THE LATE RENAL AND CARDIO VASCULAR EFFECTS OF SCARLETINAL NEPHRITIS.

BY

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INTRODUCTION.
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The author's attention was first directed to the problem suggested by the title of this Thesis by a personal experience which is doubtless common to other physicians in general practice.

Thoughtful parents of a child who had recovered from scarletinal nephritis asked pertinent questions regarding the boy's future. Was he fit to enter Sandhurst? Could he play strenuous games? Would his professional duties in India expose him to risks of impaired health in later years? Was there any danger of chronic nephritis?

A problem thus arose on which one's views were confused and indefinite, and on turning to what limited literature could be found, no consolation was extracted; in fact the literature referred to in Chapter 2 makes it abundantly clear that to give
answers representing general medical opinion was impossible.

This investigation is therefore our attempt to find an answer to two main questions.

(1) Is the acute scarletinal nephritis in childhood or youth ever the beginning of a chronic nephritis, which may manifest itself in later years? And if it does, is it a frequent termination?

(2) Does an acute scarletinal nephritis which appears to have healed, leave any traces of organic change, or functional impairment of the kidneys or other organs, in particular the cardiovascular system?

Subsidiary questions arose in the course of the enquiry and are discussed.

The problem having thus been defined, the most practical method of approach at once presented itself for consideration – as regards the kidneys, how to exclude or confirm the presence of a gross
lesion known to have been present during the scarlet-nephritis, and how best to detect the earlier stage of functional impairment.

We should state at once that — as far as the present condition of the investigated cases is concerned — we are little interested in any anatomical changes which may be a legacy of the original infection, except to consider whether, in common with the general law, a structurally damaged kidney may be less able to resist the "Sturm und Drang" period in the future.

The emphasis of anatomical change first began to take precedence over all else when Virchow almost revolutionized medical methods of investigation by his doctrines of cellular pathology. Objective evidence soon began to replace the study of symptoms, and the classification of disease is still too often based entirely on post mortem findings. Only with Mackenzie's teaching did the important fact emerge, that function is much more important than structure, and only then was what might be called the
"post mortem" method of medical study gradually succeeded by the experimental. It was realised that one should look to the living to fathom the laws of life, not to the dead.

It appeared therefore that the most rational method of approaching the problem was to examine children still living, but who had previously had scarletinal nephritis, to make a careful note of the state of health since their discharge from hospital, and to examine in particular, the renal and cardiovascular systems.

We are indebted to Dr W. T. Benson of the City Hospital, Edinburgh, from whom we were able to obtain the case records of 107 children who during the past ten years had had nephritis complicating scarlet fever. The examination and the tests employed involved at least two visits to each case and in a number of cases, the tests and examinations were repeated.

Of the cases at our disposal, eighty-four were traced and examined in the manner described in Chapter 5.
In Chapter I a brief outline is given of the pathology of scarletinal nephritis, including the associated pathological conditions of the renal and cardio vascular systems.

In Chapter II the signs and symptoms which might be expected are discussed, and an attempt is made to correlate clinical manifestations with the pathological processes in the kidney. As our main interest is the prognosis of scarletinal nephritis, a considerable section of this Chapter is devoted to the literature on this question, and as the recorded investigations on similar lines to our own, are scanty, those that could be traced are quoted in some detail.

It is mentioned in the body of this Thesis, that although the examination of the cardio vascular system would obviously proceed on conventional lines, the most reliable and practical method of forming an estimate of the condition of the kidney function, at once leads us into debatable territory. In Chapter III therefore, we have tried to classify our views regarding normal and abnormal kidney
function, particularly as towards water and dissolved substances such as urea, and stress is laid on the non-renal conditions which may modify renal function in the absence of renal disease.

In Chapter IV, renal efficiency tests are shortly referred to, and our reasons for relying on the water and urea concentration tests, are given.

Chapter V describes the method of examination adopted, and the result of the examination of each case, which are then tabulated for the purpose of easy reference.

The Discussion and Summary follow in the usual order.
CHAPTER

I. THE PATHOLOGY OF SCARLETINAL NEPHRITIS.

II. SYMPTOMS AND PROGNOSIS.

III. PHYSIOLOGY OF RENAL FUNCTION.

IV. RENAL EFFICIENCY TESTS.

V. METHOD OF EXAMINATION. THE CASES IN DETAIL.

VI. DISCUSSION.

VII. SUMMARY.

VIII. BIBLIOGRAPHY.
THE PATHOLOGY OF SCARLETINAL NEPHRITIS.
Chapter I.

The standard teaching regarding the pathological anatomy of an acute diffuse glomerulonephritis is that all the glomeruli are affected, and in a fairly uniform manner. The principal changes are, first, a swelling and dilatation of the capillary loops, followed by a total absence of red blood corpuscles and an increase in the number of cellular elements. Later the epithelial cells covering the glomeruli and capsule are swollen and show fatty degeneration, with areas of necrosis and desquamation, and of beginning proliferation.

In the early stages when the glomeruli still contain blood, there are hardly any changes to be noted in the tubules. As the glomeruli become devoid of blood, the cells of the proximal tubules
present changes in varying degree. These changes consist of swelling, fatty and hyaline degeneration and desquamation of cells. They are secondary to the changes in the glomeruli, and are the result of the diminution of the blood supply to the tubules in consequence of such changes. It is, however, possible that in cases where the changes in the tubules are very marked, they may be produced by the same causes which are responsible for the changes in the glomeruli.

In the interstitial tissue, areas of round cell infiltration are found in the early stages of the disease.

The above description covers the main pathological changes in the kidney in acute diffuse glomerulo-nephritis. Variations occur in the degree of involvement of the glomeruli and tubules. Although all the glomeruli are uniformly involved, there are borderline cases among the milder forms in which the histological picture of the glomeruli presents varying degrees of transition from the focal glomerulo-nephritis to the diffuse form.
There are four recognised types of acute nephritis following scarlet fever.

1. That in which the glomeruli are only slightly affected.

2. That in which haemorrhages occurring into the glomeruli and throughout the kidney are prominent features.

3. So-called true post Scarletinal glomerulonephritis in which the glomeruli become the seat of marked pressure owing to the proliferation of the epithelium cells about the capillaries of the capsular lining.

This proliferation proceeds until the lumen of the capillaries is practically obliterated and their walls become fused with the proliferated epithelium of the capsule by means of a fibrin network. The microscopic appearance at this stage is that of a solid mass of tissue. In some instances there are no other changes in the kidney.

This form appears to occur more frequently in scarlet fever than in any other condition.

4. The small round celled infiltration form. This
is not accompanied by a proliferation of the interstitial connective tissue cells, but is characterised by a marked infiltration of small round cells especially in the region of the glomeruli and about the blood vessels, particularly the larger veins. There are practically no changes in the tubules. This condition may develop later into a true glomerulo-nephritis in which the glomerular cells and interstitial tissues show marked proliferation, eventually assuming the type of a chronic interstitial nephritis.

Type 1 is usually considered to be present in the mild form of scarletinal nephritis, while types 2, 3, and 4 are seen in the severe forms. In Type 2 the urine is dark red or scanty and contains much albumin, casts and cell detritus. The temperature is usually septic in character.

Types 3 and 4 in which the glomeruli are much affected are characterised by marked and continued oedema. The blood pressure is always raised in these more severe cases.
The further progress of the pathological process is in two directions; either the changes in the kidney are progressive and the acute diffuse glomerulo-nephritis passes into subacute or chronic glomerulo-nephritis; or the process in the kidney recedes, the cellular elements in the glomeruli disappear, the capillaries are again filled with blood, and there is more or less complete restitution to normal. That such restitution is possible has been demonstrated, although the kidneys of the patient in which the process is in the healing stage can be rarely obtained for pathological examination. It is found that the glomerular capillaries are to a great extent filled with blood, and the cellular elements only slightly increased.

In the subacute stage the affected glomeruli are bloodless, and the cellular elements are increased. The capsular epithelium is proliferated and desquamated with the formation of crescentic masses in the capsular space.

Thrombotic masses consisting of red blood corpuscles, leucocytes, fibrin, and epithelial cells
are seen in the capsular spaces.

The tubules show degenerative changes in proportion to the degree of glomerular involvement. In the lumen of the tubules are found desquamated epithelial cells with fatty and hyaline degeneration, hyaline casts, leucocytes and red corpuscles either singly or in the form of casts.

The interstitial tissue shows an infiltration around some of the glomeruli and between the tubules, consisting of lymphocytes, and leucocytes. Where the glomeruli have become obliterated, there is an increase in connective tissue, which is at first cellular.

In the final or chronic stage, many of the glomeruli are completely obliterated and converted into round hyaline bodies. Others still may show a few normal loops containing blood and in addition there are also found normal and hypertrophied glomeruli. Many of the tubules have completely disappeared and are replaced by connective tissue and this is certainly the case with the tubules belonging to obliterated glomeruli. Other tubules, belonging
to glomeruli which are still functioning are dilated and lined with low cubical epithelium. With the disappearance of many of the tubules, the remainder are found to be grouped in the form of islands. These groups of islands project and give a granular appearance to the surface of the kidney on gross inspection. In the lumen of the tubules are found hyaline and granular casts, and desquamated epithelial cells.

The interstitial tissue is increased in proportion to the amount of destruction of the glomeruli, and tubules. The connective tissue, which is at first very cellular, gradually shrinks and surrounds the hyalinised glomeruli, and separates the tubules into groups of islands.

At any time during this insidious progress of the disease, the whole pathological process may stop, and remain at a standstill for months or years. Such a standstill might be permanent were it not for two factors, one of which again sets the pathological process into motion, and the other helps in a different
manner to reduce the functional capacity of the kidney.

The first factor is the danger of another attack of acute nephritis, and the second, the changes in the arterial system of the kidney. Any repetition of acute nephritis from whatever cause will result in more glomeruli and tubules being destroyed, thus either reducing the "safety factor" or actually impairing the kidney function. The changes that occur in the arterial system of the kidney, affect especially the small arteries, and consist of a thickening and proliferation of the intima.

Both these factors are responsible for the gradual reduction of the number of functioning elements in the kidney.
Urinary Changes during the Acute, Subacute, and Chronic Stages of Acute Scarletinal Nephritis.

In the acute stage, haematuria is in the great majority of cases, an early symptom, and the amount varies from a few red corpuscles found in the sediment, to the smoky or bloody appearance indicating the presence of large amounts.

Albumin is always present throughout the disease in variable quantities, and there is no doubt that the amount of albumin present, bears no relation to the severity of the disease. The quantity of urine is always diminished at the beginning of the nephritis, and may even be entirely suppressed. In the cases which progress favourably the daily amount of urine soon becomes increased. The specific gravity shows considerable variations. At the beginning with daily small amounts of urine, the specific gravity may be as high as 1030, but drops to a much lower figure when the urinary output
increases. In the urinary sediment are found casts of all varieties, hyaline, granular, and at times, blood and epithelial casts. The number varies, being sometimes very abundant, while at others, only a few can be found.

In the subacute stage the total urinary output remains low, and albumin is constantly present although the amount is variable. The specific gravity remains low in spite of the diminution of total daily output. Blood is almost always present and the sediment contains all varieties of casts.

In the chronic stage the only remaining symptom may be an albuminuria. Albumin is often present in very small amounts, and its presence is the only indication that recovery has not been complete.

During this stage the kidneys appear to be peculiarly susceptible to repeated mild exacerbations causing reduction in the amount of urine and nocturia, and increased albuminuria. The specific gravity becomes low and there is always the gradual tendency
for the quantity to become fixed over the twenty-four hours. The colour is then pale and the specific gravity is low, ranging from 1006 to 1016 and tends to remain at about the constant figure of 1010 or 1012.
Cardiovascular Changes.

Cardiovascular changes form a cardinal symptom of all forms of nephritis and must therefore be considered here.

It has been seen that in the diffuse glomerulonephritis all the glomeruli of both kidneys appear to be equally affected. The essential process is first, the cessation of blood flow through the glomeruli followed by an increase in the cellular elements. Although red blood corpuscles may still be seen in the glomeruli in the earliest stages, they soon disappear from them as the cellular elements proliferate. All the further changes in the glomeruli are secondary to these two processes. Whether these initial changes are due to a streptococcus or to their toxins does not concern us here.

It is presumed that blood is prevented from reaching the glomeruli by a narrowing of the arterial lumen above the origin of the afferent artery. Such a narrowing must either be organic from a proliferation/
proliferation of the arterial wall, or functional from a spastic contraction of the artery. If it were organic, the changes in the artery would necessarily be permanent and not retrogressive, such as is the case in chronic glomerulo-nephritis. In acute nephritis the changes are retrogressive and usually disappear completely.

