edema of acute nephritis, as will be discussed in the symptomatology of that condition, is often slight and may be transitory. It is often confined to the face, but it may at times become generalized. This differs from
chronic nephritis, for here when edema occurs it is apt to be generalized, extensive, and persistent. In either case, we must distinguish between renal edema and cardiac edema, for the latter is really a complication rather than a part of the nephritis.

Renal edema occurs when cardiac function is unimpaired, and it is in some way related to renal function. McCann (24) distinguishes two types of renal edema. One is the hard, non-dependent type which occurs with a depletion of the serum proteins. This type frequently succeeds the first type in glomerulonephritis, due to loss of serum proteins through abnormally permeable capillaries. It is this type of edema which characterizes lipoid nephrosis or which is seen in a patient who is kept for too long a time on low protein diet.

The extent of renal edema is not related to the severity of the nephritis. Christian (8) reports cases of severe acute and chronic nephritis, both with and without edema. There is, however, some relation between this extensiveness of the edema and the type of nephritis. In acute nephritis, there is usually a moderate amount of edema. Edema in subacute nephritis with edema is marked, while it is rare in most cases of chronic nephritis.

Renal edema also bears some relationship to glomerular lesions. It is most often present in large amounts when the kidney shows some form of proliferative lesion in the glomerulus with a degenerative lesion of the tubules.
However, glomerular lesions themselves are to inconstant to justify the belief that edema is simply the result of decreased glomerular filtration of water.

Salt retention in the tissues is one extra renal factor which plays a definite part in edema formation. However, the findings here vary with different patients. Some patients with a low sodium chloride output can have the salt intake decreased with a resulting diuresis and disappearance of edema. Another patient under the same conditions will not have the edema affected by withholding sodium chloride. Christian (8) states that salt retention is important, but that it is not known whether the salt is taken up and fixed by the tissues and then the edema develops to prevent to great concentration of the salt, or if water escapes into the tissues and the salt follows to give the needed equilibrium. It is definitely known that there is some definite relationship between the two, but this relationship still awaits complete explanation.

In the Frank Billings lecture, Christian (25) discussed at length the importance of the osmotic pressure of the blood and its relations to the intravascular pressure. When this osmotic pressure gets below a certain level, there is more intravascular force driving the fluid out than there is osmotic pressure pulling it back in and hence, edema results.
Uremia: Foster (2) defines uremia as an intoxication manifested by psycho-motor disorders, which is apt to super­vene in nephritis. The term originated from the fact that the first chemical studies of the body fluids of nephritis showed an increase in urea in the blood and cerebro-spinal fluid. While the term is inexact, it has won general usage as a description of several symptom complexes accompanying nephritis.

Foster groups nephritis into three types, each of which he believes is a resultant of a peculiar metabolic defect. (1) The convulsive or epileptiform type has headache and sudden amaurosis as frequent precursors and coma as a sequel. The convulsive seizures and not infrequently recovery are important features. (2) A second type never displays sudden onset, but is marked by gradually deepening coma, unaccompanied by psychic disorder or signs of motor irritation. (3) A third type shows visual disturbances only when demonstrable lesions of the eye are present and is prone to gastrointestinal and psychic disorders, of which the latter are commonly hallucinations and paranoid delusions. Convulsions do not occur, lethargy and somnolence are the rule, and coma is terminal.

The convulsive or epileptiform type Foster says has been known since the time of Bright. He has done extensive experimental work with this type of uremia, using a fraction of the blood of a patient with epileptiform uremia.
and injecting it into the peritoneal cavity of guinea pigs. The results of his investigations seem to indicate that the blood of patients with epileptiform uremic attacks contains an organic base which is toxic. He states, however, that the existence of a toxin in uremic blood will not have been demonstrated until its chemical identity is known.

In his pathological studies, Foster has shown that severe edema of the brain occurs with constancy in only one type of uremia; that type where stupor and coma, without psychic or motor disorder, is the prominent nervous symptom. That edema of the brain may bear a causal relation to stupor or coma is suggested by the transient clearing of the mental state following removal of cerebro-spinal fluid, which in this type of uremia is usually under increased tension.

The third type of uremia Foster refers to as asthenic uremia, and he believes it to be due to the accumulation of excretory products in a patient with nephritis. He states that Hewlett and his two associates took enough urea to raise the blood urea up to 240 mgm. percent. All suffered from the same symptoms, differing in degree only; nausea, headache, vertigo, mental irritability, apathy, and somnolence.

Foster states that in his studies of chronic nephritis with nitrogen retention, that the amount of nitrogen excreted in the urine bears a definite relation to the urine
volume. This fact was determined in this way: cases with no defect in water excretion were given diets containing a definite known amount of nitrogen, the only variable being water, and it was then observed that if they gave much water there was no nitrogen retention; but if water was limited to less than a liter per day, nitrogen was retained, and after a period, the blood analysis showed an increasing amount of urea and non-protein nitrogen.

The best illustration given of the relation of water excretion to uremic symptoms in nephritis with nitrogen retention is offered by the effects of diuresis. In this type of chronic nephritis this process of heaping up nitrogen waste is gradual and the cells become tolerant to abnormal amounts of these urinary elements. Then with a consequent water loss through diuresis, diaphoresis, or restricted fluid intake, there is a concentration of the waste products in the blood and tissues and at times a consequent uremia.

Foster concludes by stating that the clinical manifestations and their immediate causation is not as yet well understood. However, he does believe that there exists these three simple types, each a resultant upon a peculiar metabolic defect. These types frequently merge into various combinations and effect the varied syndromes that are called uremia.
TYPES OF NEPHRITIS
Acute Nephritis:

Since I am using the classification of Christian as a framework in this discussion, our first group will be acute nephritis. This is the same as the acute or initial stage of hemorrhagic nephritis which is discussed by Addis (13) and VanSlyke (22) or the acute stage of glomerulonephritis to which Volhard and Fahr (27) refer.

Etiology:

Infections of various types cause most cases of acute nephritis. Longcope (28) has followed 29 cases for from six months to seven years and has found that his findings agree with work previously published by such men as Loehlein, Volhard and Fahr, Fishberg, Branch, Baehr and Linden whom he cites. The focal form he finds to occur during acute infections. The embolic type is ascribed to the deposition of bacteria in the capillary loops of the glomeruli, where they lead to a necrosis or to an inflammatory reaction. The diffuse form of acute nephritis follows acute infections which have been proven in a large proportion of instances to be due to hemolytic streptococci. In this connection, however, Longcope brings out the point that in view of the great frequency of acute streptococci infections this must be considered as a rare manifestation. VonPirquet (29) discusses the analogy between specific complications of scarlet fever such as acute nephritis, and the occurrence of serum disease following one or two weeks after administration of horse serum. He considers that there
may also be an allergic factor in the nephritis in that there may be a heightened susceptibility of the individual to the infection. It is on this basis that Longcope explains why, with so much hemolytic streptococci infection, there is so little acute nephritis.

Of the foci where infection causing acute nephritis is harbored the tonsils are most often responsible. The sinuses, teeth, and middle ear may also be foci. Where the nephritis follows one of the acute infectious diseases, scarlet fever is the most frequent offender. Measles much less often gives rise to nephritis, and the other exanthemata are quite infrequent causes. Although it is infrequent, acute nephritis does occasionally develop following diphtheria, pneumonia, and erysipelas.

As to the pathogenicity of the infection, it is not definitely settled whether the bacteria themselves reach the kidney and act locally or whether it is the action of toxins on the renal substance. Of these two possible ways in which bacteria can act, Christian (8) believes that the evidence at hand favors the local action of the bacteria virus after it arrives in the kidney in the majority of cases.

Various toxic substances as corrosive sublimate, arsenic, and lead are capable of producing an acute nephritis. Corrosive sublimate and uranium nitrate have been injected into experimental animals and found to produce lesions of acute nephritis in every way identical with what we
find in man.

The question of nephritis in pregnancy is dealt with differently by Christian than by many authors. Some men, Addis (14), VanSlyke (22), and Epstein (30), regard the renal lesion accompanying a toxemia as a form of degenerative Bright's disease. McCann (31) states that there is increasing evidence that the renal lesions of pregnancy should be grouped with nephrosclerosis. Keith (39) notes a close parallelism between acute glomerulonephritis and nephritis in pregnancy. He believes the main difference to be the more severe toxemia in the nephritis of pregnancy. Christian (8) also discusses nephritis of pregnancy under the heading of acute nephritis, but regards it as a manifestation of eclampsia and believes that it should be discussed in that connection rather than as a form of acute nephritis.

Pathology:

The focal type of acute nephritis occurs only as a complication of subacute bacterial endocarditis caused by the streptococci viridans. Boyd (33) uses a term "flea bitten" to describe the external appearance of the kidney here. The kidneys are slightly enlarged, gray red in color, and over the surface is scattered an enormous number of hemorrhagic points, which correspond with the hemorrhagic lesions in the skin and which really account for the presence of blood in the urine. On cut sections, the same hemorrhagic spots are seen scattered thru the cortex.
Microscopically the lesion is seen to be a glomerulonephritis. It is peculiar, however, in that it does not attack all of the glomeruli, and in those which it does attack, only a limited number of the capillaries are involved. The walls of the diseased capillaries are swollen and necrosed and the lumen is occupied by a fibrinous exudate. There is a leukocytic infiltration both of the tuft and of the contiguous tissue. The capsular space contains red blood cells, leukocytes, and desquamated epithelial cells. The diseased loops become adherent to the walls of the capsular space, while those unaffected remain free. If the patient lives long enough, these damaged portions of the glomeruli become completely fibrosed, but the number involved is so small that there is no danger of renal failure.

To go extensively into the pathology of diffuse glomerulonephritis would constitute a lengthy paper in itself. However, it is of great importance in the understanding of the progress of the disease, so I am going to again refer to the work of Boyd (33).

In the first stage of diffuse glomerulonephritis which is synonymous with the acute nephritis of Christian, the kidney is usually enlarged and the capsule is tense. Due to this swelling, the kidney substance often bulges out when the capsule is cut. Upon cutting the capsule the kidney appears smooth and gray and there may be red or gray dots scattered over it. The cut surface appears moist and
in the very acute stage blood may drip from it. Looking at it with a hand lens, the glomeruli appear as gray dots, or red dots if there has been hemorrhage into the capsular space.

On microscopic examination, little change is noted in the glomeruli which is destined to influence very definitely the course of the disease. The technique of demonstrating these changes is difficult but definite if properly done. The epithelial cells outside the glomerular tuft swell and fill the spaces between the loops of the tuft. Later these may degenerate and be cast off into the capsular space. Of greater import than this swelling of the epithelial cells is the swelling and proliferation of the vascular endothelium. The obstruction which this produces is made worse by the formation of intracapillary hyalin material. As the disease progresses, these fibers of hyalin material become more coarse until they form a dense network enclosing the proliferated endothelium. When this is accomplished, we have a bloodless glomerulus.

In addition to the intracapillary changes, there may be exudate in the capsular space. This may contain coagulated albumin, threads of fibrin, leukocytes, and red blood cells. The exudate is seldom abundant. Even if the tubules show abundant hemorrhage the red blood cells are swept out by the flow of urine and collect in the convoluted tubules.

There is little tubular degeneration in this stage,
and the interstitial tissue and blood vessels are normal. In other words, the essential pathology of this acute stage is intracapillary.

**Symptoms of Acute Nephritis:**

The symptom of acute nephritis most often noted by the patient is edema. He may also notice changes in the urine, as decrease in amount, hematuria, and frequency with some irritation. Other symptoms noted are vague, as general malaise, headaches or body aches, or more rarely tenderness in the loin region. Marked fever is not common and chills are very rare.

**Gastrointestinal Symptoms:**

Nausea and vomiting occasionally appear in acute nephritis and there may occasionally be abdominal pain. Such unusual symptomatology may lead to surgical exploration.

**Edema in Acute Nephritis:**

Edema in acute nephritis shows great variability in different patients. It also varies in location, but is most commonly seen in the face. Christian (8) records the presence of puffiness of the face in forty out of forty-five cases showing edema in analysis of acute cases at Peter Bent Brigham hospital. There may also be edema of the lower extremities or of the back or buttocks if the patient is in bed.

The edema of acute nephritis varies from a transitory type to an extreme anasarca giving the patient a pale pasty appearance. With very marked renal edema, there is
a tendency for it to be especially conspicuous in the more dependent part and in the loose areolar tissue. Edema of the subcutaneous tissue so extreme as to give the patient discomfort is rare in acute nephritis.

The mechanism of edema has been discussed. (See page 19)

**Urinary Disturbances of Acute Nephritis:**

The volume of urine output is nearly always decreased in acute nephritis, but the amount of decrease shows considerable variability. With a markedly decreased volume, there may be discomfort due to the increased concentration or to the increased acidity. This discomfort is usually not marked.

Blood in the urine is a cardinal sign of acute nephritis. Addis (13) and VanSlyke (22) in their discussions do not mention the possibility of acute nephritis without hematuria. Christian (8), however, states that although they are rare, cases of acute nephritis do occur without blood in the urine. In connection with this statement, Christian does not say whether or not he has had such a case. Surely this must be very rare if it is to be correlated with the findings of Addis (14), who made a quantitative study of the urinary sediments both in health and disease. This work was done on a twelve hour dry diet, the technique of which is found in Addis' book "The Renal Lesion in Bright's Disease", page 25. He made determinations on 74 medical students and found that in these normal individuals the rate of red blood cell excretion aver-
aged 65,750 per twelve hours and varied from 0 to 425,000. This indicates that it would be unusual to have a person with an acute nephritis in the zero group. Addis (13) points out that of all the clinically observable abnormalities of glomerular nephritis, which is a broader term including acute nephritis, hematuria determined under standardized conditions is the one which is most characteristic and of most assistance in differentiating the condition from the pure degenerative (nephrosis) and the arteriosclerotic types.

In this paper, in accordance with Christian's classification, I am discussing cases with persistent hematuria as a striking characteristic under the heading "Hemorrhagic Nephritis."

Albuminuria is an almost constant feature of acute nephritis. The quantity of albumin shows great variability but it is usually moderate. The degree of albuminuria is not so good a measure of the severity of the nephritis as is its persistence, along with other evidence of the patient's renal function and general condition.

Casts are almost always found in acute nephritis, and when they are not found, disintegrated and granular detritus is seen which has the same significance. There are casts of all varieties in the acute stage, but we should look especially for casts which vary from lemon yellow to dark brown. In some of the lighter colored casts, red blood cells can be seen incorporated in the matrix, but in the majority only fused orange colored masses can be seen. These are the blood
casts which Addis (13) states are pathognomonic of hemor-
rhagic Bright's disease, of which acute nephritis is the ini-
tial stage. According to Cushny (6) granular casts show
a considerable tubular lesion besides a slight to marked
glomerular involvement.

Renal epithelial cells and leukocytes are usually
abundant in acute nephritis. Christian (8) emphasizes that
the same type of rather small epithelial cells may originate
in any part of the urinary tract, so that when they are pre-
sent in the urine, we cannot be sure whether they are from
the renal tubule, from the ureter, or from the bladder.
This must be ascertained by exclusion. Leukocytes may abound
in the urine of acute nephritis with no evidence of cystitis
or pyelitis being present.

Chloride excretion in acute nephritis is much decreas-
ed and may be practically nil. In such cases there is usu-
ally water retention causing edema, as has been mentioned.
Tests of Renal Function:

These tests show proportionately less in acute nephe-
ritis than they do in chronic nephritis. Christian (8)
says that this is due to two things: (1) That the kidney is
often hyperpermeable in acute nephritis (2) Some tests meas-
ure the result of decreased renal excretion and considerable
time is required before retention is at all evident.

In the discussion of these functional tests Addis (14)
discusses only the urea clearance test. This test is a ratio
of the urea concentration in urine.
urea concentration in blood.
He does not use the phenolsulphonephthalein test, blood creatinin or blood urea. VanSlyke et al. (34) have shown the advantages of the blood urea clearance test over other tests. The technique of the urea clearance is given in more detail in Medicine 9-1930, pp. 265-267. In their comparison they found that with diminishing renal function, the blood urea clearance shows evidence of the diminution sooner than does the blood creatinine content, the blood urea content, or the phenolsulphonephthalein excretion. They even found that this blood urea clearance usually falls below 50 percent of its normal value before any of the other three values show any abnormality. The urea ratio which is described by Mosenthal (35) and which will be discussed more in connection with chronic nephritis, is the only test comparable to the VanSlyke urea clearance as far as determining early diminution of renal function is concerned. This test uses the ratio of urea nitrogen to the non-protein nitrogen of the blood and has been proven accurate. With regard to the phenolsulphonephthalein excretion, in cases with diminishing renal function, VanSlyke and his associates found that it is likely to register entirely normal values for several weeks or months after the blood urea clearance shows less than 50 percent of average normal renal function. However, in cases improving from nephritis with severe functional deficiency, the phenolsulphonephthalein excretion sometimes shows a marked rise several weeks in advance of a rise in the blood urea clearance.
While these findings show the blood urea clearance and the urea ratio to be the most valuable functional tests, in view of the common usage of the other tests, I will summarize their value in accordance with the findings of Christian (8).

The phenolsulphonephthalein excretion is sometimes decreased and sometimes normal in acute nephritis. If the excretion of the dye is persistently low, it is indicative of a severe renal lesion. This test is of value when repeated determinations are made and considered in relation to other known data.

Blood urea nitrogen determinations give normal figures at the beginning of acute nephritis, but a little later they are usually above normal. Diet plays an important part here, because on a diet rich in protein, diseased kidneys will not keep the blood urea below the normal of 20 mgm. of urea nitrogen per 100 c.c. of blood. Severe toxic symptoms, or uremia in acute nephritis, is usually accompanied by an increase in blood urea nitrogen and a decrease in 'phthalein output. In any case, where the blood urea nitrogen is high and continues so, the outlook is bad.

The blood creatinine is usually not increased in acute nephritis.

The two hour renal test is not applicable in acute nephritis due to the small output of urine. The test may be of value in convalescence.
In discussing the urea clearance test in acute nephritis, VanSlyke (22) reports that in a study of 23 cases in the acute stage, 19 of them showed a fall of 50 percent or less of normal during the first two months after the onset. This is clearly of value in obtaining an early diagnosis, but VanSlyke states that there is no prognostic significance to the degree of functional impairment shown during the first two months. He gives one case history in which the clearance fell to 10 percent of normal within two weeks of the onset, and yet he apparently made a complete recovery.

It seems that this whole discussion of tests of renal function in acute nephritis shows mainly the value of correlation. It is of great importance to correlate the values received from the various tests with each other and also with the clinical findings.

**Cardio-vascular Changes in Acute Nephritis:**

Blood pressure is increased in severe cases of acute nephritis, but usually the increase is moderate. A rather marked increase in pressure may precede uremic symptoms. However, Christian (8) states that a systolic blood pressure of over 180 should give doubt as to the diagnosis. Many such cases are found to be acute exacerbations of chronic nephritis or acute nephritis progressing into the chronic stage.

The heart is practically always unchanged by acute nephritis. If there is any easily recognized cardiac en-
largement, murmurs, or arrhythmia in a patient with acute nephritis, it may be considered as a coincident disturbance.

There is no arteriosclerosis due to acute nephritis. This may, however, be suggested in the toxic stages due to the fact that the pulse is full and hard to compress.

**Blood in Acute Nephritis:**

In the average case with acute nephritis there is no anemia. If there is marked hematuria and a toxic condition, there may be a moderate to fairly marked secondary anemia. It is noteworthy that many patients with acute nephritis show pallor out of proportion to the hemoglobin or red blood cell count.

In the early stages of the acute disease there is often a slight leucocytosis with a slight increase in the polymorphonuclear cells. If this increase is marked, it should arouse suspicions of infection apart from the cause of the nephritis.

**Ocular Changes of Acute Nephritis:**

Blurring of vision, flashes of light, or specks before the eyes are frequent complaints of patients. Transient blindness occurs infrequently, but when it does occur, Christian (8) says that it is a central or a retrobulbar condition. It comes on suddenly and also leaves suddenly and usually completely. The opthalmoscopic examination is usually negative with such an amaurosis. In fact, it is rare to have any obvious disturbance in the fundus with
acute nephritis.

**Diagnosis of Acute Nephritis:**

Diagnosis of nephritis is not difficult, but the main difficulty comes in determining whether the condition is primary or whether one is dealing with an acute exacerbation of a chronic nephritis. Christian (8) points out several points significant in differentiation. If there is high blood pressure, plus cardiac hypertrophy, it points to the chronic type. Extensive retinal changes indicate a chronic nephritis. Renal function, decreased out of proportion to other disturbances, suggests that there was a preceding chronic attack. Previous symptoms, as nocturia, also help to make a diagnosis of an acute exacerbation. All of these factors and the patient's general condition must be considered, as the two cannot be distinguished by urine analysis.

Renal infarction or chronic passive congestion are other conditions which may give a urine identical to that of acute nephritis. Evidence of circulatory failure and the results with cardiac treatment remove doubts as to diagnosis here.

Orthostatic albuminuria may also cause difficulty in diagnosis. This has been discussed on page 10.