We presume therefore that the narrowing of the arterial lumen is of the nature of a spastic contraction of the arteries. This spastic contraction occurs uniformly throughout both kidneys and by obstructing the flow of blood causes an ischaemia of all glomeruli. This explanation lends itself easily as a basis for the explanation of the pathological physiology of the disease, the oliguria, anuria, oedema, and the cardiovascular changes.

In the majority of cases the blood pressure is increased and this usually occurs at, and sometimes even before, the onset of the nephritis. Rolleston\textsuperscript{1} found the blood pressure subnormal in 25\% of a series of cases of scarlet fever, the extent and duration of the depression being as a rule in direct
relation to the severity of the original attack. In only a minority of his cases of nephritis (12 out of 33) was the blood pressure above normal, and the hypertension was never extreme, nor of long duration.

Ernberg² found that the raised blood pressure, when present, was fairly large.

An abnormal blood pressure is usually absent in mild cases of scarletinal nephritis, and is also occasionally absent in a severe case without apparent reason. In most cases however, there is a rise in blood pressure occurring at the onset of the disease. It is usually not high being from 20 - 40 mm. above the normal, and it usually returns to normal before the other manifestations of the disease have disappeared.

The heart does not show any changes at the beginning of the disease, except for an accentuation of the aortic second sound. When the increase in blood pressure is considerable and prolonged over several weeks the heart hypertrophies, the apex beat being forcible and outside its normal position. Heart failure is rare in acute nephritis.
In the subacute and chronic stages there is a tendency for the blood pressure to increase. At first there may be considerable variations from day to day, but later the pressure remains constantly high. Both the systolic and diastolic pressures are high — with a systolic reading of 180 - 200 — the diastolic is usually as high as 120 - 140 — which contrasts strongly with the blood pressure figures in primary renal arterio-sclerosis without renal insufficiency where with a systolic pressure of 200, the diastolic is rarely above 100 or 110.

The heart is hypertrophied in all cases, the more so the longer the condition has lasted. The apex beat is forcible, the aortic sound accentuated and a mitral systolic murmur is often present. When the hypertension is of long duration evidence of arterio-sclerosis of the peripheral arteries may be found.
SYMPTOMS AND PROGNOSIS.
Chapter II.

SYMPTOMS AND PROGNOSIS.

Symptoms.

As all the cases followed up were carefully interrogated regarding their general health since having had scarletinal nephritis, we should next consider the clinical course of a chronic diffuse nephritis. Only a knowledge of the possibilities enable us to put what are of necessity leading questions.

The clinical course of a chronic diffuse nephritis may conveniently be subdivided into three stages.

First, the period following apparent recovery from the original acute attack. The great
majority of our cases fall in this category. Second, the period of persistent hypertension and increasing loss of kidney reserve, and third, the terminal period of absolute renal inefficiency.

Following the attack of acute scarletinal nephritis, there is apparently complete recovery. Oedema disappears, the blood pressure returns to normal, the blood chemistry is unchanged and the presence of albumin in the urine is the only indication that recovery is not complete. At this stage, functional kidney tests are quite normal.

This period may last for many months or years, and the patient usually first comes under the observation of the physician when albumin has been found in the urine on routine examination.

The second period, which may also last for many years, is characterised by a persistent and gradually increasing hypertension - both the diastolic and systolic pressures being high. With the persistent hypertension there is cardiac hypertrophy corresponding to the duration of the
hypertension, a forcible apex beat, accentuation of the aortic second sound and frequently a systolic apical murmur. When oedema is present it may be due either entirely to renal, or cardiac conditions, or to both.

In cases without oedema the urinary output is either normal or increased. The specific gravity varies with the quantity and the progress of the disease; as the loss of kidney reserve progresses, the specific gravity becomes lower and tends to become "fixed". Albumin is present in varying amounts and casts, leucocytes and occasionally blood cells are found.

The functional tests at this stage show a distinct reduction in kidney reserve, and the presence of a relative renal insufficiency. This may be very slight at first but increases with the progress of the disease and shows itself by a prolongation of elimination time, and by a reduction of the ability to concentrate the urine. The water test shows smaller quarter hour quantities and the elimination
of the total intake is prolonged. The specific gravity is low and shows little variation and the urea concentration test shows a diminution in urea percentage.

All these tests will show all variations from only a slight reduction of kidney reserve to a very considerable degree of relative renal insufficiency.

But the characteristic of this period, which separates it from the third stage, is the absence of absolute renal insufficiency. The non-protein nitrogen of the blood is still normal.

A temporary increase in the non-protein nitrogen of the blood may occur either during a recurrent attack or with a too liberal protein intake, and there is by this time a moderate degree of anaemia present.

These changes are accompanied by their clinical manifestations. Headache, fatigue, loss of appetite, dyspnoea on exertion, and blurring of
vision, are the predominant symptoms.

In the third or terminal period, there is superadded a persistent elevation of the non protein nitrogen in the blood, which cannot be reduced to the normal level. With the still higher blood pressure, the signs of cardiac hypertrophy are accentuated and cardiac failure may occur.
Correlation Between the Clinical Manifestations and the Pathological Processes in the Kidney.

The morphological changes which occur in a kidney during an acute or chronic nephritis are essentially simple and straightforward, and should be able to be correlated with the clinical manifestations of the disease.

We have seen that the pathological changes in the kidney are:—
1. The gradual hyalinisation and obliteration of the greater number of the glomeruli.
2. The disappearance of the corresponding tubules with their replacement by connective tissue.
3. Changes, chiefly in the afferent arteries of the glomeruli resulting in the thickening of their walls.

In studying the clinical manifestations of the disease one finds essentially the following symptoms:—
1. A gradual and persistent increase in blood pressure.

2. A gradually increasing loss of the variability of kidney function, which manifests itself by a compensatory prolongation of elimination time – by polyuria and nocturia – and by a diminution in the ability to concentrate.

3. A gradually increasing renal insufficiency, at first relative and later absolute as shown by the blood chemistry and the functional tests.

4. Termination with true chronic uraemia.

Under normal conditions, the function of the kidney is to eliminate the waste products of protein metabolism, to maintain the normal composition of the blood, and to aid in the neutrality regulation of the body. The important element in a pathological condition of the kidney is the gradual loss of the variability of kidney function. It begins to lose its power of sudden, efficient bursts of work – it begins to "take its time".

With the gradual hyalinisation and obliteration
obliteration of the glomeruli, the number in which filtration is possible is reduced.

In the early stages of the disease when there is still a sufficient number of functioning glomeruli, the loss of variability in function constitutes simply a loss in the reserve power of the kidney. But a sufficient number of glomeruli and tubules are still left to perform the function of the kidney under ordinary conditions without an undue load.

Under such conditions, any added load, such as excess intake of water or protein, or such an end product as urea, must necessarily result in the prolongation of elimination time.

As the reserve power is further reduced, the extra load of water or waste products which the kidney can eliminate even with prolongation of elimination time becomes smaller and smaller, and waste products accumulate temporarily in the blood. As soon as the load is reduced, however, they are reduced to a normal level. This stage is an exact analogy
to the hypertrophied heart, which is compensated at rest, but decompensated on exertion.

With the reduction of the functioning elements of the kidney to $1/3$ or $1/4$ of the total, the reserve power is entirely gone, and only the minimum amount of waste substances can be eliminated—and this only with all the remaining functional elements continuously active night and day. The remaining glomeruli are continuously active under conditions similar to that of a diuresis following the intake of large quantities of water. The filtrate comes down into the tubules in a flood. Because of this, the filtrate does not remain sufficiently long in the tubules for proper re-absorption of water to occur and is therefore not sufficiently concentrated. The result is an increase in the amount of urine which is of low specific gravity.

In the last stages, the removal of waste products and excessive water from the blood is impossible, because of the sheer lack of glomeruli to do the work. The excess of water is
accomodated in the tissues, although oedema may not actually be present, because of the many extra renal methods of its elimination (chiefly lungs and skin). But the non protein waste products cannot be eliminated in this manner, and are accumulated in the blood.

The essential facts therefore are. It is the function of the kidney to excrete urine, and this function is possessed by the parenchyma of which the kidney is composed. A disturbed function of the kidney can therefore only come to pass as the parenchyma has been involved.

If a poison capable of causing nephritic changes, circulates in the body of a patient — whether it be the toxins of a pregnancy nephritis, or artificially introduced bichloride of mercury, it will, in passing through the kidney, affect the entire kidney at once, and uniformly. This is in other words a generalised parenchymatous nephritis, and since the whole kidney is involved, we see under these circumstances the greatest interference with function, and therefore the greatest decrease in
urine excretion, even perhaps to the point of complete suppression. This is not an uncommon event in scarletinal nephritis. At the same time, such urine as is excreted is heavily charged with albumin, casts, and possibly blood.

If the causes operating to produce the nephritis pass away, the kidney recovers, and so the urinary output rises again, and casts and albumin disappear. But if through prolonged or particularly intense action of the agencies producing the nephritis, irrecoverable changes occur in the parenchyma then the involved cells die and are absorbed. If the kidney does not recover then death of the whole kidney is not the only alternative. Larger or smaller pieces may die and be replaced by connective tissue, while the remainder of the kidney recovers. There will then ultimately result a kidney, which contains normal parenchyma but in diminished amount. This is the "secondarily contracted kidney", "the chronic interstitial nephritis" and the "small red kidney" of the pathologist.

In our opinion therefore it is hardly
possible for a soluble poison (as occurs in scarlet fever) to enter the kidney and not affect it uniformly, with the subsequent possibilities as have been outlined.
Prognosis.

Opinions on the prognosis of scarletinal nephritis, and in particular on the relation between it and a subsequently found chronic nephritis are as the poles apart. Most of the opinions expressed, are by authorities who after many years of experience in dealing with large numbers of cases of scarlet fever, simply record the impressions they have formed on this question. They have an intimate knowledge of the immediate prognosis of scarletinal nephritis but have, or have not, as the case may be, heard of such cases subsequently developing a chronic form of nephritis. The number of actual investigations carried out after a number of years on patients who have had scarletinal nephritis is not large, and the conclusions are equally at variance.

Kerö says that the vast majority of patients recover completely. "A chronic nephritis
sometimes occurs in adults, but must be regarded as an unusual sequel".

Ker\textsuperscript{4} says that he has seen one case of chronic nephritis result from scarlet fever. The patient was an adult and died of nephritis two years later. He adds "I am however, unable to say in what proportion of cases, if any, albumin returns later on". He considered that the out-look as regards nephritis is as a rule extremely good and the chances of the albuminuria becoming chronic, especially in children exceedingly remote.

Rolleston\textsuperscript{5} says that the prognosis of scarletinal nephritis is on the whole good, except in ambulatory cases, in which it is usually unfavourable.

Osler\textsuperscript{6} says that while recovery may take place, not infrequently a chronic interstitial nephritis follows. He further states, in speaking of chronic parenchymatous nephritis, that it is met with most often in young adults, and by no means infrequently in children as a sequel to scarletinal
nephritis.

Stroink examined twenty-two patients who had had scarletinal nephritis. Of these,

1. 7 were discharged 2 - 5 years ago.
2. 12 " " 6 - 10 years ago.
3. 3 " " 11 - 15 years ago.

Of Group 1. 6 or 86% still had albuminuria.
" " 2. 7 or 58% " " "
" " 3. 1 or 33% " " " and chronic nephritis. Of six discharged albumin free, three were again passing albumin.

He came to the conclusion that fourteen, or 64% had signs that the kidney was still affected. One died of uraemia fourteen years after his scarletinal nephritis. Of the fourteen cases, only three were albumin free on leaving hospital. It may be remarked here, that Stroink only examined three of these cases for orthostatic albuminuria, and that it was present in two. He observed that most of these cases felt well, and that apart from the urine changes only one case showed albuminuric retinitis, and only one showed any cardiac hypertrophy.
None of these cases had been under observation since their discharge from hospital. He is, however, in no doubt as to the connection between scarletinal nephritis and the albuminuria in later life and is of the opinion that the condition frequently ends in interstitial nephritis.

Stroink also mentions three cases of chronic nephritis seen post mortem at three, fifteen and sixteen years after having had scarletinal nephritis. Two of these cases left hospital still passing albumin. Each of these three cases showed the existence of a chronic interstitial nephritis.

1. Girl 20 years. Scarletinal nephritis at 5 years. Good recovery but constant albuminuria. Never in bed since discharge. 15 years later oedema and uraemia.