**Prognosis of Acute Nephritis:**

For most cases of acute nephritis the prognosis is good. A large number recover completely. However, there are a few that go directly to chronic nephritis with a fatal outcome, and a few others that go into the latent stage
and finally develop a chronic nephritis. With regard to this latent stage, Murphy, Grill, and Moxon (36) report that the sedimentation rate is of prognostic value in that it is a distinct aid in showing whether a renal lesion is going on towards healing or going into chronic nephritis in a patient who is in a transitional state.

Uremic symptoms in the acute stage do not have the bad prognosis that they have in the chronic. There may be a persistent albuminuria or hematuria over a long period of time and then ultimate recovery. Renal function tests may show poor results in this stage without a fatal outcome. With special reference to the urea clearance test, VanSlyke (22) states that the essential for a good prognosis is that within four months after the acute onset the clearance, if it has fallen, shall have begun a consistent climb backward toward a normal level.

Certainly it is difficult to give a satisfactory prognosis in early stages. Renal function tests must be repeated and correlated with the general condition of the patient, to arrive at a satisfactory prognosis. It is certain that nitrogen retention that persists over a period of time indicates a much damaged kidney and is of bad import.
Subacute Nephritis with Edema; Nephrosis:

Introduction:

Subacute nephritis with edema in Christian's classification is used to indicate a type of case intermediate between acute and chronic nephritis, in which the essential feature is an early developing and persistent edema of renal origin.

McElroy (42) discusses the fact that the term nephrosis was suggested at a meeting of the German Pathological Society in 1905 by F. von Muller. He suggested its use to distinguish the degenerative from the inflammatory lesions in the kidney. Clinical manifestations of this type of pathologic lesion were not known at this time. In 1913 Munk (43) also cited by McElroy (42) worked out the clinical symptoms of degenerative lesions laying stress on the presence of double refracting bodies in the urine in one rather characteristic clinical syndrome. This he called lipoid nephrosis. In 1914 the monograph of Volhard and Fahr appeared and McElroy quotes Fahr's (44) work as the most satisfactory to explain clinical and pathologic facts. Fahr would regard nephrosis as a generic term to express the primary degenerative lesions that occur in the kidneys by virtue of their function as excretory organs. He classifies them as follows:

A. Simple nephrosis
   (a) First stage; albuminous degeneration.
   (b) Second stage; hyalin droplet degeneration.
(c) Third stage; necrosis.

B. Distinctly characterized nephrosis.
(a) Lipoid nephrosis.
(b) Amyloid nephrosis.
(c) Pregnancy nephrosis.
(d) Storing nephrosis.

In most of the literature that I have been able to read, the nephrosis were dealt with extensively only from the standpoint of the pathologist and the pathological classifications of nephritis. They have not used the term, nephrosis, to mean a clinical entity but have followed the meaning which Fahr uses and made it a generic term for degeneration. To get away from the omnipresent controversy, Addis (13) has omitted the term nephrosis entirely and made a large group of degenerative Bright's disease under which he has six subdivisions. The first is cryptic degenerative Bright's disease, which is synonymous with the subacute nephritis with edema of Christian, the lipoid nephrosis of Munk, the genuine nephrosis of Fahr, and the chronic nephrosis of Epstein.

In spite of the fact that I am discussing this subject from a clinical standpoint and using Christian's very clinical classification as a framework, I can hardly pass up the subject of nephrosis without some reference to the attitude of the pathologists. In Christian's classification, (45) subacute nephritis with renal edema or nephrosis is the name of a syndrome which has the following important feat-
ures: "insidious onset, marked edema, decreased basal metabolism, oliguria, marked albuminuria, decreased blood proteins with relative increase in globulin reversing the usual globulin:albumin ration, lipoidemia (hypercholester- emia), good phenolsulphonephthalein excretion, no increase in non-protein nitrogen of the blood, cylindruria but no hematuria, doubly refractile lipoid droplets in the urine, and normal blood pressure."

I believe that it would be well right here to consider where Christian in his clinical classification puts all of the extra subgroups that are found under the generic nephrosis of the pathologist. Let us take for comparison the classification of nephrosis used by Bell (5).

1. Nephrosis
   (a) Lipoid
   (b) Chemical
   (c) Infectious
   (d) Pregnancy
   (e) Amyloid

   (a) Lipoid nephrosis, as has been stated, is synonymous with subacute nephritis with renal edema.

   (b) Chemical nephroses are placed by Christian in the class of acute nephritis, as he says that many of these substances when injected into animals produce renal lesions quite identical with acute nephritis in man. Simple toxic substances, such as corrosive sublimate and uranium nitrate, injected into animals produce both degenerative and prolif-
erative lesions of glomerular and tubular epithelium.

(c) Infectious nephrosis as discussed by Bell would only fit into a clinical classification as a very early stage of acute nephritis. Bell (5) states that there is often a slight swelling of the glomerular endothelium and when this becomes sufficiently pronounced it is called glomerulo-nephritis. This, I believe, we can dismiss from our clinical classification.

(d) The nephrosis of pregnancy. Christian (8) states that clinically when this condition is advanced there is decreased urine with abundant albumin and casts, edema is usually present and may be excessive, the blood pressure is generally high, and the patient is toxic. Marked hematuria is not constant, but the sediment may show a few red blood cells. Bell states that anatomically, aside from some glomerular changes which are not constant, the picture is that of lipoid nephrosis. Christian says that it is not the picture of the usual acute nephritis although it is an acute renal disturbance. He believes that it should be considered as a toxemia of pregnancy, the cause of which is entirely unknown. He would consider the kidney lesion of pregnancy as a manifestation of eclampsia and describe it in that connection.

(e) Amyloid nephrosis, according to Bell, is usually secondary to chronic suppuration, and it is related to glomerulo-nephritis. There is no dissension here, as Christian (45) states, "all of our patients who have had extensive
edema of the nephrotic type and who died have shown glomerular lesions, either those usual to glomerulonephritis or an amyloidosis of the kidney including the glomeruli."

This attempt at the correlation of the pathologist's classification of nephrosis is naturally imperfect. It is made difficult first by the fact that all pathologic lesions cannot be diagnosed clinically and second by the difference in terminology. When a tissue shows a reaction of degeneration in contrast to that of inflammation, the pathologist takes the lesion out of the nephritis group and puts it in with the nephroses. Christian (8) in his definition has said that he regards inflammation in its broadest sense as a reaction of a tissue to injury, and so he includes degenerative changes as well as cellular infiltration and tissue proliferation under the term nephritis.

Etiology:

Various workers in the field of nephritis have very different opinions as to the etiology of this condition. Addis (13) says that it is unknown and discusses only its course. Epstein (19) says that it is due to a profound metabolic disturbance, the pathologic changes in the kidney being the consequence and not the cause. Christian (8) says that the syndrome follows a prolonged protein deficiency in the blood which in turn is due to a renal lesion.

Epstein (19) states that the term nephrosis is inappropriate in describing this disease because it accords undue importance to the kidney in the evolution of the con-
dition. He suggests the name "diabetes albuminuricus" because he believes that the albuminuria of nephrosis is not of renal origin but is the expression of a profound and general metabolic change. He states, "Because of an alteration in some or all of the cells of the body, or a modification (chemical, physical, or biologic) in the serum protein itself, as a result of which the body is unable to utilize it for whatever function protein serves, it is excreted by the kidneys from the blood stream as a foreign substance which can serve no normal or useful purpose."

He also believes that the lipoidemia arises from a peculiar disturbance in the protein metabolism and that it has a common origin with the lipoidemia of myxedema.

Christian (8) in contradistinction to this states, "there seems to be no justification for regarding nephrosis as other than a variety of kidney disease, a form of nephritis." He bases this statement on the following logical sequential reasoning.

(1) Barker and Kirk (18) working in Christian's laboratory have lowered the plasma proteins on dogs by repeated bleeding and prevented subsequent anemia by returning the washed red blood corpuscles. By this technique they have produced edema, lowered basal metabolic rate, decreased blood protein with a reversal of the albumin-globulin ratio, and increased blood lipoid.

(2) Clinically the most common cause for a blood protein deficiency such as was obtained experimentally is
marked and prolonged albuminuria.

(3) The cause of such albuminuria is a renal lesion. Christian (8) stated that this lesion is often obviously in the glomeruli but that there are cases in which the glomeruli show slight or no demonstrable lesions while the tubules show extensive degenerative changes. His explanation for this last type is hypothetical, but he believes that in so far as the actual daily amount of albumin in the urine is far in excess of what could possibly come from degenerating renal epithelium, that there is a functional change in the permeability of the glomerular capillaries of which the microscope gives no evidence.

Leiter (46) in a careful consideration of both of these attitudes believes that neither the view that nephrosis is a primary renal lesion nor that it is a general metabolic disorder has been adequately proven. However, he seems to definitely favor the idea of a renal lesion over that of a metabolic disorder.

Wolbach and Blackfan (47) report eight cases which were autopsied and no glomerular lesions found except what they believed would be due to terminal infection. They state that while offering no substitute, they believe that any name implying renal origin such as nephrosis or tubular nephritis is inappropriate to this disease.

There is one other point in regard to etiology on which Christian and Epstein again differ. Christian (8) states that from a practical point of view it is to be
remembered that a few patients with the nephrosis syndrome are benefited greatly by appropriate antisyphilitic treatment. Epstein (19) reports only three cases of nephrosis with syphilis and in those cases he believed that the nephrosis was an independent condition and had nothing to do with the syphilis.

**Pathology:**

Christian (8) states that the gross appearance of the kidney depends somewhat on the duration of the disease. Those dying within a few months of the onset show a pale, often yellowish kidney of normal size, or one moderately swollen. As the condition progresses there is a gradual diffuse increase in the interstitial tissue, so that the more slowly fatal cases show varying degrees of shrinkage of the kidney.

Microscopically Boyd (48) states that the striking change is the degenerative lesions of the convoluted tubules, the cells of which are swollen and contain both neutral fat and cholesterol ester. A fine work in connection with the glomeruli has been done by Bell (49) who used an improved technique. He found a proliferation of the endothelium lining the glomerular capillaries and a thickening of the basement membrane just as in glomerulonephritis. It differs from ordinary nephritis only in that the vascular obstruction is incomplete instead of complete. Bell also brings out the fact that there are some nephrotic
tubules in every case of glomerulonephritis.

Symptomatology and Physical Changes:

The most prominent symptom in subacute nephritis with edema is an early edema which increases to an extensive anasarca. Christian (8) states that when ascites is present, it is commonly a pseudo-chylous ascites, the fluid being opalescent due to excess of lipoids in suspension. With this extensive edema goes the characteristic pale, pasty appearance, but anemia by blood count is slight. Christian (8) states that while the cardiovascular apparatus is normal at first, high blood pressure develops later and some cardiac hypertrophy follows. This is contrary to the experience of VanSlyke (22). He states that in his series of cases of nephrosis, both hypertension and hematuria have been uniformly absent. The urine is lessened in amount, contains much albumin and many casts of all types. Christian's finding with regard to red blood cells again does not correspond to the findings of VanSlyke. He states that red blood cells may be absent at times and that they are usually few in proportion to other cellular elements in the urine, but very exceptionally they may be numerous enough to give macroscopic hematuria. It is difficult to see why there should be this discrepancy between such accurate men unless VanSlyke has adhered closely to Addis' (14) statement of what he includes under degenerative
Bright's disease. Addis says that he includes under this title all of the very numerous conditions that are associated with the appearance of evidences of degeneration of the renal parenchyma without bleeding. Hematuria is then ruled out by definition. Then if we accept Bell's work showing that there is some glomerular involvement in every case of nephrosis these non-hematuric cases must be early cases or cases with as yet very little glomerular involvement and hence would not have an opportunity to develop any hypertension. If hematuria appears, according to this definition, the case would be thrown out of this type of nephritis and would go to what Addis and VanSlyke call hemorrhagic Bright's disease.

Toxic symptoms in subacute nephritis with edema are few. When they appear it is mainly toward the end of the disease in the fatal cases, and at that period there may be a definite uremia. Renal function, as measured by blood nitrogen and 'phthalein excretion, is surprisingly good, as contrasted with the patients general appearance of serious illness, until late stages. The prominent and chief renal disturbance is an inability to excrete water and often there is salt retention.

**Diagnosis:**

To diagnose the nephritis here is obviously easy. Having diagnosed the nephritis the following characteristics are given by Christian (8) to determine the sub-grouping of the patient into the nephrosis syndrome:
"marked generalized edema; decreased basal metabolism, often down to -35 to -42; normal blood pressure; oliguria; marked albuminuria; urine sediment showing many casts of all sorts, fat droplets, usually double refracted by polarized light, and many round cells and leucocytes but few or no red blood corpuscles; decreased blood proteins with relative increase in globulin reversing the usual albumin to globulin ratio; no increase in nonprotein nitrogen, urea, uric acid, or creatinine in the blood; increase in blood lipoids; normal excretion of phenolsulphonephthalein; very slight or no anemia not withstanding the patients' pale, pasty pallor."

**Prognosis:**

The prognosis in subacute nephritis with edema is poor. While a few recover, more die in the course of a few months. A large majority progress steadily downward or progress downward by exacerbations and remissions, each exacerbation leaving the patient in a poorer condition. Christian (8) states that a few cases do eventually recover, but he knows of no way except by the verdict of time to distinguish these few from the more numerous with a poor prognosis.

In this connection, Epstein (50) definitely disagrees. He states that in cases of true nephrosis, which Christian states that he has never seen, the outlook is good. He says, "Barring complicating infections, which are not infrequent, it is my firm conviction that the condition is not only amen-
able to satisfactory treatment, but is capable of complete cure."
Hemorrhagic Nephritis:

Introduction:

This is a type of nephritis which is characterized by showing a persistent slight to moderate hematuria. This one finding is predominating in these cases and the condition in general differs so markedly from the usual features of nephritis that this special grouping of these cases is justifiable. Christian (8) regards it as a form of subacute nephritis because the duration of the process in the majority of cases is too long to be called an acute process; some cases being really chronic. O'Hare and Walker (37) define the condition as "a type of case in which microscopic bleeding continues for a varying length of time during and in the wake of an acute nephritis." These men consider this as a special type of acute nephritis, which may go on to subacute or chronic stages. Other writers as Addis, Vollhard and Fahr, and VanSlyke do not make any special note of this condition but merely consider it under the broad terms of hemorrhagic Bright's disease or glomerulonephritis.

Hemorrhagic nephritis is the most frequent form of nephritis in children. Hill (38) has shown that 25 percent of nephritis cases studied in the children's hospital at Boston were hemorrhagic nephritis. O'Hare and Walker state that the diagnosis of hemorrhagic nephritis was possible in 21 percent of a series of 86 consecutive cases of acute nephritis entered into the Peter Brent Brigham hospital.
Etiology:

O'Hare and Walker (37) state that the etiology is similar to that of ordinary acute nephritis. Of their eighteen cases nine had "sore throat" as the cause. Two were due to "colds", two to "scarlet fever", and one each to the following: otitis media, parotitis, pneumonia, septic miscarriage, and abortion. They believe that the streptococcus is the responsible agent most often. O'Hare (39) cites the work of Derrick and O'Hare (40) in which they found that 22 out of 37 cases of this were definitely skin sensitive to either the hemolytic or viridans type of streptococcus. With reference to etiological foci, Hill (38) states that in his experience tonsilitis is by far the most frequent cause of nephritis in childhood.

Pathology:

Very little is known about the pathology of hemorrhagic nephritis in the acute stage because practically no patients die in this stage. O'Hare and Walker (37) discuss their findings in two specimens, one an autopsy specimen and one obtained at a therapeutic decapsulation. They state that the pathology in these cases was essentially that of sub-acute and subchronic glomerular nephritis with "bands of anastomosing cicatrices enclosing sclerosed glomeruli and atrophic tubules." The glomeruli showed all stages of destruction up to complete obliteration. In many there was a proliferation of capsular epithelium with hyaline connective tissue masses adhering to the tuft and with blood con-
fined to a small portion at the periphery. Occasionally blood cells were seen to form a lake in the center of a lobule. Thrombosis of small vessels leading to glomeruli were not uncommon. The vessels through the kidney showed varying degrees of sclerosis, although many normal vessels were noted. As a rule the tubules showed atrophy but no degeneration, accounting for the absence of brown granules in the casts. They explain the scarcity of casts in the urine by the slowness of the process and the few glomeruli affected at any one time.

**Symptoms and Findings:**

In the onset these patients have much the same picture as acute nephritis in which edema is not a prominent symptom. There may be a sense of unusual fatigue, listlessness, anorexia, slight headache, and backache. O'Hare (37) emphasizes the fact that most cases show no symptoms except tiredness and that the diagnosis frequently must be made on the urine alone.

Physical findings are often entirely absent, but O'Hare (39) discusses some that may be present. There may be a little puffiness about the face or a little edema of the ankles. The skin may feel a bit hot, but the temperature is rarely over 100 degrees F. When fever is present a slight leucocytosis of 10,000 to 12,000 is common. In the acute stage there is no anemia and rarely any increase in blood pressure, but as the condition goes on into the chronic stage a mild secondary anemia develops, and we note
a moderate rise in blood pressure.

In the cases reported by O'Hare and Walker (37) there was nothing at all in the volume of the urine, its specific gravity, or its albumin content that differed in any way from that found in any acute or chronic nephritis. However, in the acute stage the urine may show an abnormally large number of red cells or a continuation of the red cells while the other elements are disappearing. It is the second or subacute stage where the diagnosis is most frequently missed. In this stage the persistent finding of a sediment consisting exclusively of a varying number of red blood cells together with a rare nongranular red blood cell cast or a rare hyalin cast is sufficient. There may, of course, be cases in which there is a continuously active and diffuse condition in the kidneys, which give rise to brown granular casts as well, but the diagnosis is less frequently missed in that type of case.

The renal function as tested by the urea nitrogen and phenolsulphonephthalein excretion is not much altered in the first and second stages of hemorrhagic nephritis. However, the second stage gradually merges into the third stage, and here there is a definitely diminished renal function. Increase in blood pressure and decreasing renal function in this type of nephritis indicates either an acute exacerbation of a chronic process or a merging into the third or chronic stage of hemorrhagic nephritis.
Diagnosis:

The diagnosis here differs markedly from that of acute nephritis or nephrosis. There the diagnosis of nephritis was easy, and the only difficulty came in determining the type. Here the diagnosis of nephritis is often missed and the patient told that there is nothing wrong. This is the type of case where the urine sediment shows only a rare red cell and a rare hyalin cast on a single examination. A few days after this one might find numerous red cells, and the process might go on to a very serious condition without indicating it by any symptoms.

More usually there is a definitely recognizable number of red blood cells and the diagnosis then depends upon finding a few casts, especially red cell casts among them. O'Hare and Walker (37) emphasize that the casts are rare but that the diagnosis depends on them and if they can be found, papilloma of the bladder, early tuberculosis, hypernephroma, and other conditions of this type can be ruled out without subjecting the patient to cystoscopy.

Prognosis:

Hill (38) states that in children suffering from hemorrhagic nephritis the prognosis is good. There is little tendency toward uremia and the process tends toward recovery, although occasionally chronic nephritis may develop.

O'Hare and Walker (37) state that while the prognosis for life is usually good, most of the patients are left with some residual of their nephritis. Christian (8) re-
minds us that the progress in many cases is likely to be slow and many gradually progress downward as a chronic nephritis without edema.

Baehr (41) states that the prognosis is excellent and that in the fourteen cases that he has studied none have shown the slightest evidence of a disturbance of renal function. This is only an apparent disagreement with O'Hare and Walker, for Baehr states that he is discussing a type of nephritis in which neither edema nor hypertension develops at any time. This means that he is not including cases such as O'Hare and Walker would place under chronic hemorrhagic nephritis and this very obviously would improve the prognosis.
Chronic Nephritis:

Introduction:

Christian (8) has grouped his cases of chronic nephritis into cases with edema and cases without edema. He acknowledges, however, that there is some overlapping so that cases are met which, while showing the main characteristics for chronic nephritis without edema, yet show edema and vice versa. These cases must be considered as a mixed type, constituting exceptions to the general grouping that is possible for most of the patients with chronic nephritis.

Chronic nephritis with edema, meaning by that renal edema, is a rare condition. Christian (50) reports that from approximately 1,650 cases of chronic nephritis studied in his clinic only about five have been placed in the group of chronic nephritis with edema. There have been 54 cases placed under the heading of subacute nephritis with edema, however, and Christian makes no very definite demarcation there. We can say then that most of the cases of chronic or subacute nephritis with edema, if classified by Addis (13) or VanSlyke (22) would be grouped mainly as chronic active hemorrhagic nephritis, although some might fall in their terminal group. If these cases were classified by Volhard and Fahr (27) they would be called chronic diffuse glomerulonephritis of a nephrotic type. If these cases were grouped according to the classification popularized by Osler (52) they would fall under chronic parenchymatous
nephritis. Still further back under the morphological classification, they would be called one of the large white kidneys.