2. Girl 8 years. Scarletinal nephritis at 4 years. Also constant albuminuria, uraemia and death.

3. Child 16 years. And at 32 uraemia and death.

Ernberg examined cases fifteen to twenty-three years after having acute nephritis of various origins and he examined thirty-three who had had
scarletinal nephritis between the ages of 2 – 19 years.

Of these, thirty-one showed no signs of renal inefficiency.

One, a girl of nineteen had been discharged still passing albumin after four months treatment. On examination twenty-three years later, symptoms of chronic nephritis were found — albumin in quantity, casts and a systolic blood pressure of 210. During two pregnancies at twenty-five and thirty albumin was present, otherwise she appeared healthy until at thirty-five years she contracted syphilis and was treated with mercury for four weeks. Ernberg thinks the syphilis responsible for the later nephritis.

The other case in this series was a young man who had albuminuria nineteen years after scarletinal nephritis. He had been discharged albumin free, but had later suffered from a psoas abscess, so that his albuminuria was probably not due to his scarletinal nephritis. Ernberg also mentions
four cases who had died. Two of them six years after discharge and two eleven years after. Two died of pulmonary tuberculosis, and two of pneumonia. Ernberg's work is one of the most interesting on account of the long periods over which his observations were extended. Yet even his investigations give no indication of the relation of scarletinal nephritis to orthostatic albuminuria.

Rosenfeld⁹ examined ninety-three children and young persons who had had scarletinal nephritis within the past ten years.

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<th>Number of Patients</th>
<th>Years after scarletinal nephritis</th>
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The authors say "none of the examined cases showed any signs of severe chronic nephritis, but some had albuminuria of a nephritic character".

Here also, of the ten cases with albuminuria only three had the night as well as the morning urine examined, so that one cannot exclude the possibility of their being chiefly orthostatic cases, especially as in nine of the ten, the blood pressure was normal. In some of this series who had no albuminuria the blood pressure was high and the authors conclude "that they cannot avoid the conclusion that acute scarletinal nephritis can cause a lasting pathological condition of the kidney".

Hansborg had the opportunity of investigating the records of 14,339 cases of scarlet fever admitted to the Blegdam Hospital in the years 1911 - 1920. Of these, 612 had acute haemorrhagic nephritis. Of these, 25 died in the acute stage and 7 died after leaving hospital. These seven cases all had normal urines on leaving hospital, and subsequently had no symptoms of renal trouble. Three died of acute rheumatism, and endocarditis. Two of
tuberculosis, one of diphtheria, and the cause of the other death was unknown. 588 cases of scarletinal nephritis were discharged and of these he was able to examine 284. These cases could be divided into the following groups.

**Group 1.**

259 showed no renal trouble, of these 235 were discharged albumin free, and 24 were still passing albumin on leaving hospital.

In 225 there was at no time between discharge and re-examination any evidence of renal dysfunction. 7 had had at some time or other influenza, measles, etc., and a transient albuminuria. 2 had had a slight recurrence of nephritic symptoms, but later recovered.

**Group 2.**

One case of permanent albuminuria observed 5 years after scarletinal nephritis. This was a girl of 12 admitted in 1919. On admission she had a slight albuminuria which disappeared in a few days, but which returned on the 12th day. On discharge she was still passing albumin, and had a systolic blood pressure of 110. She was frequently examined subsequently, but always had albumin. She felt well, and made no restrictions in her diet.

In 1921, heart normal. Blood pressure 105, albumin present, and not orthostatic. Sodium chloride excretion normal and the specific gravity varied from 1001 - 1027.


Ureteral catheterisation showed the right kidney with only traces of albumin, but the left passing large amounts. She was then still in good health.

**Group 3.**

One case of chronic nephritis. A girl who had a mild scarletinal nephritis, and re-examined at the age of 25 years, 9 years later. During her stay in hospital she developed acute rheumatic fever with endocarditis, and was discharged still passing albumin, and blood, and with mitral disease. Two years later admitted with diphtheria, and then had mitral stenosis, and symptoms of cardiac decompenation. Blood pressure 150. Urine contained blood, albumin and casts. Lowest specific gravity 1002. Highest 1028.

**Group 4.**

23 cases had orthostatic albuminuria.

This work of Hansborg is one of the few recorded investigations carried out systematically on a large scale, and its interest and value are our justification for a somewhat detailed quotation. We are in some doubt as to the significance of the case of permanent albuminuria (Group 2), but whether or not this case continues to remain symptomless like the other 282, or whether it becomes a chronic nephritis, this investigation bears out the view of Ernberg,
that the prognosis of scarletinal nephritis is extremely good, and that the risk of chronic nephritis almost negligible.

As scarlet fever is a common disease, and as most patients are quite vague not only as to whether they have had scarlet fever, but still more so on the possibility of scarletinal nephritis having occurred, it is obvious that a mere history of scarlet fever is of no value etiologically when given by chronic nephritics.

Campbell examined the records of 1,500 consecutive cases of the Montreal General Hospital and found -

(a) 1. Cases giving a history of scarlet fever, but having no signs of chronic nephritis while in hospital - 111.

2. Cases with signs of chronic nephritis, but no history of scarlet fever - 82.

3. Cases with signs of chronic nephritis and giving a history of scarlet fever - 10.

(b) Of 450 consecutive cases of chronic nephritis there was a history of scarlet fever in 46, i.e. 10%.

(c) As pregnancy throws a strain on the kidneys, 1,500 consecutive cases were taken from the Montreal Maternity Hospital. In three groups these also showed.
1. Patients with a history of scarlet fever, but no evidence of nephritis during pregnancy or puerperium - 182.

2. Patients showing evidence of nephritis during pregnancy or puerperium, but with no history of scarlet fever. - 30.

3. Patients with nephritis of pregnancy and with a history of scarlet fever - 10.

A statistical study based on the figures from these two hospitals showed that the incidence of chronic nephritis in cases with a history of scarlet fever was little greater than is in accord with the law of averages. This was shown by applying calculations based on the probability of current events.

Savill \(^\text{12}\) says that as a rule scarletinal nephritis clears up entirely, and that the supervision of chronic nephritis is rare.

Dingwall Fordyce\(^\text{13}\) points out that the prognosis in cases of acute nephritis differs considerably in scarletinal and non-scarletinal cases. "In scarletinal cases it is largely a question of "kill or cure" and fortunately in about 95% of cases the result is cure, but in some cases the tendency to become latent is met with".

Beattie and Dickson\(^\text{14}\) in describing subacute
diffuse nephritis say that in scarletinal nephritis, the patient may die during the acute stage, but more commonly not till the disease has become subacute e.g. three to four weeks up to many months after the onset of the fever. The condition may become more chronic and may last from two to six or seven years; in which case the condition of the kidneys may come to resemble that found in chronic granular contraction, with fibrous tissue overgrowth, adhesion of the capsule, thickening of the vessels and atrophy of the secreting structures.

Osler and McCrae\(^{15}\) consider that chronic renal disease is not infrequently caused by scarlet fever, and the possibility of such a termination should always be kept in mind.

James\(^ {16}\) examined sixty-seven patients who had had an acute nephritis from all causes. Nine of the sixty-seven or 13.3% ended in the chronic type, and of this series of nine, four followed scarlet fever.

He concludes from his investigation that in acute nephritis the greater percentage recover completely, although one is not justified in saying that
a child is cured after one negative urinary finding, until the child has been under ordinary conditions on a regular diet for a considerable period. He points out that diseased portions of a kidney may recover, even if there is considerable degeneration, and neighboring portions of the kidney may hypertrophy and carry on the extra work — that in other words, an anatomically imperfect kidney may function efficiently.

Price17 says that in some cases the albuminuria persists and a chronic interstitial nephritis may ensue.

Taylor18 says that recovery from slight cases is common, but that death may result from twelve to eighteen months later.

Holt19 states that the general opinion prevails that acute diffuse nephritis in childhood, whether it is primary or a complication of scarlet fever is rather frequently followed by the chronic form of the disease. He, however, believes that this is uncommon. "Considering the frequency of acute nephritis in the course of scarlet fever, it is remarkable how few cases of serious chronic nephritis are observed".
Conybeare\textsuperscript{20} says that although a certain number of patients die during the acute disease, the great danger is that it may pass into the chronic form.

Campbell\textsuperscript{21} quotes Duval\textsuperscript{22} as being of the opinion that the great probability is that scarletinal nephritis is one of the forerunners of Bright's disease.

Still\textsuperscript{23} found that twenty-two out of one hundred consecutive cases of nephritis in children were scarletinal in origin, but that only a very small proportion reappear with albuminuria. A very large majority are completely cured before leaving the fever hospital and it would seem that the prognosis of scarletinal nephritis, apart from the risks during the acute stage is altogether more favourable than that of the non-scarletinal variety. It is indeed quite exceptional to meet with a prolonged albuminuria lasting for years as a result of the scarletinal form. In his opinion although the non-scarletinal cases in childhood tend to run a much more prolonged course and in this respect
have a worse prognosis, they at least have the ad-
vantage that a fatal ending rarely occurs as speedily
as in scarletinal nephritis.

Caiger 24 says that although in a large
proportion of cases of scarletinal nephritis complete
recovery ensues after from four to eight weeks, as is
evidenced by the complete disappearance from the
urine of albumin, etc., and by the absence of oedema
and anaemia — in exceptional cases albuminuria
persists in slight degree for several months. This
is often unattended by any other signs of renal af-
fection. Most of such cases lose their albuminuria
after a time and eventually make a satisfactory re-
covery. On the other hand they may not do so.
"The presence of progressive changes in the kidneys
of a permanent character, should always be suspected,
if the albuminuria persists for more than three to
four months".

It is thus seen that there is much diverg-
ence of opinion regarding the prognosis of scarlet-
inal nephritis, and its relationship to the chronic
nephritis. Some authors consider the prognosis excellent, and are convinced that there is no relationship other than an accidental one, between it and a subsequent nephritis, while others blame scarletinal nephritis either wholly or in part for the chronic nephritis found in later life.

The mere history of scarlet fever, and even of scarletinal nephritis is in our opinion of little value, and the many conflicting "impressions" held on the question suggest that they too are unreliable.

The most accurate method — as far as any such method can claim accuracy — of ascertaining how often scarletinal nephritis becomes chronic, is to examine a number of patients over a number of years after they have had scarletinal nephritis, and to determine how many of them suffer from chronic nephritis, or how many, showing some functional impairment, may be presumed to be candidates for a chronic condition at a later date.

The only way of avoiding the possibility that the child has not contracted nephritis since his discharge from hospital, and apart from his
scarletinal nephritis, would be to examine all such patients at regular intervals. This is, however, hardly practicable.

To repeat what was said in the Introduction, it is this lack of unanimity of opinion which made an investigation of such cases appear desirable, and possibly of value.
PHYSIOLOGY OF RENAL FUNCTION AND THE OUTPUT
OF WATER AND DISSOLVED SUBSTANCES BY THE
IMPAIRED KIDNEY.
Chapter III.

PHYSIOLOGY OF RENAL FUNCTION AND THE OUTPUT OF WATER AND DISSOLVED SUBSTANCES BY THE IMPAIRED KIDNEY.

Although the method of examination in the case of the cardio vascular system has obviously to proceed on conventional lines, the method of choice in attempting to estimate the renal efficiency at once leads us into debatable territory. What follows in this chapter represents briefly the author's conception of the ability of the normal and the impaired kidney to deal with, in particular, such substances as water and urea, and of the variations of such renal function in the presence of extra renal factors.

The anatomy, structure and blood supply of the kidney need not be recapitulated, but it is
important to remember that the nerve supply has no
direct influence on renal activity except by modify-
:ing its blood supply, although grey fibres from the
excitor cells in the renal ganglion are said to have
been traced to the tubules.

Heidenhain's original theory of the
secretion of urine demanded that the glomeruli
secreted the water with its dissolved salts, such as
sodium chloride, and that the tubules added the urea,
uric acid pigment and any foreign substance artifici-
:ally introduced.

Ludwig's theory attempted to explain
the secretion of urine by the activity of purely
physical forces. Ludwig regarded Bowman's capsule
as a simple filter, through which water and the salts
soluble in it, as well as the specific constituents
of the urine are filtered. The protein, fats, and
those salts which are combined with them, are pre-
vented from passing through the capsule. In the
tubules this dilute filtrate is concentrated by the
diffusion of water through the cells of the tubules.
The fact that the constituents of the urine are in different proportion than they are in the bloodstream, Ludwig explains with the assumption that some of the substances such as sodium chloride permeate more readily than does the urea through the epithelium of the tubules.

Neither of these views has been considered adequate by many physiologists. Physical forces, such as in Ludwig's view, seemed insufficient to explain the amount of work performed by the kidney, while the vital activity of Heidenhain seemed to be a mystic force to which any form of activity might be attributed.

Physiologists seem gradually to have picked out what is best in both theories, and attempted to combine them. Such a view is that of Metzner 27. He assumes filtration in the capsule, the filtrate being a deproteinised plasma, with reabsorption in the tubules. Absorption is not a passive diffusion, but an active process. At the same time active secretion occurs in parts of the convoluted tubules.
by which uric acid and foreign substances in the blood are eliminated. The urea is secreted in the same way, but is also filtered through the glomeruli.

The inadequacy of these theories led Cushny to the elaboration of the "modern theory". The modern theory "accepts the general scheme of filtration and reabsorption of Ludwig, but appreciating the inadequacy of the known physical forces, supplements them, as far as is necessary by the vital activity postulated by Heidenhain".

Filtration occurs in the glomeruli and is purely a physical process. The energy is supplied by the blood pressure in the glomerular capillaries which suffices for filtration. The filtrate in the capsule contains unchanged the constituents of the plasma with the exception of the colloids. It is a deproteinised plasma. The filtrate on passing through the tubules is altered by the absorption of water and certain solid constituents. The energy for the absorption is supplied by the cells.
themselves. It is not a passive diffusion but an active absorption by the cells, dependent on their vital activity. Cushny denied that any excretion of urea or other substances was affected by the tubules, and considered that the whole of the concentration was effected by the absorption of water from the glomerular filtrate back again into the blood. As the water is reabsorbed, the solution becomes more and more concentrated. If water alone were reabsorbed however, each substance would be concentrated exactly the same number of times. It can easily be shown that in any individual, urea may be concentrated eighty to ninety times, while the uric acid in the urine may not be more than twenty times that in the blood. It is assumed therefore that uric acid is only partially reabsorbed, and that in general, these substances which may be of further use in the body are partially reabsorbed with the water, while definitely harmful substances such as urea are all excreted.

Although this is a useful working theory, it does not coincide with all the known facts of
normal and abnormal excretion, and is not accepted by all authorities in its entirety. It seems therefore in describing both normal and abnormal renal function, to be convenient to consider the functions of the glomeruli and tubules separately.
The Functions of the Glomeruli.

If the process in the glomeruli is one of a simple filtration, then the amount of the filtrate must depend chiefly on the pressure and on the rate of the flow of the blood in the glomerular capillaries. Numerous investigations have been made to determine the relation of the circulation to kidney activity since Goll's first experiment in 1854. It is only recently that the factor of blood pressure and rate of flow have been separated. These, along with other factors affecting the function of the glomeruli should be briefly referred to.

1. Blood Pressure and Rate of Blood Flow.

Richards and Plant, elaborated a method for perfusing the rabbits kidney in situ by means of a perfusion apparatus capable of pumping a pulsating stream of fluid. Its volume out-put was
controllable within fairly wide limits regardless of the the resistance offered, by the blood vessels. It was possible for them to alter the pressure within the kidney vessels by various means without altering the volume flow or the velocity of blood in the vessels. When this method was applied, and the renal vein was then partly occluded, there was no stagnation of blood in the glomerular capillaries. The pressure in them was increased and there was an increase in the urinary flow. Since there was no change in the rate of blood flow, they attributed the increase in urinary flow to an increase in blood pressure. It was also found possible by this method to obtain an increased flow of urine on raising the blood pressure by means of adrenalin, and by stimulating the splanchnic nerve, while at the same time the blood flow was not changed. It was found that when the perfused kidney is treated with a large dose of adrenalin, the result is a constriction of the vessels with shrinkage in the volume of the kidney. But small doses, which still result in some constric-

:tion /
constriction of the vessels, show either no change or a distinct swelling in the kidney volume. The explanation which Richards offers is as follows -

Both the afferent and efferent arteries of the glomeruli contain smooth muscle fibres, and both are supplied with nerve fibres to their muscle cells. It is possible that adrenalin in large doses acts on both vessels, causing constriction, and shrinkage in the volume of the kidney. Small doses would act only on the efferent glomerular artery causing its constriction, which would result in a passive dilatation of the glomerulus proximal to it, and thus lead to swelling of the kidney. In support of this view is the observation made by him that on the frog's kidney, the adrenalin constricts the blood vessels peripheral to the glomeruli.

In the excretion of urine, the blood flow is certainly equal in importance to the blood pressure. It is known experimentally (Wearn and Richards 32), that constriction of the renal vein, although it raises the glomerular pressure, has the effect of greatly reducing the blood flow through
the kidney, and diminishing the excretion of urine. The asphyxial condition damages the glomerular epi-
theilum and so alters its permeability that albumin and blood are allowed to escape. The engorged veins, by their pressure on the tubules, prevent the reabsorption of fluid. Clinically a similar condition is seen in the last stages of heart fail-
ure, causing renal congestion, oliguria and edema. Normally at night, when both factors, namely the blood pressure and the circulatory rate are reduced, the amount of urine excreted is much lessened.

The whole effect of both the blood pressure, and the rate of blood flow through the kidney, on urinary function can be best expressed by saying that the normal urinary excretion is absolutely dependent upon an adequate oxygen supply to the kidney parenchyma. Any interference with this oxygen supply leads to a decrease in urinary excre-
tion, even to the point of suppression. Through a particularly favourable oxygen supply to the kidneys, an excretion of urine may be increased to above what is considered as normal.
Nature has, of course, provided that the kidneys shall have a plentiful supply of oxygenated blood by endowing them with large renal arteries. It does not matter how the interference in the oxygen supply to the kidneys takes place, it invariably results in diminished excretion. It may be brought about by a change in the action of the heart itself, such as a decrease in the number or force of the heart's contractions, or both, such as occurs in myocarditis, valvular disease and dilation. But clinical experience teaches that abnormal urinary constituents, and renal function occur only in the late stages of cardiac disease.

Or the deficiency in oxygen may be brought about by haemorrhage, and most effectively of all, the oxygen supply to the kidney may be diminished to any degree by compression of the renal artery from without, or occlusion from within (arterio-sclerosis, embolism, etc.,). The same result occurs if the outflow of blood through the renal veins is sufficiently impeded, either experimentally by ligation, or
by passive congestion due to heart disease.

Rowntree 33 found that slight experimental chronic passive congestion was characterised by the excretion of a normal quantity of urine, with a trace of albumin, occasionally a few casts, and sometimes a few blood cells; and that the functional capacity remained normal: but that a marked congestion resulted in a very scanty urine with much albumin, casts and blood cells, and that the functional capacity was definitely reduced. This leads one to the conclusion that although such an extra-renal factor may, and does, affect urinary excretion, without any actual renal defect being present, it will if long continued result in irrecoverable kidney dysfunction. An adequate oxygen supply to the kidney on the other hand favours the secretion of urine. This is evidenced by the fact that the removal of the various conditions outlined above, provided that they have not acted too long, is followed by a re-establishment of the urinary secretion to normal.
2. Osmotic Pressure.

It has been shown that filtration ceases when the blood pressure falls to forty millimetres of mercury. The osmotic pressure of the proteins in the blood is about thirty millimetres of mercury (Starling 34) and it varies with the fluid content of the blood. The intravenous injection of saline causes marked diuresis although the blood pressure shows only a slight and transient rise. As the blood flow to the kidney is also not appreciably affected by the injection of saline, the diuresis must be due, as has been suggested by Cushny, partly to dilution of the plasma proteins, enabling quicker filtration to take place in the glomeruli, and partly to the fact that the fluid passes so quickly down the tubules that the tubular epithelium has no time to absorb the normal amount of water.

This delicately adjusted balance between the fluid content of the body and the osmotic pressure also occurs when large quantities of water are taken by the mouth. The excretion of the water
takes place so quickly that the diuresis is accompanied by very slight dilution of the blood, (Priestly 35). And the excretion of water is dependent mainly on the diffusion pressure of water in the blood. Whether the fact that the kidney may excrete a urine in which the diffusion pressure of water is much lower than that of the blood, is simply due to its rapid flow down the tubules, or to some modification of the diffusion process, is unknown. Starling 36 considers that some substances with an action similar to that of pituitrin may normally be present, and that it serves as a means whereby the kidney is controlled in its function of regulating the output of water. He ascribes this rather puzzling reaction of the kidney to an inhibition of the normal process of water reabsorption — possibly to a neutralization of some hormonal influence.

The excretion of water naturally involves elimination of solids and although during the initial diuresis there may be a temporary slight increased excretion of urea and chloride this is compensated for by a lessened rate of excretion immediately after
the diuresis. Adolph 37. The total amount of solid excreted in twenty-four hours after the exhibition of a large amount of water is the same as in twenty-four hours when no water is taken.

As the osmotic pressure of the blood proteins is thirty millimetres of mercury, and the lowest blood pressure which will allow a kidney to excrete any urine is about 40 millimetres of mercury, it follows that in the capsule there are two forces, opposed in their action to each other. The blood pressure striving to drive the filtrate on, and the osmotic pressure of the blood proteins holding it back. It can be shown experimentally that when the osmotic pressure of the blood protein and the blood pressure coincide, there is no excretion of urine, so that the nett filtering force must always be the difference between these two.

3. The Physico-chemical Factor in Filtration.

If the process in the glomeruli is one of filtration in which the osmotic pressure of the colloids of the blood must be overcome, it is obvious that the other factors remaining the same, any change
in the concentration of the colloids must involve a change in the rate of filtration. A lessening in the concentration of the blood colloids must therefore result in an increase of the glomerular filtrate, while an increase of the glomerular filtrate will diminish it. The effect of a diminution in the concentration of the colloids on filtration can be seen in the diuresis caused by the injection into the blood stream of an isotonic solution of a threshold substance such as sodium chloride. Such a solution simply dilutes the colloids of the blood, and the diuresis which is produced is a dilution diuresis. When solutions of a non-threshold substance such as urea are injected into the blood stream, there is in addition to the dilution diuresis, a diuresis due to the retention of water in the lumen of the tubules, due to the fact that not being absorbed, these substances prevent the absorption of a certain amount of fluid in which they are dissolved. That the dilution diuresis is due to a lower concentration of the blood colloids is shown by several well known experiments. The removal of the blood
plasma, and its replacement with Ringer's solution is followed by diuresis, although the blood pressure remains the same. Dilution diuresis can be abolished or reduced by the addition of gum acacia or gelatine to the injected saline — and this is referred to later when the excretion of water is discussed. The intravenous injection of saline solution at the same time causing the blood pressure to be reduced, causes a urinary flow even with a blood pressure as low as twelve or thirteen millimetres of mercury. Barcroft and Straub have shown that during dilution diuresis the oxygen consumption of the kidney is not higher than in the resting kidney — the conclusion being that the work of the kidney during the dilution diuresis is not due to increased kidney cell activity. In the case of kidneys with the tubules poisoned they considered that the evidence points rather to their having lost the power of secretion, than to their having lost that of reabsorption. If the process in the glomeruli is one of filtration, then an increase in the rate of filtration would increase the
rate of flow of the filtrate through the tubules. The tubules would have thus less time to concentrate the filtrate. The greater the flow, the more nearly must the urine resemble a deproteinised plasma in composition. In such a case all the constituents of the urine are increased in absolute amount per unit of time, but are reduced in percentages.

4. Permeability of the Membrane.

Any condition which renders the membrane more permeable will allow blood and protein to escape. This is seen in all forms of acute nephritis — from that caused by metallic poisons to that caused by a haemolytic streptococcus. The effect of an asphyxial state due to congestion has already been referred to.

5. Filtration Surface.

It is a factor of importance in the adjustment of renal function to the excretory requirements
of the body that the extent of the filtration surface in the kidney is variable. Richards and Schmidt observed microscopically the circulation of the glomeruli in the frog's kidney and noticed that the number of the glomeruli through which the blood flows at any one time, and hence which function at any one time, may be a fraction only of the total number of glomeruli in the kidney.

Although the modern theory is that the glomeruli do not secrete, but simply filter out from the blood what is essentially deproteinised plasma, this theory is also not universally accepted and Maclean doubts if this process is an ordinary filtration. He considers that many facts are more in accordance with the view that the glomeruli epithelium has a selective action, and that while the passage of water may be a filtration, the glomerular cells have the power of concentrating to different degrees the various substances brought to them in the blood.
Function of the Tubules.