Chronic nephritis without edema is a much more common condition. Christian (51) believes that in contradistinction to chronic nephritis with edema this group of patients are not really suffering from chronic nephritis but are suffering from a general vascular disease, in which the renal disease is but a local manifestation. In this last contention most men whose work I have read agree, but in the idea that subacute and chronic nephritis with edema is practically always a disease localized almost entirely to the kidney, there is definite disagreement by such men as Mosenthal (53), Blackfan and Wolback (47), and Epstein (19). If these cases of chronic nephritis without edema were classified by Addis (13) or VanSlyke (22), they would be called either chronic active or terminal hemorrhagic nephritis, but more would be considered terminal than in the case of chronic nephritis with edema. Volhard and Fahr (27) would place these cases under chronic diffuse glomerulonephritis. In the classification popularized by Osler (52) they would be one type of chronic interstitial nephritis, being placed in this broad group with the vascular and senile cases. In the old morphological classification this group would fall under the heading of secondarily contracted kidney.

As this separation of chronic cases into those with
edema and those without edema is a division entirely on a clinical basis, it can be applied only to the description of symptoms, physical findings, diagnosis, and treatment. The etiology and pathology will be discussed for chronic nephritis in general.

Etiology:

The etiology of chronic nephritis seems to be a subject about which much has been said but little has been proven. There have been cases in which an antecedent acute or subacute nephritis has been proven, but these cases are greatly in the minority. Christian (8) states that few cases of chronic nephritis develop as a recognized progression from an acute nephritis. Newburgh (54) says that in spite of the fact that so few cases of chronic nephritis develop as sequels of infections that first make themselves manifest in the form of acute nephritis, still many observers believe that much or even most chronic nephritis is a product of infection. It is assumed that infections, usually in themselves to trivial to attract the patient's notice, are capable of elaborating poisons whose slow hidden action finally comes to light in the form of a sclerosed and atrophied kidney. While such a hypothesis is both interesting and possible, it does not carry proof and hence does not solve the problem.

Christian (8) states that chronic nephritis with edema much more frequently than the other group has an easily assigned, definite onset, but even here close relation to
infectious disease is infrequent. He states, however, that pathologists think that kidneys with extensive glomerular lesions often give evidence of bacterial cause for the process. Even this possible etiological relationship is often absent in chronic nephritis without edema.

It has been suggested that diet may play a part in etiology and Newburgh (54) has produced renal lesions in rabbits by the use of a diet very high in protein. As a further basis for his idea that too much protein may be a factor, he tells of a wave of hemorrhagic nephritis which broke out in the British Expeditionary force during the world war. Subsequent study showed that there had been no acute nephritis in the contingent from India although the Indian troops had been more seriously affected by respiratory infections than had the British. When the rations were compared, it was found that the British were daily consuming 180 grams of protein whereas the Indians only ate about 90 grams of protein a day. Newburgh (54) also discusses a letter from a Dr. P. W. Harrison who has practiced for ten years among the inland shepherd Arabs. These people have a very low protein intake and this doctor has just had one case of nephritis, and that an acute juvenile case. These instances are not controlled experiments and so are subject to error, but they provide food for thought.

Christian (8) concludes his discussion of etiology by stating that we really have little information of the subject and so far as the individual patient is concerned, we
can rarely do more than guess a cause. Newburgh is more definite and states that in his opinion chronic nephritis is, generally speaking, caused by the combined effect of infection and abuse of protein.

Pathology:

Christian (8) states that grossly the kidney of chronic nephritis is usually smaller than normal. However, in the cases which he classes as chronic nephritis with edema there may be a large pale kidney. Kaufman (65) states that large white kidney is much more frequent than the large red kidney and that it may even be two or three times the normal size. Christian says that when the red kidney is found it is less often due to hemorrhage than to the fact that with the atrophy of the tubules a vascular connective tissue framework is left. The surface of these chronic kidneys may be either smooth or granular. In those cases which show renal edema, the surface is usually smooth and pale and the capsule strips easily leaving a smooth surface. The granular red kidney is more likely to be found in those cases without renal edema. In these cases where the kidney is not smooth, the capsule is difficult to peel off due to the connective tissue dipping down into the kidney substance in continuity with the connective tissue framework of the kidney, which has become increased in focal areas. The exceptional cases where this does not work out are often those in which it is difficult to tell between renal and cardiac edema.
Christian (8) states that the microscopic picture in these kidneys is a varied one. The glomerular changes are proliferative or atrophic for the most part. One may see in atrophied tubules, evidence of proliferation that preceded the degenerative change. The connective tissue portion of the glomeruli is usually increased in amount. The glomerular capillaries show varying degrees of thickening of the wall and various stages of thrombosis. Often one can see many sclerosed remnants of the normal glomeruli.

Kidneys with marked glomerular changes generally scattered through the cortex tend to be pale, fairly smooth, and during life these patients usually have marked renal edema. In this group of cases the tubular epithelium shows extensive degeneration of various sorts, spread rather diffusely and uniformly through the cortex.

In the other general type of chronic kidney, the sclerosed glomeruli are scattered in groups with intervening groups of more normal glomeruli. These kidneys are generally red and granular and during life the patient tends to be free from extensive renal edema. In this group the atrophy of the tubules is more marked, but it has occurred in groups connected with sclerosed glomeruli. Between these groups are normal tubules and some with higher than normal columnar epithelium. There is some evidence that there has been an actual hypertrophy of some of these glomeruli and tubules.

In each of these types of nephritis the connective
tissue overgrowth is directly proportional to the number of glomeruli and tubules which disappear. This connective tissue is cellular depending upon the activity and duration of the proliferation.

In all of these kidneys the arteries show secondary changes, some of which are marked. Kaufmann (55) states that the larger vessels show endarteritic, obliterating, and atheromatous changes, and the arterioles hyalin thickening and narrowing.

It is important to remember that this also involves the interlobular arteries and the vasa afferentia of the glomeruli as well. These changes in themselves may now cause atrophic processes in the remaining renal parenchyma and thus contribute to the contraction and diminution in size of the organ.
Chronic Nephritis with Edema:

Symptoms:

Edema:

Edema is the most prominent symptom and physical finding in this group of cases. As in acute nephritis the edema is usually first noted about the face, but it may occur anywhere. After the edema is first noted, it comes on with variable rapidity, at times gradually, at other times very rapidly. In some cases there is an extensive accumulation of fluid in the body cavities. Christian (8) states that it is not known what factors determine the localization of this fluid but that probably local conditions not directly associated with the nephritis play a part. Addis (14) states that the edema in the chronic stage is a soft pitting type in contrast to the hard edema of acute nephritis. The fact that this edema is accompanied by a protein excretion of several grams per twelve hours, adds to the evidence that this particular type of edema is due to a lowering of the plasma protein concentration. Other factors besides this lowered plasma protein no doubt also play a part. Mosenthal (53) believes that the fact that this edema parallels oliguria and the associated diminished elimination of salt in the urine very closely is significant.

Whatever the cause, this edema gives to the patient a very characteristic appearance. Christian (8) rather vividly described such a patient. "He is pale and pasty;
skin folds that give facial expression are lacking; his eyes are watery; he is truly a sad picture. His skin is tense, often shiny in appearance where it is most swollen. Sometimes the skin bursts and exudes a thin serous fluid. In the very loose areolar tissues such as those beneath the eyes and about the penis and vulva, there may be a curious semi-translucent appearance. In the most swollen parts there is no evidence of vascularity of the skin and even on incision there is almost no bleeding."

**Circulation and Blood Findings:**

Christian (8) states that blood pressure in chronic nephritis with edema is almost always increased in some stage of the disease. In many cases the increase is moderate until late, and in exceptional cases it remains normal for a long time. It is this type of case with normal blood pressure that is especially likely to be confused with lipoid nephrosis. The arteries in this type of chronic nephritis only exceptionally show physical signs of change. The heart shows no disturbance until late, when with the blood pressure high, it develops a hypertrophy and later a progressive failure of function occurs.

In the earlier stages of this condition with marked edema, anemia is more apparent than real. Later, however, anemia does develop.

**Digestive Disturbances:**

Digestive disturbances are marked in all forms of nephritis but they are often especially marked here.
Christian (8) attributes it here in part to edema of the wall of the stomach and intestine

**Urinary Findings:**

I have quoted Mosenthal's emphasis with regard to a marked oliguria in edematous cases of chronic nephritis. Both he and Christian (8) bring out the fact that there is a low urinary sodium chloride output and a high plasma chloride. The specific gravity of the urine is normal or above normal. The urine contains much albumin and many casts of all varieties. While there may be numerous leucocytes and red blood cells, gross hematuria is uncommon. Mosenthal (53) states that the blood chemistry is normal or slightly elevated in this stage. Christian (8) points out that the two hour renal test, being satisfactory only in those cases with a fairly large twenty-four hour amount of urine, is not always practical here.

**Uremia:**

According to Christian (8) uremia is much more infrequent here than in those cases without edema. It is usually late in appearance and does not develop unless hypertension has occurred. Headache, drowsiness and nausea, which in other types of nephritis are uremic in origin, here may be due to cerebral edema and be relieved, temporarily at least, by lumbar puncture.

**Eyes:**

As with uremia, exudate and hemorrhage are much less frequent in this group than in chronic nephritis without
edema. Exudate is observed more often than hemorrhage. There may be edema of the optic disc in this group of cases without other changes in the retina.

**Basal Metabolism:**

The basal metabolic rate is often decreased in chronic nephritis with edema as well as in subacute nephritis with edema.

**Diagnosis of Chronic Nephritis with Edema:**

Christian (8) only recognizes one difficulty in diagnosis here and that is from cardiac cases with edema. Here the therapeutic test of response to digitalis with disappearance of edema and change in the urine picture to approximately normal is of value. Another test he recommends is the use of small doses of diuretin or theocin, which will produce little or no diuresis if nephritis is an important causative factor in edema, while a prompt diuresis shows the kidney quite well intact.

Leiter (46) and Addis (44) and VanSlyke (22) recognize another difficulty. Since Christian believes that nephrosis is just one form of subacute nephritis, he does not consider the differentiation of a subacute form from a subchronic one of any great import, but these other men who believe lipoid nephrosis to be a purely degenerative tubular condition, see great importance in the differential diagnosis from a prognostic point of view. This differentiation may be very difficult in a chronic case with-
out hypertension or nitrogen retention. Addis believes that the differentiation can be made by examination of the sediment and the finding of red cells or the remains of red cells. Leiter believes that in some cases the differentiation cannot be made clinically and may require careful pathologic examination.

Prognosis in Chronic Nephritis with Edema:

The prognosis in chronic nephritis with edema is bad. Christian (6) states that many cases run their course within three years, a few survive for five years or longer, but that it is doubtful if any recover. In giving prognosis in this condition, we must realize that the result of tests of function are usually relatively good in proportion to the patient's actual condition, although repeated tests which show a failing function are helpful as indicating rate of progression in the disease, and form a rough estimate of the probable duration of life. Christian, however, believes that in these patients, general appearance and urinary findings are of far more use in determining prognosis than are tests of function.
Chronic Nephritis without Edema:

Symptoms and Physical Findings:

Christian (8) states that in contrast to chronic nephritis with edema, this group has no dominating symptom. The most frequently observed abnormal physical finding is high blood pressure. Strictly speaking, he says that nocturia is the only renal symptom of this group. Often there are no symptoms at all and the condition is discovered accidentally through finding high blood pressure, albuminuria, or retinitis during a routine physical examination. When symptoms do appear, their onset is usually insidious. The patient may notice a loss of weight, a lack in strength or energy, a growing nervousness, or a gradually developing nocturia as the first indication of the disease. With the loss of weight there is often an associated sallow complexion and definite gastrointestinal disturbances. This gives the appearance of a neoplasm and Christian (8) states that these cases are occasionally operated on for carcinoma of the stomach or intestine.

With regard to the insidious onset of this condition one of Richard Bright's (56) paragraphs is especially interesting. "It is indeed a humiliating confession that although much attention has been directed to this disease for nearly ten years yet little or nothing has been done toward devising a method of permanent relief.........I believe that our want of success in what are considered the more recent attacks is frequently owing to the fact that the disease is
far more advanced than we suspect when it first becomes the object of our attention; and I am most anxious in this present communication to impress upon the members of our profession the insidious nature of this malady."

**Disturbances of the Alimentary Tract:**

Christian (8) discusses a large number of alimentary disturbances which are not always thought of in connection with nephritis. A sore mouth and a persistent bad taste is frequent in advanced chronic nephritis. Superficial ulcerations and a dirty greyish membrane are also common. Smears from the necrotic material often show organisms common to Vincent's angina. A similar ulcerative condition may occur in the vagina, colon, or rectum.

Nausea and vomiting are often present and may be persistent. They usually are considered to be of toxic central origin, although in the late stages chronic passive congestion from cardiac failure brings additional gastro-intestinal symptoms. Hiccough is common late in the disease and often difficult to stop. There may be either constipation or diarrhea. With the diarrhea ulcerative colitis may be found.

**Cardio-vascular Disturbances:**

Cardio-vascular disturbances are very common in chronic nephritis without edema and sooner or later develop in almost every patient. VanSlyke (22) states that hypertension occurs in most cases of chronic active and terminal Bright's disease but that it does not always occur in either case and
that in his experience, its presence or absence does not alter the prognosis as concerns renal failure or uremia. It does indicate that the patient may die a circulatory death before renal failure is complete.

Christian (8) states that hemorrhages, particularly epistaxis, are frequent occurrences in this group of patients, due in part to high blood pressure, in part to vascular degeneration. These nose bleeds are often copious, difficult to control, and may be the first evidence of an existing chronic nephritis with hypertension. Retinal hemorrhage, subconjunctival hemorrhage, hemorrhage into the internal ear, and cerebral hemorrhage are often observed. There may be marked renal hemorrhage. Hemorrhages from other locations are less frequent.

Changes in the heart, sooner or later, can be detected in almost all patients with chronic nephritis without edema. Christian states that in many cases the hypertension is noted long before there is any evidence of cardiac enlargement, but as time goes on marked enlargement will be noted in many patients. This muscle after a time shows some degree of insufficiency and cardiac edema comes on to increase the confusion of the clinical picture.

Anemia:

Ashe (57) believes that the factor of anemia is often neglected in seeking a cause for the symptoms of the patient. He states that traces of albuminuria, dyspnea, anorexia, slight edema of the ankles, vertigo, weakness, apathy, and
even some diminution of the concentrating power of the kidney may be the results, not of nephritis or hypertension, but solely if not in part, the effects of the anemia which coexists.

He states that the blood count is usually of the "chlorotic" type with a low color index. There are, however, rare instances of cases with a color index over one which, with the lemon yellow color of the patient, makes the disease simulate pernicious anemia. The degree of anemia is found to be proportional to the extent to which the renal function has been impaired and to the length of time the renal insufficiency has existed. Thus, if a patient with nephritis with normal kidney function manifests anemia, some other cause for the anemia should be sought. On the other hand, if renal insufficiency of moderate or marked degree is present and there is no anemia, we may conclude that the impaired renal function is of recent origin.

**Eyes in Chronic Nephritis without Edema:**

Various eye symptoms as black specks, flashes of light, dimming of vision, and transitory blindness are often complained of in this condition. Christian (8) discusses ophthalmoscopic examination as being very important here as it detects vascular and retinal changes in a period when symptoms are few. Thickening, tortuosity, and obstructions of the arteries and veins can be seen here. One can determine here early evidence of arteriolar sclerosis,
which is suggestive of similar changes elsewhere, particularly in the nearby cerebral vessels.

Christian (8) states that in no form of nephritis is retinitis so common. O'Hare (57) reports retinal lesions in 30 out of 32 cases of chronic glomerulo nephritis who he has followed over a period varying from six months to almost 14 years. It may be found when there are few, if any other signs of a renal lesion. The patches of whitish or yellowish color intermingled with hemorrhagic areas in the retina are easily recognized and there are relatively few conditions to be confused with it. These retinal changes are especially significant as indicating that chronic nephritis is not merely a kidney disease, but a process widely spread and profoundly affecting the body tissues as a whole.

**Urine in Chronic Nephritis without Edema:**

Christian (8) states that nocturia is one of the early urinary disturbances in this type of chronic nephritis. Later, as a rule, there is also noted increased frequency during the day.

The urine is almost always pale in color, of lowered specific gravity, and contains only a slight amount of albumin. The specific gravity tends to become fixed at a constant level. When the urine becomes sufficiently dilute the hyalin casts, which up to this time have been so numerous, must necessarily dissolve. Addis (14) says that it is easy to explain the disappearance of the hyalin casts and cells, but he cannot explain why, as the blood urea concentration rises higher.
and higher the casts tend to become broader. Oliver and Luey (58) have explained this phenomena. They have found that with the fibrosis of a glomerulus the blood goes through the vessel of Ludwig, which acts as a shunt between the afferent arteriole and the tubular capillary bed. This brings a type of concentrated waste material into the tubule and obstruction of the lumen is frequent. Now in a kidney whose structure has been altered by obstruction at a number of places along various nephrons the further passage of casts toward the pelvis of the kidney is blocked. What occurs is progressive clogging of even larger collecting tubules and, although this obstruction allows urine to filter through, it holds back the formed casts from the smaller tubules. Hence, with progressive renal damage the casts are "casts" of larger tubules until finally the very large renal failure casts are all that can be found. Addis (14) points out that even renal failure casts will disappear if the urine is to dilute, and they are sometimes missed because water is given in such large amounts.

Addis (14) states that in spite of the diluteness of the urine, red cell excretion is always abnormally high. He does not mention the periodic bleeding, which Christian (8) says occurs quite often in this type of nephritis. Following this periodic bleeding, the cause of which is not definitely known, clots may occur in the pelvis or ureter and passage of these clots cause colic as with renal
calculi.

Christian (8) also discusses the hematuria of acute exacerbations. Here there is likely to be oliguria, more albuminuria, and more cellular and granular casts. With periodic hemorrhage there is no other change in the urine.

When passive congestion occurs due to coincident cardiac insufficiency, the urine picture is again changed from that typical of this group. Here there is oliguria, darker color, increased specific gravity, increased albumin, more casts, and more red cells. At this stage the patient shows cardiac edema, and resembles a case of chronic nephritis with edema. This resemblance disappears, however, if digitalis relieves the cardiac insufficiency.

The total solids are decreased in the urine in this type of nephritis. Christian (8) remarks about the fact that there is often a reduction of the sodium chloride content of the urine here without developing edema; the so-called dry-salt retention. This indicated that there is not a necessary causal relation between salt retention and renal edema. The nitrogen output is usually normal for some time after the reduction in sodium chloride output has taken place, but later the nitrogen output is decreased.

Glycosuria is frequently seen in chronic nephritis without edema, especially with hypertension. This is explained by a hyperglycemia, which often reaches a high degree and is quite out of proportion to the glycosuria.
Renal Function Tests in Chronic Nephritis without Edema:

Mosenthal (53) states that the earliest signs of diminished renal excretory power are an elevation of the blood uric acid and the presence of nocturnal polyuria. To determine nocturnal polyuria requires measurement and Mosenthal (53) states that the normal has been found to go as high as 725 c.c. although the upper limit of normal is usually considered 400 c.c. or less. Christian (8) does not agree as to the value of the uric acid determination and sets 600 c.c. as the maximum night urine. He also states that early in the disease the two hour renal test shows a functional disturbance.

Mosenthal (53), page 325, gives the technique for this two hour test. The level of specific gravity will be found to be slightly less than normal for the different specimens and there will be a variation of less than nine degrees in the various samples. Kirkland (59) believes that Volhard's dilution and concentration test is the best to determine whether or not the deviation of fluid is due to renal or extra renal factors. The main difference between the two techniques is that the dilution and concentration tests involve a forced amount of fluid and is contraindicated where there is much cardiac failure, while the two hour renal test is done under rather normal conditions.

Later, as the nephritis progresses, all of these changes become more marked, specific gravity falls lower and there
is less fluctuation between samples. Then sodium chloride excretion diminishes and still later nitrogen excretion does the same.

In the early periods of chronic nephritis without edema, phenolsulphonephthalein excretion is normal, but as time goes on it gradually decreases until in the late stages its excretion is very slight or practically nil. Christian (8) states that drops in 'phthalein excretion usually accompany periods of circulatory failure and with improvement in circulation the excretion again rises.

Christian (8) states that the nitrogenous constituents of the blood increase in much the same relation to the course of the disease as the 'phthalein excretion diminishes. He uses the urea nitrogen determination as it is simpler, and he believes as valuable as the nonprotein nitrogen.

VanSlyke (22) considers a patient in the chronic active stage of glomerulonephritis, if at the end of four months there has been no definite tendency for the blood urea clearance to rise. He states that of the patients whom he has seen in this group only one has improved, the rest progressing gradually toward a terminal uremia.

Mosenthal (35) has checked his urea ratio:

\[
\frac{100 \times \text{urea nitrogen}}{\text{nonprotein nitrogen}}
\]

with the VanSlyke urea clearance test and found it to compare favorably as an index of renal efficiency. It is very
simple to carry out as only one specimen of blood is needed. With normal function the index is 44 or less; maximal impairment of renal function gives a value of 80 or higher. With progressive renal impairment there is a rise in the ratio, while it drops if renal function improves.