The evidence for the absorptive function of the tubules can best be found in the study of tubule diuresis produced by the injection into the bloodstream of non-threshold substances such as sulphate or urea. When a solution of sodium sulphate is injected intravenously a diuresis is produced which lasts longer than a corresponding sodium chloride diuresis. The sodium chloride diuresis persists only till the colloid dilution has disappeared and the concentration of the blood colloids has returned to normal, whereas the sulphate diuresis persists after the blood has again become concentrated. In chloride diuresis the percentage of chloride in the urine rises at the beginning and sinks towards the end, while in the sulphate diuresis the sulphate content of the urine increases in percentage towards the end.
Further evidence of the absorptive function of the tubules was produced by Cushny by the obstruction of one ureter, thus causing the kidney to eliminate urine against a pressure in the ureter. It was found that the obstruction lessened the chloride in the urine more than the urea and still more than the sulphate. This could only be the result of the greater absorption of the chloride due to the filtrate remaining longer in the tubules.

Barcroft and Straub 41 showed that when diuresis is produced by dilution such as after Ringer's solution or of a solution of sodium chloride, there is no increase in the oxygen consumption of the kidney above the normal. This is in accord with the view that the work of the tubules is to separate water from the non-absorbable substances such as urea or sulphate.

Most convincing experiments have been done by Richards and Wearn 42. They were able, with the aid of a microscope, to insert a pipette into the glomerular spaces in frogs, and to collect and
analyse uncontaminated specimens of the glomerular filtrate.

Their analysis showed that normally protein was not filtered into the capsule, but that where blood stasis was present there was some leakage of plasma, and that sugar was normally found neither in the filtrate, the blood nor the urine. When injected into the blood in amounts below the threshold, sugar is filtered through the glomeruli, but reabsorbed in the tubules, but when above the threshold (0.05%) it was not all reabsorbed.

Starving frogs kept in distilled water eliminated a bladder urine free from chlorides, whereas the glomerular urine contained chlorides - the conclusion being that chlorides were absorbed by the tubules.

Starling and Verney 45 showed that the activity of the tubules could be inhibited by perfusing the isolated kidney with a solution of hydrocyanic acid, and it was found that the glomerular filtrate under these conditions was identical with the blood plasma.
Water, chloride and sugar were shown to be reabsorbed by the tubules, while urea, although largely filtered through the glomerulus, appeared to some extent to be excreted by the tubules. In this experiment, a kidney was perfused with cyanised blood for two minutes, thus inhibiting activity in the tubules. During this time the urea excreted was estimated. It was found that there was a marked fall in the total urea eliminated per unit of time, and this could only be explained on the assumption that it was actively secreted by the tubular epithelium.

It was demonstrated that sulphate, and, if present in the plasma, phenolphthalein, were secreted by the tubule cells into the glomerular filtrate.

Rowntree and Geraghty \(^44\) also showed that phenolphthalein can be excreted by way of the cells of the tubules in frogs, and presumably in mammals, because those substances which appear to act by stimulating the renal cells, cause an increased output of phthalein, while those diuretics which act
only mechanically as by changing the blood pressure or osmotic tension do not influence the out-put.

Atkinson,\textsuperscript{45} investigating the functions of the urinary tubules in the frog, concluded that transmission of urea and sulphate can take place from the intertubal vessels to the urine, whereas that was not the case with glucose, and that chlorides normally pass from urine to intertubal vessels.

We therefore assume that in its passage through the tubules the glomerular filtrate becomes concentrated with the absorption of water and of the threshold bodies. Most of the water is reabsorbed as is shown by Cushny's finding that sixty-one litres of water were reabsorbed for every litre excreted. The solid substances are not reabsorbed indiscriminately, but in definite proportion depending on their concentration in the plasma. The non-threshold bodies such as urea and sulphate are not reabsorbed, and are therefore highly concentrated. If the threshold bodies such as chloride or glucose in the blood plasma are higher in concentration than normal,
their contents in the glomerular filtrate will also be higher; but as the tubules absorb in a definite optimal proportion, the excess of the threshold bodies will appear in the urine.

The extent of the absorption in the tubules may be changed by several factors, just as it has been seen that the glomerular function is affected. The chief factors influencing the tubal function are:

(1) The amount of any unabsorbable substance, namely, the non-threshold bodies, the most important of which is urea.

(2) The presence of a threshold substance such as sugar in excess of its normal content. The extent of the absorption of water is limited by the osmotic force which these substances exert. The urine can therefore never exceed a certain concentration, namely, that at which the osmotic resistance is equal to the power of absorption.

(3) Absorption depends on the length of time during which the glomerular filtrate remains in contact with the tubular epithelium. The more abundant the filtrate, the more rapid is its flow through the tubules, and the less time it is in contact with the absorbing cells.

As the reabsorption of water takes place against the powerful resistance of the osmotic pressure of the urea containing fluid in the tubules, the more powerful as the fluid becomes more concentrated/
concentrated during its course down the tubules - it must be due to the vital activity of the tubular cells. It is due to this vital process that substances which are of value are kept back, while harmful substances such as urea and sulphates are allowed to pass to the bladder.

Summing up all the recent experimental data, the conclusion can be drawn that in a glomerulus a process of filtration occurs by which water and the soluble diffusible constituents of the blood plasma are separated from the proteins. This process is disturbed by a number of factors, which are not, in themselves, of renal origin. The amount of filtrate depends largely upon the pressure, and the rate of flow of the blood in the glomerular capillaries, and upon the colloid content of the plasma.

In its passage through the tubules this filtrate undergoes extensive changes, some of its
constituents, water, salt, and sugar, (substances of value to the body), being reabsorbed, while other constituents such as urea are possibly excreted from the blood. In either case this is an active and selective function rather than a simple process of osmosis. The difference in the structure of the epithelia in certain portions of the tubules, and the striking differences in the distribution of the blood vessels, strongly point towards a difference in the functions of portions of the tubules.

As in every disease impairment of function precedes structural change, renal disease will be more apt to manifest itself first in a derangement of its vital function, and that therefore the earliest sign is likely to be a lack of its power to concentrate.

It will be seen in a subsequent chapter that in investigating the renal function, we have attempted to do so by estimating the capacity of the kidney to deal with either water, or urea, or both.
We have therefore to consider how the normal and the impaired kidney react in the presence of these substances.
The Output of Water and Dissolved Substances by the Normal Kidney.

The output of water by a kidney depends on the amount and manner in which water is "held" in the blood, and in body tissues and is therefore subject to variations by a number of non-renal conditions.

It is a commonplace that the excretion of urine practically ceases during absolute starvation. If the colloids of the body as a whole are holding on to all the available water, if, in other words, an amount more than necessary to saturate them is not present, then none is left over to be excreted.

On the other hand, in an organism whose colloids are saturated with water, an amount of urine is excreted (ignoring that lost extrarenally by skin, lungs and bowel), which is equivalent to the amount
of water drunk, and if this does not occur, then oedema develops.

It does not matter how this water is consumed. It may simply be swallowed, or have been experimentally introduced into the gastro-intestinal tract, or it may have been injected into the peritoneal cavity, under the skin, or directly into the blood. By a process of absorption by the blood colloids, all these become reduced to one, namely to the presence of water in the blood. In its passage through the lungs, the venous blood coming from the alimentary tract, loses carbonic acid gas, which is responsible for the increased hydration capacity of its colloids. As soon as this has happened, the blood contains more water than its colloids are capable of holding, and so this separates off as urine. The amount of water thrown out by the kidney depends not only on the state of hydration of the body tissues, but in the case of injection of such a solution as sodium chloride solution, on its concentration.
If equal amounts of sodium chloride solution of increasing concentration are injected into an animal's circulation, the water output of the kidney increases, the more concentrated the solution; and in sufficiently high concentrations the animal will lose actually more water than was injected.

The explanation of such results is undoubtedly that the injected concentrated solution decreases the capacity of the body colloids for water. The higher the concentration of salt in the injection, the higher it will be in the blood, and after diffusion in all the tissues of the body, so that the tissues are actually forced to give up water. This "free" water is then added to that injected and it is the sum of the two which appears as urine.

If instead of injecting a simple salt solution in which the water is "free" one injects a colloid solution, no increased flow of urine takes place. Such an absence of diuresis after the injection of normal blood was first recorded by Magnus.46 Without appearing to have realised
its practical value, he found that if the volume of the blood was increased, the venous and capillary pressure in the kidney being also raised, by a transfusion of blood, no diuresis ensued. But that as soon as a solution was transfused which altered the composition of the blood, the diuresis at once occurred.

This difference in the effect of simple solutions of salts, and of colloid solutions has its practical application in the treatment of shock — in which according to Fraser and Colmell the ideal injection fluid is the solution the colloid added, preferably one containing sodium bicarbonate and six per cent acacia. The injection of the ordinary simple salt solutions causes only a temporary alleviation of shock, as the free water escapes, thus preventing the restoration of the blood-volume, which is the object aimed at.

It is to be noted that in some experimental work on the normal water excretion, it has been found that little or no diuresis may occur. In
several such recorded investigations, an anaesthetic has been used. The absence of diuresis is undoubtedly because all anaesthetics produce a state of lack of oxygen, so that the tissues have an increased capacity for holding water, and so do not excrete that which has been absorbed by the alimentary tract or peritoneum.

The continuance of an absorption of water from the gastrointestinal tract, while little or none is being excreted through the kidneys, is explained by the increased hydration capacity of the body tissues through the effect of the anaesthetics. The invariable thirst after anaesthesia is a familiar manifestation of the process.

The excretion of water as a test of renal function was pointed out by Schlayer, 48 & 49 and the method was used clinically by Monakow. 50

An excretion of dissolved substances by the kidney is possible only so long as water is supplied to the organism, and an excretion of water is necessary before any excretion of dissolved substances/
substances can occur.

When salt is taken by the mouth there is a slight increase of sodium chloride content of the blood, and the kidney immediately throws out the excess. If on the other hand the amount of salt tends to fall below 0.6% the necessary concentration in the blood is maintained by the kidney throwing out water. The retention of sodium chloride in the system, of necessity involves the retention of water as well, so that the condition is soon indicated by oedema. Tests therefore for sodium chloride excretion are superfluous, especially as, when large doses of sodium chloride are given by the mouth, its excretion in a given time depends as much on extra-renal, as on renal factors. Widal 51 showed that the ingestion of a large amount of salt does not necessarily mean that an equivalent amount is excreted by the kidneys. The amount of salt excreted after a given dose, depends on the state of the body tissues with regard to fluid. The amount of fluid present in the body varies consider-ably/
considerably at different times, the actual amount being possibly dependent to some extent on the quantity of sodium chloride available. If the body happens to be low in fluid, the injected salt is retained in order that the fluid may be increased.

Rowntree investigated the salt excretion in fifty-seven patients. Among these were cases which were purely nephritic, cardiac, and cardio-renal. Sodium chloride added to the diet in considerable amounts appeared to be excreted normally in a large number of cases. In advanced nephritis it was excreted in amounts less than those ingested, while in cardiac renal cases its excretion varied, some cases retaining it whether there was oedema or not, whereas others, of more advanced nephritis clinically, excreted more than was ingested.

The study of salt excretion as a test for function is therefore of little value on account of the many extra renal factors to which it is subjected.

The whole question of excretion, both of water and dissolved substances is summed up by
First, that "a diseased kidney has a more constant function than a healthy one, and the greater the destruction of its parenchyma, the less does its function vary from time to time", and secondly — a corollary of the first — that "as a result of any passing stimulus whatsoever to renal function the increased renal activity which results there from is always more marked in the healthy than the diseased kidney".
The Output of Water and Dissolved Substances by the Impaired Kidney.

Although conflicting views are still held and are supported by impressive arguments, the consensus of opinion today leans to the view that in the diseased kidney, all the excretory functions are involved - Maclean even maintaining that if one test gives evidence of inefficiency, then the others will, if sufficiently delicate, do the same. As against this view of the unitary nature of impairment of renal function, is that first put forward by Widal 54 and Strauss, 55 and Fischer, 56 that in impaired renal function there is found an isolated injury to individual functions, while other excretory functions are satisfactory performed - thus leading to a selective retention.

It has been stated (Myers 57), that of the
non-protein nitrogen constituents, a selective action occurs at successive periods in cases of renal failure—that uric acid is first retained, then urea, and finally creatinine.

The fact that the normal kidney excreted some substances in a higher state of concentration than others, was explained on physico-chemical grounds, but if the vital function of the kidney cells is impaired, it appears unnecessary to suppose that the concentrating power towards one dissolved substance, would be more markedly affected than another.