Christian (8) concludes his discussion of this phase of chronic nephritis by saying that these various tests often do reveal serious disturbances in renal function not suggested by other features of the case, and where they do, they are of great diagnostic and prognostic value. However, as in all phases of nephritis, it is the trend of repeated tests that are of most value.

**Uremia:**

Uremia occurs with far greater frequency in chronic nephritis without edema than in any other type of nephritis. Christian (8) states that provided the patient does not die of apoplexy, cardiac failure, or of intercurrent infectious disease, he is practically sure to develop uremia.

**Diagnosis of Chronic Nephritis without Edema:**

The diagnosis of this condition is discussed in brief by many authors, but none of them compare with differential diagnosis given by Christian (8) which I will review in abstract form.

The frequency and nocturia of chronic nephritis are symptoms suggestive of prostatic enlargement. The back pressure upon the kidney may cause albuminuria and depressed
renal function further complicating the picture. If the change in the prostate is one such as an enlarged median lobe without much palpable enlargement, it may be particularly difficult to distinguish from a simple chronic nephritis unless cystoscopic examination is made.

Confusion with chronic cardiac disease has been referred to in the renal function tests, but here a therapeutic test with digitalis will clear up the diagnostic difficulty.

It may be difficult to tell whether the urinary picture is due to arteriosclerosis or whether the arteriosclerosis is secondary to the chronic nephritis. Renal function tests help here and will be discussed later under essential vascular hypertension and arteriosclerosis.

The periodic hematuria which may occur in chronic nephritis may resemble renal calculus or neoplasm. X-ray studies and cystoscopy will help here. Absence of hypertension is suggestive of the latter conditions.

Cerebral tumor, cerebral hemorrhage, cerebral syphilis, cerebral aneurism, and epilepsy may be confused with chronic nephritis in those nephritics who have cerebral edema, uremic attacks, or transitory circulatory disturbances. Christian reminds us here that a convulsive seizure or suddenly developing coma from whatever cause, is accompanied by albuminuria, glycosuria, and cylindruria. Actually it is often impossible to determine the presence or absence of nephritis until the seizure is over. Frequently a lumbar puncture will give data that will help greatly in diagnosis.
of this group of cases.

Chronic nephritis and neurasthenia have been confused. The point in diagnosis here is not to overlook the usual signs of chronic nephritis because symptoms are of such a nature as to suggest neurasthenia.

Christian states that gastrointestinal symptoms in chronic nephritis to often lead to the mistaken diagnosis of acute or chronic indigestion. It is the neglect of a careful physical examination that causes physicians to treat only the most prominent symptom in this group of cases.

Pernicious anemia with its sallow pallor, its gastrointestinal symptoms, slight pitting edema of the ankles, and its albuminuria with a few casts and low renal function as measured by the two hour renal test, may simulate chronic nephritis very closely, and the true diagnosis only be made when the patient is studied with the possibility of this condition in mind.

**Prognosis in Chronic Nephritis without Edema:**

The prognosis is better here than in chronic nephritis with edema. Eventually the chronic nephritis or the associated cardiovascular disturbance kills, but Christian (8) states the duration is often one of years. VanSlyke (22) quotes a personal communication from Addis saying that he has seen several active chronic cases improve to the latent condition and VanSlyke has just had one such case.
It has been stated that renal function tests are of definite value but to be most valuable prognostically and diagnostically they must be repeated and correlated with clinical findings. VanSlyke (22) states that the prognosis in the majority of their cases with a urea clearance of 20 percent of normal or less has been less than one year and in only two out of 17 cases has it exceeded two years.

Intercurrent infections and cardiovascular disturbances frequently play an important part as the cause of death here, and they must be carefully evaluated.

Christian (8) states that ophthalmoscopic examinations are of much prognostic importance. Retinal hemorrhages are of less serious import. O'Hare (57) found the average duration of life after either arteriosclerotic retinopathy or hypertensive neuroretinopathy appeared to be seven months. The maximum was 23 months. From the condition of the retinal vessels we can form some idea as to the probability of cerebral hemorrhage, often the terminal event in chronic nephritis without edema.
Essential Vascular Hypertension:

Introduction:

In accordance with Christian's plan of classifying the nephritides, I will discuss essential hypertension here. Fishberg (3) defines essential hypertension as "those cases of chronic hypertension which neither clinically nor anatomically can be demonstrated to have evolved from antecedent inflammatory disease of the kidneys or urinary obstruction." Christian (8) justifies its discussion here by saying that actually we do not know the cause of high blood pressure nor its relation to the changes which we observe to take place, both in the cardiovascular structures and in the kidneys, during the progress of the condition. It is sufficiently independent of nephritis to justify the term "essential", yet the association of high blood pressure with renal disturbances is close enough to warrant describing the condition in this place.

Fishberg (3) has said that the very term essential hypertension is a confession of ignorance, and that is its chief virtue. In this discussion we understand it as high blood pressure not obviously secondary to any demonstrable cause in contradistinction to the high blood pressure that gradually develops in chronic nephritis, or rapidly develops in acute nephritis, apparently in close relation to renal insufficiency.
Etiology:

The literature on the etiology of essential hypertension seems to be based largely on theories propounded by various men. However, much work has been done on this problem, and Fishberg (3) has given a very effective discussion of this work. He states that there is not only one essential hypertension but there are essential hypertensions and the following groups may be tentatively differentiated:

The group which seems to be most important numerically is a constitutional, familial, and hereditary disease, which has been termed constitutional hypertension. Of the figures cited the work of O'Hare, Walker, and Vickers (60) included the largest number of cases. They elicited a family history of vascular disease in 68 percent of 300 patients with hypertension but in only 37.6 percent of 437 controls. In these cases, however, apart from the fact of hereditary predisposition, we know little of the cause of the hypertension.

In another group of cases, the hypertension is the result of dysfunction of endocrine glands. Fishberg (3) states that the most common of this group are the cases coming on in association with the menopause, in the production of which the cessation or perversion of ovarian function is probably of great importance. However, it is very probable that the group of ovarian and constitutional hypertension overlap.
Fishberg (3) believes that there are accessory factors in the causation of essential hypertension which, while they do not in themselves cause hypertension, make themselves manifest or exaggerate the high blood pressure in predisposed individuals. He believes the most probable of such contributory causes are emotional and other psychic strains, overeating, and obesity. How they act is not known.

Pathology in Essential Hypertension:

Nothing is known of the very early stages of essential hypertension as patients do not die then. Christian (8) states that when they do die fairly early in the course of the disease, usually due to vascular accident, there is diffuse thickening of the smaller arteries but not much change in the larger arteries. The kidneys are red but appear essentially normal except for thickening in the smaller arteries and an occasional atrophic and sclerosed glomerulus.

Christian (8) states that later in the disease kidney changes are more evident. The cortex is slightly thinned; the kidney surface is slightly granular; the kidneys are beefy red; sclerosed glomeruli and atrophic tubules are more numerous; blood vessels are more generally thickened. The kidney lesions, however, are much less marked than what is found in the ordinary type of chronic nephritis and would seem to be the result rather than the cause of vascular dis-
turbance. In this latter statement Fishberg (3) agrees but in more positive terms. He states that formerly renal lesions of essential hypertension were not differentiated from chronic glomerulonephritis, both being united in the concept of chronic interstitial nephritis. However, later investigation showed conclusively that in essential hypertension the changes in the kidney are secondary to disease of the small arteries, the so called arteriosclerosis, and in recent years the term arteriolosclerotic kidney has been appropriately applied to the renal lesions found in the vast majority of cases of essential hypertension.

DeWesselow (61) in a lecture before the Royal College of Physicians agrees in regarding it proven that in essential hypertension the renal lesion is secondary to the vascular one. In referring to this renal lesion here he endorses the term "ischaemic nephritis" which recognizes the purely secondary nature of the changes in the kidney.

Christian (8) has found that the more advanced cases have many resemblances both to cases of degenerative arteriosclerosis and to cases of chronic nephritis. Very probably hypertension, arteriosclerosis, and nephritis are often intermingled in the same patient, and it is not possible from autopsy evidence to reconstruct the type, sequence, and progression of the lesion. He reminds us that our pathology is largely of the late or end stages and that essential vascular hypertension is a condition that may persist without very disturbing symptoms; hence, we
have very little knowledge of the anatomical changes, if any are present, in the earlier period of the condition.

This type of kidney just described is the kidney of benign nephrosclerosis of Volhard and Fahr (27). While there are signs indicating damage to the kidney there is never any serious impairment of renal function here. In this sense it is very different from malignant nephrosclerosis in which there is renal insufficiency and the patient may succumb to uremia. This latter group which Fishberg (3) has found to constitute less than ten percent of the fatal cases of essential hypertension, is characterized anatomically by the presence of necrosis and endarteritis of the renal arterioles.

**Symptoms in Essential Vascular Hypertension:**

Mosenthal (53) states that the first symptom of essential hypertension is an elevated blood pressure. This is obviously true if we consider that signs and symptoms presented in general are secondary to increased arterial pressure. However, the sphygmomanometer often detects the presence of the hypertension a long time before the patient has any related complaints. When he does begin to have complaints they vary greatly and are not well defined. Mosenthal (53) states that they are often confused with the symptoms of neurasthenia or those ascribed to focal infections because they are so indefinite. Cardiac palpitation, slight dyspnea, precordial heaviness, headaches,
vertigo, failing memory, fatigue, dyspeptic symptoms, nocturia, and many others occur, varying according to the part of the circulatory system in which the disease is developing most rapidly. Mosenthal goes on to say that epistaxis or hemorrhage elsewhere, apoplexy or angina pectoris, may be the first signal of a marked hypertension.

Cardio-vascular Changes:

Christian (8) states that physical examination, besides the hypertension, usually shows demonstrable cardiac enlargement, chiefly to the left. Palpable vessels often feel very normal and marked arteriosclerosis is the exception. O'Hare and Walker (62) have worked on the relation of these peripheral vessels to high blood pressure and found that they play little or no part in the hypertension whatever may be their state. They have studied 50 cases of advanced peripheral arteriosclerosis with normal retinal vessels and found no hypertension to exist. Usually the ophthalmoscope reveals changes in the retinal arteries even when nothing unusual can be palpated, but this is not always true. Those cases without retinal arteriosclerosis are believed by O'Hare and Walker to be early cases of hypertension. Fishberg (3) writes that there are many cases of essential hypertension in which the hypertrophied heart muscle copes adequately with the increased work confronting it, and at no time during the course of the disease are there complaints referable to
the heart. However, he says that it is decidedly more common that cardiac symptoms make their appearance sooner or later. In fact, many individuals with essential hypertension present a clinical picture that is completely dominated by the manifestations of disease of the heart, and from beginning to end they are "cardiacs". In this connection Christian (8) states that vascular hypertension is a general circulatory condition, so as it progresses we may expect to find evidence of changes throughout the body. However, while the condition is generalized, the effects are far more marked on one organ than on another, so that we may speak of a cerebral or cardiac or renal type of hypertension in accordance with whether the brain, heart, or kidney undergoes the more marked degenerative disturbances. The danger in these expressions of type is that one may focus his attentions on the point from which the symptoms arise and forget that we have here primarily a general vascular disturbance.