In those cases in which there appears to be a circumscribed injury to the ability to excrete individual substances, the cause of the retention is probably not primarily a renal defect, but is due to some extra renal factor such as the accompanying cardio vascular changes resulting in a diminished supply of the substance to the kidney, or to the metabolic changes caused by the accompanying hyper tension. It is noteworthy that most cases in which such conclusions are drawn, refer to patients
with advanced kidney disease, where the extra renal factors are most likely to be present.

It is obvious that normally, some control of the kidney function is necessary, when it is recalled that, with constant variations in food and water intake the volume and composition of the blood remain normal. It is said that the human kidney has about a million glomeruli. In the normal kidney at the height of its activity, such as after drinking large quantities of water, one may presume that all the glomeruli are active. But, as already mentioned only a fraction of the number of the glomeruli are needed for the normal variations of every day life.

It is highly probable that the vaso motor supply of the glomeruli constitute the main control of glomerular activity. Tubular activity is on the other hand entirely dependent upon the rate and composition of the glomerular filtrate supplied by the corresponding glomerulus. It is true that nerve fibres have been traced to the basement
membrane of the tubules and even to the individual cells of the tubules, but their function is unknown.

Another method of glomerular control was suggested by Richards. By observing under the microscope the active glomeruli of a frog's kidney, he found that the number of active glomeruli varied continuously, and could be made to vary with the injection into the blood of various substances. A glomerulus showing a multiplicity of channels with a rapid flow, could be changed, by the injection of adrenalin in constrictor doses, into one with fewer loops and slower flow. An intermittence of the blood flow through the glomeruli could also be observed, and this intermittence persisted after complete destruction of the central nervous system. Richards concluded that the capillaries of the glomerulus possessed the power of contraction independent of the nervous system. This extremely sensitive vaso motor mechanism is therefore the key which opens and shuts the gates to the glomeruli.
It regulates the amount of fluid to be filtered with the object of keeping the blood volume constant. Any increase in the blood of those substances which have to be removed, at once results in the activity of a greater number of glomeruli. This increase in the number of active glomeruli can be demonstrated after the injection into the blood stream of an isotonic salt solution, urea, caffeine and other substances. One of the most important of the non-threshold substances with which the kidney has to deal is urea, and also any excess in the blood above their threshold value, of water and chloride. Any increase in these substances above their normal level in the blood causes the activity of a greater number of glomeruli. So sensitive is the kidney, that it responds at once with a dilute urine to a fluid intake which dilutes the blood so slightly that it cannot be detected by ordinary methods (Oushmy). The importance of water in causing variations in the function of the kidney is seen on
studying the composition of the blood and urine in the acute febrile diseases. These diseases are characterised by a toxic destruction of protein which results in an increased production of urea, and its accumulation in the blood. With normal kidneys the urea should be immediately eliminated, and yet it is found that the concentration of the urea in the blood is often two or three times its normal amount. The explanation is that in the acute febrile disease, water leaves the blood and tissues so that the total volume becomes reduced. The kidneys at once reduce the work of the glomeruli to the minimum despite the greater quantity of urea to be excreted, with a consequent maximal saving of water to help to maintain the blood volume.

This variability of kidney function constitutes the "safety factor" which is normally possessed by every organ. When for instance the kidneys have all their glomeruli intact and capable of performing their function, the variability of the kidney function or its safety factor, is normal. So
that if a large quantity of fluid is given the kidneys will at once respond with a highly dilute urine, and when fluid is withheld from the body over a considerable length of time, the kidneys will respond with a highly concentrated urine, one with a high specific gravity.

Any disease of the kidney, in which its functional capacity is reduced, will result in an alteration of this variability. Suppose for instance that the glomeruli in both kidneys, along with their corresponding tubules have been reduced to half their original number: What would be the effect on the kidney function, first, under ordinary conditions with a minimum intake of fluids and food, and secondly, with a maximum intake of fluids and food?

Under ordinary conditions of minimum intake, there will be little evidence of disturbed kidney function. As only a portion of glomeruli and tubules are normally doing the minimum work, there will be in this case a sufficient number left to do
the work, and even possibly to carry a moderate load, although the rest period for the individual functioning part will be diminished. With a maximum intake, kidney function will be disturbed. If we give an intake of water which calls into play the whole reserve power of the kidney, that is, all the glomeruli and tubules, it is normally eliminated as a very dilute urine within about four hours. With only half the glomeruli and tubules active, and working to their fullest capacity, a similar fluid intake will necessarily take about eight hours. In the same way a definite amount of waste products such as urea formed after an intake of a large amount of protein, or given as such, will also be eliminated over a longer period than normal. In other words such a kidney compensates its inability to elaborate a urine of normal molecular concentration, by excreting the same amount of the substance over a longer time, and in a urine of lessened concentration. This is a true compensatory process and if renal failure
is taken to mean inability to excrete the substance, such a kidney has not failed. There is no renal insufficiency. It is in a state of compensated hypofunction and such a patient will have a diminished concentrating power, although the blood reaction will be normal.

If the glomeruli and tubules have become still more reduced in number, then increased water intake will be eliminated over a proportionately longer time as will also the waste products after an increased protein intake. Concentration by the tubules will be proportionately lessened. Such kidneys however may, still be able to eliminate properly the minimal intake of such substances as water and urea, provided that the number of glomeruli and tubules do not fall below a certain minimum. This will no longer be possible if the number falls below a minimum which has been shown in animals to be about one fourth of the total functioning capacity of both kidneys; when this occurs, even the necessary minimum intake will take a long time to be eliminated,
and even after complete abstinence from protein intake, even the products of endogenous protein destruction will be in part retained. The concentrating function of the tubules will be almost entirely lost. Such a kidney may be said to have reached the stage of renal decompensation, and just as the cardiac patient only begins to have symptoms of oedema, dyspnoea, etc., when compensation breaks down, so does the renal patient now for the first time have symptoms.

The condition of compensated hypofunction may vary from a slight diminution of the variability of kidney function to a point where the normal level of the non-protein nitrogen in the blood can only be maintained with a minimum food and fluid intake. Moderate degrees of renal insufficiency are often difficult to determine and it is for their recognition that the numerous tests for kidney function have been evolved. So far, we have no standard
of what a normal kidney can do. According to Cushny, both kidneys can, in man, eliminate an intake of twenty-four litres of water in twenty-four hours, and can concentrate an albumin and sugar free urine to a specific gravity of 1036 and above. These are the extreme variations. The tests which have been evolved for the determination of slight variations can only show the diminution in the variability of kidney function, that is the prolongation of elimination time, or the lessening of concentration.
RENAL EFFICIENCY TESTS.
Chapter 4.

Renal Efficiency Tests.

That renal efficiency tests are important can hardly be doubted, although many clinicians are strongly of the opinion that if careful consideration is given to the various clinical aspects, that is, careful history taking, proper physical examination, blood pressure measurements, etc., renal efficiency tests do not add much to the understanding of the case. It is now realised, however, that anatomical integrity is not a necessary requirement for functional efficiency, which is the chief concern of the clinician. An analogy may be found in the well recognised concept of cardiac pathology, where
where the chief clinical concern is not the anatomic-
al nature of the heart lesion. Prognosis is not
necessarily measured by the size of the heart nor by
any particular valvular defect, but is measured chief-
ly by its functional efficiency — the amount of
work the individual can do without getting short of
breath.

Unfortunately there is no such simple index
of efficiency in the case of the kidneys. Various
tests must be employed and the principles upon which
they are based must be understood.

In studying the functional ability of the
kidney it must always be kept in mind that deficient
excretion of a substance does not necessarily in-
dicate impaired function of the kidney itself and
the pathological significance of such extra renal
conditions has been emphasized recently by Vaquez
and Volhard.

The kidney is the most important link —
but only a link — in an excretory chain which
begins with the alimentary canal and ends with the
bladder. A link whose output is affected by the efficiency of such varied organs as the skin, lungs, bowels and heart — which organs in themselves vary widely in activity under normal and pathological conditions. Roth 61 came to the conclusion that normally 60% of the water was lost in the urine, and that 40% was lost by the skin, lungs and bowel. The greater part of this 40% is excreted by the skin, in the form of invisible sweating. He showed that the "perspiratio insensibilis" is due to molecular changes in the body fluids and is dependent on such diverse factors as the temperature, humidity, diet, activity of muscles, cardiac action and psychic states. He quotes Paessler 62 who noticed that in several cases of nephritic oedema, when the diureses began there was less urine passed than would have been expected by the loss of weight. One such case of acute nephritis losing 7 kilogrammes in 1 day, while the quantity of urine in the same time only increased by 900 cubic centimetres. This
case had no diarrhoea and no heavy sweating, there must have been a greatly increased "invisible sweating".

Douglas and Priestly 63 quote Moss 64 as having found that miners may lose as much as 1½ kilogrammes of sweat per hour, containing 0.2% sodium chloride, i.e. 5 grams of salt.

Although when necessary the healthy kidney can quickly eliminate water, under circumstances in which a quick loss is not required, the lungs and skin can excrete the necessary amount of water. In pneumonia, chlorides may practically disappear from the urine, and the urea excretion is often very low in severe liver disease, despite in each case the functional integrity of the kidney.

Most of the calcium and magnesium is eliminated through the bowel and from what we know of the "safety factor" of almost all the bodily functions it is clear that in the case of these substances elimination will be completed by the vicarious activity of the extra renal organs despite complete
cessation of kidney activity.

With the exception of potassium, all the substances which in renal defect, accumulate in the blood, are either taken in food, or are products of catabolism. Therefore although they continue to be produced they can be materially lessened by alterations in the diet. On the other hand, those which do not increase in renal insufficiency can be made almost to disappear by eliminating them from the diet. It is thus easily understood why such substances as chlorides do not increase in uraemic states, but are in fact decreased, as the patient has usually been kept on a salt free diet.

The nitrogenous urinary constituents on the other hand are hardly at all eliminated extra renally, and any extra renal excretion which does take place certainly cannot be increased enough to compensate for defective renal function.

It has also been shown that quantitatively the excretion of a substance may be completely carried out despite functional impairment of the
kidney by means of a **compensatory polyuria**.

It is obvious that these factors will affect the excretion of substances by the damaged as well as by the healthy kidney and in discussing the tests for renal functions, and out choice of tests, further reference will be made to them.

Renal efficiency tests had their origin in the very simple clinical observation made one hundred years ago, that when a substance such as turpentine was exhibited to a healthy individual, it imparted a characteristic odour to the urine subsequently passed, while it was absent or less marked in patients with diseased kidneys.

Since then a great number of tests and combination of tests has been devised for the recognition of renal dysfunction. Their multiplicity itself suggests that the position is unsatisfactory, and most of them have, after careful investigation, become obsolete.
Many give such contradictory results in cases where the degree of renal damage is known, that they are of doubtful value, and it still appears to be a common procedure, not only to apply kidney tests without having as far as possible excluded any extra renal factor, but even to carry out such tests in patients where such factors undoubtedly exist. The importance of excluding such factors has been referred to, and the omission to do so obviously nullifies any conclusions as to the value of the test.

Many tests are difficult and tedious to perform, and a study of the vast literature which has grown around this subject seems to indicate that so far, none has led to any conclusion which could not be arrived at by simpler means. Others again such as the estimation of the blood urea give valuable information only in more or less advanced cases of nephritis.

The great majority of tests for renal function belong to one of two varieties. They are either balance tests or concentration tests.
In the former, a known quantity of a substance which is excreted in the urine is given orally or by injection, and the quantity eliminated in the urine in a given time is measured. Such substances as potassium iodide, sodium salicylate, sodium thiosulphate, various dyes, as well as urea, chlorides, creatinine and water have all been advocated, and some are still largely used.

The two tests, most widely used, and representative of this class are the phenol sulphone phthalein test introduced in 1910 by Rowntree and Geraghty, and the water test of Volhard.

The phenol sulphone phthalein test depends on the ability of the kidney to excrete the dye at what has been found to be a normal rate. The pigment, in alkaline solution has a bright red colour. It is usual to give the patient 200 - 400 cc. of water to drink about half an hour before 6 milligrams of the dye is injected intravenously or intramuscularly. In health 40 - 60% should be excreted during the first hour and 10 - 25% in the second, i.e. 50 -
85\% during the first two hours.