Urine and Renal Function:

Mosenthal (53) states that in the early stage of every case of essential hypertension and throughout the great majority of the cases, there are no signs of kidney involvement in the urine in the form of albumin or casts, nor is there the slightest indication of any impairment of renal function in the blood chemistry or on other tests. Fishberg (3) reports that only seven percent of his cases ver-
ified at necropsy died of uremia, which is the only form of death from essential hypertension that can be ascribed to the kidneys. Paulin (63) in a study of 76 cases of essential hypertension concludes that renal involvement in the late stages of this disease is usually very slight, and he states that only one of this series died because of renal failure. Christian (64) also believes that few of these patients die as a result of uremia or have manifestations of chronic nephritis. His percentage is somewhat higher than Paulins, however, as from 131 cases, 70 of which were checked at necropsy, six or 4.5 percent died of uremia or had extensive chronic nephritis.

Christian (8) believes that if there is to be any change in function, it will most likely be detected in the two hour test by a slight departure from normal toward an increased night excretion. Fishberg (3) agrees that this is the most accurate test and states that many errors have been made by relying on the phenolsulphonephthalein test here. The excretion of the dye is frequently subnormal while the concentration test shows the kidney in good condition. In such cases the phthalein excretion is due to cardiac weakness, and we must remember that cardiac failure is a much more frequent event in essential hypertension than is renal failure. Water excretion is often deficient in these patients so that the two hour test may show diminution in the diluting power unaccompanied by deficient concentrating ability, which again is to be attributed to
the heart and not to the kidneys. With good functioning capacity of the kidneys the nonprotein nitrogen is not elevated, unless severe cardiac weakness with oliguria causes it to rise.

**Hemorrhage:**

Hemorrhages are a striking feature in many cases of essential hypertension. Obviously the most important form of hemorrhage in this disease is cerebral hemorrhage. Rhomberg and Lippman cited by Fishberg (3) found hypertension to be almost invariably present in individuals who had a cerebral hemorrhage.

Fishberg states that epistaxis is frequent in essential hypertension and in some instances is an initial symptom. Christian (8) has found that it is frequently followed by striking relief from symptoms.

Other types of hemorrhages also occur. Retinal and subconjunctival hemorrhages are not uncommon. Renal hemorrhage may also occur and when it does local renal and bladder disease as neoplasm and tuberculosis must be ruled out.

**Dyspnea:**

Christian (8) states that dyspnea here is of the ordinary cardiac type and comes on with increasing cardiac enlargement. He also states that usually although not always, with this dyspnea there is quite marked evidence of renal insufficiency, suggesting that this type of dyspnea
is also of central toxic origin. Fishberg (3) believes that with failure of the left ventricle there occurs stasis and increased pressure in the pulmonary circuit which gives rise to a hypertrophy of the right ventricle. It is this strain on the right heart which he believes to be the cause of the dyspnea. Stieglitz (65) differs from both of these views and believes that the dyspnea is due to left ventricular failure causing an inadequate cerebral circulation and hence causing dyspnea by hyperstimulation of the respiratory center.

**Diagnosis of Essential Vascular Hypertension:**

It is agreed by most writers that in the majority of cases there is little difficulty in establishing the diagnosis of hypertension. Having recognized the hypertension, it is important to determine renal function to see whether the condition is to be regarded as essential vascular hypertension or hypertension of chronic nephritis. A careful history will help to differentiate the malignant type of hypertension from chronic nephritis. Christian (8) has found that the hypertension of hyperthyroidism sometimes may be confused with this form of high blood pressure. Basal metabolic determinations are very helpful here in diagnosis, although borderline cases are a difficult problem.
Prognosis in Essential Vascular Hypertension:

The clinical duration of essential hypertension varies between extremely wide limits. However, as Fishberg (3) states, the person with elevated blood pressure is exposed to many dangers, and his expectation of life is distinctly shorter than if his blood pressure were normal.

The sex is of importance in prognosis of this disease. Paulin (63) in the 71 cases that he followed from five to 17 years found the mortality for men was 47.2 percent and for women 9.2 percent. Fishberg (3) found the mortality about twice as high in men. This may be partially explained due to the rather benign hypertension in women about the time of the menopause.

Fishberg (3) believes that in general the younger the individual with essential hypertension, the more serious the prognosis. Hypertension detected in the sixties or later often pursues a mild course and may not shorten the patient's life.

Fishberg (3) quotes the work of May (66) in the Prudential Life Insurance Society to show that in general the prognosis is worse with a very high blood pressure. Christian (8) emphasizes that the height of the diastolic pressure is much more significant than that of the systolic.

I have discussed the fact that myocardial insufficiency is one of the most frequent serious complications of essential hypertension. If this is slight it frequently responds well to treatment and even the severe cases often
respond well the first time. However, it has been noted by Fishberg (3) that after several attacks of myocardial insufficiency therapeutic measures are usually of no avail and the patient becomes bedridden most of the time. Following this, the condition may soon terminate fatally or may last for years.

The occurrence of anginal attacks due to arteriosclerosis of the coronaries is always a serious event. The prognosis is made much worse if following a coronary closure in a patient with hypertension the blood pressure drops and remains low.

When the renal concentration test shows impaired renal function in a patient in the thirties or forties the outlook is very poor. As a rule, these patients run an acute course, and Fishberg (3) states that autopsy reveals them to have been in the malignant phase of the disease with arteriolar necrosis.

The ophthalmoscopic examination is of great value in telling the condition of a group of small vessels in intimate association with important cerebral arteries. Changes here indicate possible cerebral hemorrhage. Christian (8) states that prognosis depends on the condition of the cerebral vessels, myocardium and coronary arteries, and on renal function rather than on height of blood pressure.
Renal Arteriosclerosis:

The more significant points with regard to this condition have already been discussed. Here we are dealing with arteriosclerosis in contradistinction to the arteriolosclerosis of essential hypertension. Addis (14), VanSlyke (22), and Volhard and Fahr (27) quoted by VanSlyke would all call this lesion benign nephrosclerosis.

Christian (8) deals with this condition in a very brief manner. With arteriosclerotic changes in the intrarenal arteries there are degenerative changes in the glomeruli and tubules. The kidney is red and granular, slightly to moderately decreased in size, and the blood vessels stand out prominently with gaping lumina and thickened walls. The urine shows a little albumin and a few casts. Renal function may be normal or moderately decreased.

VanSlyke (22) says that the symptoms of this benign form of arteriosclerotic Bright's disease are almost entirely those attributable to circulatory changes, and death usually comes from circulatory rather than renal failure. Christian (8) states that while there is evidence of a renal lesion in most arteriosclerotics, it plays relatively little part in the symptom complex of arteriosclerosis and the renal factor needs no special attention in the treatment of that disease.
CONCLUSION
The symptomatology of the various types of nephritis has been considered according to Christian's classification. In connection with each of his subdivisions, an effort has been made to show what terminology other authors would use. This comparison of terminology may be condensed into a table such as the following:
<table>
<thead>
<tr>
<th>Christian</th>
<th>Volhard &amp; Fahr</th>
<th>Addis</th>
<th>Van Slyke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Nephritis</td>
<td>Acute focal Glomerulonephritis</td>
<td>Acute Stage Hemorrhagic Bright's Disease</td>
<td>Initial Stage Hemorrhagic Bright's Disease</td>
</tr>
<tr>
<td></td>
<td>Acute Diffuse Glomerulonephritis</td>
<td>The following Degenerative Bright's Disease 1. Pyogenic 2. Non Bacterial 3. Bacterial</td>
<td>The following Degenerative Bright's Disease</td>
</tr>
<tr>
<td>Subacute Nephritis with Edema</td>
<td>Genuine Nephrosis</td>
<td>Cryptic Degenerative Bright's Disease</td>
<td>Lipoid Degenerative Bright's Disease</td>
</tr>
<tr>
<td>Subacute Nephritis: Hemorrhagic Nephritis</td>
<td>Subacute Glomerulonephritis</td>
<td>Hemorrhagic Bright's Disease Late acute Latent Early chronic</td>
<td>Hemorrhagic Bright's Disease Late Initial Latent Early chronic</td>
</tr>
<tr>
<td>Chronic Nephritis with Edema</td>
<td>Chronic Diffuse Glomerulonephritis with a Nephrotic Tendency</td>
<td>Chronic Active Hemorrhagic Bright's Disease</td>
<td>Chronic Active Hemorrhagic Bright's Disease</td>
</tr>
<tr>
<td>Chronic Nephritis without Edema</td>
<td>Chronic Diffuse Glomerulonephritis</td>
<td>Terminal Hemorrhagic Bright's Disease</td>
<td>Terminal Hemorrhagic Bright's Disease</td>
</tr>
<tr>
<td>Essential Vascular Hypertension progressing into Chronic Nephritis</td>
<td>Nephrosclerosis Benign type Malignant type</td>
<td>Arteriosclerotic Bright's Disease</td>
<td>Arteriosclerotic Bright's Disease Arteriolosclerotic Type</td>
</tr>
<tr>
<td>Renal Arteriosclerotic Benign Nephrosclerosis Progressing into Chronic Nephritis</td>
<td>Arteriosclerotic Bright's Disease</td>
<td>Arteriosclerotic Bright's Disease Arteriosclerotic Type</td>
<td></td>
</tr>
</tbody>
</table>
The only difficulty which arises in comparing the classifications of Volhard and Fahr, Addis, and VanSlyke with that of Christian comes in trying to name any condition described by any of these four men which corresponds to the hemorrhagic nephritis of Christian. True, both Addis and VanSlyke refer to hemorrhagic Bright's disease, but when they do, they include not only the hemorrhagic nephritis found in Christian's classification but also his acute and chronic nephritis. It would seem that the type of patient who would fall under hemorrhagic nephritis in Christian's classification might be classed as subacute glomerulonephritis by Volhard and Fahr and as a late acute, latent, or early chronic hemorrhagic Bright's disease by Addis and VanSlyke.

It is evident from this discussion that the main variation that exists between these classifications is one of terminology and not of concept. If we can just keep the various terms sufficiently in mind to be able to interpret the literature we will do well to adhere to Volhard's (67) conception that "it is more essential to attain clarity concerning the nature of the disease than to be meticulous concerning the etymology of its name."
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