The method is open to certain objections. It can only determine a prolongation of elimination time and a lessened output is only of value as a test for prolonged elimination time due to kidney disease when there are no other factors which interfere with the dye reaching the kidney. It has been shown that good excretion does not necessarily mean good renal function. For instance Hill 68 found that in chronic nephritis in children it was possible for severe kidney damage to exist with a phthalein output of 60 - 70\%. And poor excretion is not always an indication of poor renal function. The introducers of the test admit that in myocardial insufficiency, when the blood flow is retarded, or in cases with marked oedema where the dye will be side tracked in the oedema fluid, there is apt to be a lessened output in the urine, although the variability of the kidney function may not be diminished at all. It is quite possible for a normal quantity
of the dye to be eliminated in two hours in the com-
:ponsated stage of impaired renal function.

In general, therefore, this test appears to be of less value in determining the degree of
renal insufficiency then the water or urea concentra-
tion test.

A choice of renal efficiency tests for this study was necessary and obviously difficult, since
any one test alone is apt to be unreliable. In addition our test or tests of choice had to be chosen
not only with a view to their reliability, but also
to their simplicity.

Simplicity in the technique of a test, and the practicability of its application to patients in their own homes, and following their vocations was obviously of much moment.

Any test, imperfect as it may be was ac-
ceptable if (a) it measured a very prominent func-
tion of the kidneys, (b) if the effects of extra renal factors could be reduced to the minimum and
(c) if it readily detected the characteristic.
impairment of the kidneys in the particular disease being searched for.

The urea concentration test fulfills these postulates, at least fairly well, and on it and the water test, the conclusions and opinions which follow have been based. Complicated physical, chemical, and calorimetric tests were quite unsuitable, and for this reason the popular and useful phthalein test was discarded.
The Urea Concentration Test.

This test depends on the power of the healthy kidney to concentrate urea. The apparatus used is a Gerrad's ureometer as modified by McLean. 23 cc. of 40% sodium hydroxide, with a bulb containing 2 cc. bromine, are mixed with 4 cc. urine. The CO₂ evolved being absorbed by the alkaline hypobromite solution, the N causes a sinking of the level of the water in the burette. Each cc. of N is calculated as being equal to 0.0625 grm. urea per cent in the sample of urine examined.

The patient is given 15 grm. urea dissolved in about 100 cc. water. The bladder is emptied immediately before, and no fluid is taken for 8 - 10 hours before the test is carried out. Any diuresis caused by the urea usually occurs in the specimen passed after one hour, so that for practical purposes
it is better to use that passed after two hours. The percentage urea is estimated by the urease or hypobromite method.

In health, the amount of urea in urine, unless in the presence of severe diuresis, amounts to about 2.5%, whereas the concentration in the blood is 0.015 to 0.04%. It is thus considered that in the case of urea, the normal kidney has the power of affecting this degree of concentration.

Broadly speaking, a maximum concentration of 2% or over, indicates a kidney which at the time of the test, can concentrate satisfactorily. Under 1% shows a kidney which definitely cannot. A figure below 1.5% is considered to show strong presumptive evidence, and a figure between 1.5 and 2 has been taken to point to the possibility of some kidney deficiency.

These figures should not be assessed, divorced from the general clinical picture, and in the case of low readings, from other tests.
The advantages of using urea as a test of renal function are manifold. Urea is a true end product, and is not chemically altered within the body. The urea concentration of the blood and tissues may be markedly increased without disturbing any essential equilibrium of the body. It is excreted by the kidneys only, and it has been shown to be excreted by the proximal convoluted tubules. Its presence is easily recognised and the quantity easily determined, and it has been argued by Addis that the excretion of urea throws a greater strain on the kidney than of such substances as the dyes.

It is assumed that the speed and facility with which the urea is eliminated is characteristic of the kidney's capacity to eliminate the whole of that group of waste products of which urea is an important member. If this were not so of course, the test would be of no value, for urea alone is not the cause of uraemia – indeed by itself it appears to have very little harmful effect, as is shown by the fact that the blood urea may be reduced by
dietetic means to the normal, and yet the patient die of uraemia (MacLean 70). It is only one of a number of toxic bodies which accumulate in the blood, but the ability or inability of the kidney to get rid of it is taken to represent the renal efficiency in dealing also with other members of this group.

The greater part of the energy required to cause the necessary changes in molecular concentration of substances from those existing in the blood to those found in the urine is expended in concentrating urea, and the greater the degree of concentration, the greater the work done per gram. This work has been calculated by Rabinowitch 71 and was found to vary inversely as the concentration of urea in the blood.

In normal individuals the kidneys do an average of seventeen kilogrammes of work in this process, for every gram urea excreted.

The relative amount of work done may be judged from the fact that he calculated that of
thirty-nine kilogramme metres of work done in concentrating urea and sodium chloride during a two hours period, 37.2 kilogramme metres was expended in concentrating urea.

He also assumes that the excretion of water does not, as compared with that of urea, require so much work by the kidneys.
The Water Test.

This test depends on the power of the kidney to perform its primary function of eliminating water. As the excretion of all dissolved substances is secondary to the excretion of water, one might say that the efficiency of a kidney can be gauged by its ability to excrete water.

There are a number of modifications of Volhard's procedure - the usual practice being to give the fasting patient at 8 a.m. 1½ litres of water to drink. Thereafter he passes water into a series of glasses every half hour for four hours. The quantity and specific gravity of each of the eight specimens are measured.

As we found 1,500 cc. a rather too copious draught for young children, 500 cc. was for the sake of uniformity, used in each case. As in other
renal tests, so here also must non-renal factors be excluded if the results are to be of value, and it is particularly important to begin the test with the patient in a state of "fluid equilibrium".

If the patient's body tissues have not been previously saturated with water, or if exercise, sweating, diarrhoea, fever or prolonged lack of water intake have temporarily increased their water holding power, then "free" Water, will only slowly appear in the blood.

The best time therefore to make a water test is about two hours after breakfast, or two hours after the last water was drunk. It appears to take a normal person about this time to eliminate whatever free water exists in his body. When this state has been attained, but not one beyond this, in which the tissues are beginning to become dehydrated, the patient empties the bladder and 500 cc. of water are consumed. A normal person, (or one having what may be called a normal kidney efficiency), should
excrete 400 - 500 cc. of the consumed water within the next two hours.

For the purpose of having a standard this test was carried out on twenty-five healthy children (Boy Scouts), between the ages of ten and eighteen. The average result was as follows:

<table>
<thead>
<tr>
<th>Time</th>
<th>Urinary output</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.15</td>
<td>29</td>
</tr>
<tr>
<td>0.30</td>
<td>54</td>
</tr>
<tr>
<td>0.45</td>
<td>70</td>
</tr>
<tr>
<td>1.00</td>
<td>76</td>
</tr>
<tr>
<td>0.15</td>
<td>65</td>
</tr>
<tr>
<td>0.30</td>
<td>65</td>
</tr>
<tr>
<td>0.45</td>
<td>52</td>
</tr>
<tr>
<td>2.00</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td><strong>441 cc.</strong></td>
</tr>
</tbody>
</table>

An excretion of water above the 500 cc. consumed means that free water over and above that consumed existed in the body at the time the test was started, or that water was drunk during the test.

The individual portions have a specific gravity which may be as low as 1002.
With slight relative renal insufficiency, the above amount of water may still be eliminated quantitatively within the two hours, but the individual portions are more uniform in quantity and there is not the rapid rise of the diuretic curve as in the normal.

As the renal insufficiency becomes more severe, the individual portions become smaller and smaller and the specific gravity of each portion does not vary much. Elimination is prolonged in proportion to the severity of the relative renal insufficiency.

In interpreting the results of this test, it can be said that if 400 - 500 cc. of urine is excreted within two hours, then the kidneys are able to deal adequately with water. If no such diuresis occurs, then the whole gamut must be run of causes lying without or within the kidney which may be responsible for such lack of function.
METHOD OF EXAMINATION.
Chapter V.

METHOD OF EXAMINATION.

In this investigation eighty-four children, who during an attack of scarlet fever had contracted scarletinal nephritis, were examined. The time since their discharge from hospital varied from one to ten years.

The cases were selected to the extent that where a choice was possible on account of numbers available, it was thought advisable to select the more serious forms of nephritis — cases in which the child had been acutely ill with oliguria and oedema, and in which blood and casts were present in
quantity. Although there is doubt as to the relation between the severity of the original attack, and the existence of permanent cardiovascular, or renal damage, it was though advisable to approach the problem from the point of view that if after a period of years such cases showed relatively little, or no evidence of abnormality, then a fortiori the milder cases would not.

Each case was examined in the following routine manner.

1. The general condition of the patient was noted, and a careful history taken of the state of health since the attack of nephritis. Leading questions were put for symptoms which might be referable to renal or cardiovascular inefficiency, with special enquiry for any history of oedema.

2. The heart was examined, and the position of the apex beat and left border noted. Any abnormality of function was recorded.

In each case the blood pressure was taken. Bearing in mind conditions normally affecting blood
blood pressure, the following routine was adopted.

A mercury column instrument - the Baumanometer - was used in the majority of cases; in some an anaeroid type (Barton) was employed.

The pressure was taken in the sitting posture with the arm resting on a table, and the auscultatory method was used in every case. Although it has been claimed that the pressure readings are influenced by the width of the cuff, we found it most convenient to use the standard 12 cm. armlet of the instrument except in the very young children, when it was folded to a width of 8 - 9 cm. We were unable to record any definite alterations in readings when both widths were used. The systolic readings were taken during release of pressure, and the first regular sounds were taken to represent the true pressure. The first reading was always discarded and the second one recorded. The diastolic pressure was taken at the fourth stage, and not at complete silence, and the readings were made as quickly as possible. None of the children
appeared to be alarmed in any way, but if the pulse rate was abnormally high, the whole procedure was interrupted and repeated a few minutes later.

3. 15 grms urea and 3 bottles were left, along with a printed slip of the following instructions.

**INSTRUCTIONS.**

I. Evening meal about 6 p.m. with only one cup of tea of other fluid.

II. Empty the bladder before going to bed. This need not be kept.

III. At a.m. pass water into Bottle 1. before getting out of bed.

IV. Then take the powder dissolved in half a cup of water - after this the child may get up.

V. At a.m. empty the bladder into Bottle 2. At a.m. empty the bladder into Bottle 3.

It will be noted that instructions II and III enable us to deal with orthostatic albuminuria before the carrying out of the test.

Specimens 1 and 2 were examined for the
presence of albumin. If albumin was present, the specimen was centrifuged and examined for abnormal constituents. The urea concentration test was carried out on the lesser of Nos. 2 and 3 - which was usually No. 3.

4. When the water test was used, the patient was provided with eight numbered bottles, and 500 cc. of water, along with the following instructions.

**INSTRUCTIONS.**

I. The test begins about 2 hours after the last water was drunk.

II. Drink the measured quantity of water, after emptying the bladder.

III. Empty the bladder in exactly 15 minutes into Bottle 1, and exactly every 15 minutes into Bottles 2, 3, 4, 5, 6, 7, and 8.

The amounts and specific gravities were subsequently measured.
5. In one case only was a blood urea estimation necessary.

6. In the one case who had died since being discharged, the cause of death and clinical facts were obtained from the various Hospitals at which he had been admitted. This case is referred to individually in a later section.
THE CASES IN DETAIL.
Case 1.

Boy 8 years. S.N. 3 years ago.
53 days in Hospital. Urine albumin and blood.
Albuminuria for 10 days. No complication.
Mild case.

Has been well since discharge except for an attack of chorea for which he was admitted to Hospital. Occasional headaches. No oedema.
A robust healthy looking child.

Heart - Apex 5th space in nipple line. Forcible systolic shock. Soft mitral systolic murmur, with an accentuated aortic second sound.

Blood pressure - 118. 90.

Urine - All specimens albumin free. Acid.
Urea concentration 2.2%.
Hourly specimens - Gravity 1022, 1020, 1018.
Water Test - 530 cc. Specific gravity varies from 1020 - 1006.
Case 1. (Contd)

Remarks — The systolic murmur probably indicates organic valvular change — rheumatic in origin. Cardiac hypertrophy is present. Blood pressure above the normal range. Urinary examination and renal function normal.
Case 2.
Boy 15 years. S.N. 7 years ago.
62 days in Hospital. Albuminuria 30 days, blood.
No complications. Mild case.

Has been well since discharge. No symptoms of any kind. No oedema. General physique and appearance good.

Heart - Apex beat forcible. Inside nipple line.
Mitral presystolic murmur.
Lordosis not marked.

Blood pressure - 135. 100.


Urea concentration 3.2%.

Remarks - No history of rheumatism to account for the beginning mitral stenosis. Blood pressure
Case 2. (Contd)

above normal range.

Orthostatic albuminuria - possible cause being slight renal congestion.
Case 3.

Boy 9 years. S.N. 2 years ago.
49 days in Hospital. Albuminuria on admission (18th day) and for 26 days. Albuminuria, blood, granular casts.

Heart. Apex 5th space in nipple line. Mitral systolic murmur. Rhythm regular.

Well since discharge. Has been puffy in the face in the morning. Eyesight good.
Heart - Normal outline. Sounds closed.
Blood pressure - 125. 90.
Urea concentration 2.7%

Remarks. - Urinary findings and renal efficiency test normal. Blood pressure above the normal limits.
Case 4.

Boy 15 years. S.N. 10 years ago.
75 days in Hospital. Albuminuria 9 days.
Urine — Blood and albumin.

No illness since discharge. No oedema, cough or headaches. Sight good.
Not examined, but passed a strict medical examination for his job — heavy work.

Urea concentration 2.1%.

Remarks — Albuminuria but no other evidence of renal impairment.
Case 5.

Boy 8 years. S.N. 2 years ago.
37 days in Hospital. Albuminuria on admission on 12th day - and for 23 days.

Urine - albumin, blood, granular casts.
Heart - Apex 4th space inside nipple line.
          Sounds closed. Regular rhythm.
Subsequently pleurisy and empyema, left side. 40 cc. of pus withdrawn. Organism - pneumococcus.

Well since discharge. No symptoms of any kind.

Heart - Apex 5th space inside nipple line. Sounds closed.

Blood pressure - 100. 75.


Urea concentration 2.8%.
Case 5. (Contd)

Remarks - Cardio vascular condition normal.
Blood pressure within normal range.
Renal efficiency test normal.
Case 6.

Boy 12 years. S.N. 5 years ago.
81 days in Hospital. Albuminuria 4 days.
No blood or casts. No complications. Very mild case.

Has only been in fair health. Enuresis since childhood. No other acute illness.
Is a congenital syphilitic under treatment.
Very pale. No lordosis.

Heart - Normal size and action.

Blood pressure - 112. 66.


   No pus or casts.


Urea concentration 3.5%.

Water Test - 632 cc. S.G. 1020 - 1004.

Case 7.

Boy 11 years. S.N. 1 year ago.
62 days in Hospital. Albuminuria 10 days. Blood.
Granular casts.

Heart - Normal on admission, but during
nephritis, left border 1/4 in outside
nipple line. Mitral systolic murmur.

Subsequently tonsillectomy with secondary
haemorrhage 3 days later. Chicken pox.
Mastoid operation. Discharged albumin free.

Since discharge general health good.
Active and plays games. Eats well. No other ill-
ness. Ear still discharges occasionally.

Heart - Normal.

Blood pressure - 110. 70.

Urine - Specimen 1. S.G. 1022. No albumin.
2. S.G. 1018. No albumin.

Urea concentration 3.75%.

Remarks - Renal and cardio vascular systems
unaffected.
Case 8.

Girl 17 years, S.N. 8 years ago.
51 days in Hospital. Albuminuria 28 days.
Blood and granular casts.

Has been well since discharge. No other illness.

Heart - normal.
No lordosis. General physique good.

Blood Pressure - 136. 86.

2. S.G. 1014. Acid. Trace of albumin. Large number of epithelial squames. No pus or casts.

Urea concentration 3.4%.

Water Test - 406. S.G. 1022 - 1008.

Case 9.

Girl 14 years. S.N. 6 years ago.
Rash very slight and first sent to Hospital with oedema. In Hospital 70 days.

Has been well since. No other illness.

Heart - normal.

Blood Pressure - 116. 64.


Urea concentration 37.

Remarks - Renal and cardio-vascular systems unaffected.
Case 10.

Girl 15 years. S.N. 8 years ago.
56 days in Hospital. Albuminuria 13 days.
Blood and casts.

Has been well since. Is a shop assistant.
No other illness. No oedema. Sometimes
complains of pains in knees.

Heart - normal.

Blood Pressure - 126. 60.


Urea concentration 2.5%.

Remarks - Renal and cardio-vascular systems
unaffected.
Case II.

Girl 13 years.  S.N. 6 years ago.
49 days in Hospital.  Albuminuria 17 days.

Blood.

Has been well since.  No other illness.
No oedema.  A pale, thin, badly developed girl.

Heart - First sound rough and prolonged.  Apex inside nipple line.  Sounds closed.

Blood pressure - 82. 48.

Urine - Specimen 1.  S.G. 1024.  Acid.  Trace of albumin.  Large number of urates and some epithelial squames.
No pus or casts.


Urea concentration 2.6%.

Water Test - 485 cc.  S.G. 1024 - 1006.

Remarks - Albuminuria but renal efficiency tests normal.  Blood pressure below the normal range.
Case 12.

Girl 9 years.         S.N. 2 years ago.
63 days in Hospital.  Albuminuria 35 days.
Blood but no casts.

Heart - Normal in size.  Sounds closed.
Nasal discharge for 3 weeks.

Has been very well since discharge.  No symptoms.  No other illness.

Heart - normal.

Blood pressure - 120. 90.


Urea concentration 2.6%.

Remarks - Albuminuria but renal efficiency appears normal.  Diastolic blood pressure is just above normal range.
Case 13.

Boy 7 years.  S.N. 3 years ago.
58 days in Hospital.  Albuminuria 26 days.


Heart and lungs normal.

No illness since.  No oedema or headaches although there was oedema for 2 months after discharge from Hospital.

No lordosis.  General appearance fair.

Heart - Apex beat forcible but localised in fifth space in nipple line.  Sounds closed.

Blood pressure - 135.  58.


Urea concentration 3.1%.
Case 13. (Contd).

Remarks - Renal efficiency tests normal. Diastolic blood pressure, within normal range.

Orthostatic albuminuria. The history of oedema suggests extensive renal damage three years ago, and the large pulse pressure may be a factor.
Case 14.

Girl 4½ years. S.N. 1 year ago.
50 days in Hospital. Albuminuria 16 days.

Blood. Epithelial and hyaline casts.
Heart - Sounds closed. Rhythm regular.

Well since discharge but nocturnal enuresis. No other illness except whooping cough. Eats well and is active. A healthy looking girl.

Heart - normal.

Blood pressure - 103. 50.

Specimen 2. S.G. 1016. Trace of albumin.

Urea concentration 3.45%.

Remarks - Albuminuria with renal efficiency test normal, and the blood pressure within normal range.
Case 15.

Boy 21 years. S.N. 9 years ago.
60 days in Hospital. Albuminuria 20 days.

Well since discharge. No symptoms.

Heart - Apex beat very forcible in sixth space inside nipple line. Systolic mitral area propagated into axilla. 2nd sound accentuated in all areas.

Blood pressure - 165. 110.


Urea concentration 3.4%.

Water Test - 673 cc. S.G. 1016 - 1002.

Remarks - No history to account for the systolic murmur. Cardiac condition not noted during stay in hospital. Blood pressure grossly abnormal. Renal efficiency tests normal.
Case 16.

Girl 14 years. S.N. 10 years ago.

39 days in Hospital. Albuminuria on admission (30th day) and for 20 days. Urine contained blood.

No illness since discharge. Occasional headaches. Rather puffy face.

Heart - Apex 6th space in nipple line, and forcible. Accentuated 2nd sound.

Blood pressure - 145. 110.


2. S.G. 1013. Acid. Albumin +

Urea concentration 2.9%.

Water Test - 394 cc. S.G. 1026 - 1014.

Case 17.

Girl 8 years. S.N. 2 years ago.
57 days in Hospital. Albuminuria 23 days.

Urine contained blood and casts.

Heart not enlarged, but a mitral systolic murmur is present. Chicken pox on eighth day after admission.

Has been well. Never off school and no serious illness. No oedema. Occasional enuresis. A pale, anaemic child.

Heart - normal in size and action, but a systolic murmur over the pulmonary area.

Blood pressure - 74. 42.

Lordosis marked.

3. Acid.

Urea concentration 2.8%. 
Case 17. (Contd).

Case 18.

Boy 15 years. S.N. 1 year ago.
78 days in Hospital. Albuminuria 44 days.
Urine contained blood, cellular casts, and 2 grs. albumin per oz.

Heart – both sounds closed.

Quite well. Works as a message boy.
No other illness.

Heart – normal in size and action.

Blood pressure – 110. 80.

Urine – 2nd hour specimen acid, S.G. 1020. No albumin.

Urea concentration 3.85%.

Remarks – Renal and cardio-vascular systems unaffected.
Case 19.

Boy 12 years.  
S.N. 3 years ago.

54 days in Hospital.  
Albuminuria 21 days.

Urine contained blood.

Heart - normal.

Well since discharge.  Often has headaches and pains in back.  Eyesight good.

Heart - Apex 5th space inside nipple line.  Sounds closed.  Apex beat forcible and aortic 2nd sound accentuated.

Blood pressure - 130. 85.


2.  S.G. 1018.  Acid.  Trace of albumin.  A few epithelial squames and some bacteria, but no casts or pus seen.


Urea concentration 3f.

Case 19. (Contd).

Remarks - Blood pressure within normal limits.
Renal efficiency tests normal. Orthostatic albuminuria - no obvious cause.
Case 20.

Boy - died aged 6 years. S.N. 6 months before death.

112 days in Hospital and discharged still with albuminuria. No casts. Albumin 0.3g.

Heart - 5th space in nipple line. Sounds closed.

Blood pressure - 152. 105.

Earlier History.

He had been well until a year before having scarlet fever. Then suddenly had convulsions and was unconscious for 2½ hours. Admitted to Leith Hospital and treated for five weeks. Was discharged feeling well except for pains in the head. Headaches became worse and two months later he was again admitted for six to seven weeks. Two months later, scarlet fever. After discharge he was again in Leith Hospital for ten weeks, but on this occasion made no progress - still headaches and vomiting. Subsequently admitted to Royal Infirmary, developed uraemia with convulsions and died.

Remarks - Previous nephritis.
Case 21.

Boy 11 years, S.M. 1 year ago.
59 days in Hospital. Albuminuria on admission (7th day) and subsequently for 32 days. Admitted comatose and unconscious and taking fits.

In good health since discharge, but occasional headaches. An active boy. No oedema.

Heart - Normal outline and action.

Blood pressure - 104. 68.

Urine - 2nd hour specimen - S.G. 1014. No albumin.

Urea concentration 2.45%.

Remarks - Renal and cardio-vascular systems unaffected.
Case 22.

Girl 17 years. 3.N. 6 years ago.
72 days in Hospital. Albuminuria 36 days.
Blood in urine.

In good health since. Plays hockey, etc.
No other illness.

Heart - normal.
Blood pressure - 115. 75.
Urine - 2nd hour - no albumin.

Urea concentration 3.25%.

Remarks - Renal and cardio-vascular systems unaffected.
Case 23.

Boy 9 years.        S.N. 3 years ago.
99 days in Hospital.  Albuminuria 63 days.

Urine contained much blood and many casts.

Has been well since discharge, but any cold
"goes straight to his kidneys" causing cloudiness and
deposit in urine. Often has headaches. Eyesight
good and no history of oedema.

Heart - Not enlarged. Apex beat 5th space inside
nipple line. Sounds closed.

Blood pressure - 120. 90.

No lordosis.

2. S.G. 1024. Acid. Albumin +
A few pus cells, fair amount of
bacteria. No casts seen.

Urea concentration 3.1g.

Water Test - 604 cc. S.G. 1020 - 1010.
Remarks - Diastolic blood pressure slightly above normal range. Orthostatic albuminuria - no obvious cause. Renal efficiency tests normal.
Case 24.

Boy 6½ years. S.N. 1 year ago.
47 days in Hospital. Albuminuria on admission
(14th day). Albumin 2 grs. per oz..

Quite well since. No other illness except measles. Lordosis present.

Heart - normal.

Blood pressure - 90. 54.

Urine - Specimen 1. No albumin.


Urea concentration 2.35%.

Water Test - 687 cc. S.G. 1018 - 1002.

Remarks - Blood pressure below average but within normal limits. Renal efficiency tests normal. Orthostatic albuminuria with lordosis.
Case 25.

Boy 13 years. S.N. 1 year ago.
63 days in Hospital. Albuminuria 27 days.

Urine contained blood and casts.

Heart remained normal.

Has been well since. No headaches or oedema.

Heart - normal.

Blood pressure - 80. 48.

Urine - Specimen 1. No albumin.


Urea concentration 2.80%.

Remarks - Renal efficiency test normal, but blood pressure below normal limits.
Case 26.

Girl 10 years.               S.N. 6 years ago.
66 days in Hospital.        Albuminuria 13 days.
Urine contained blood.      Granular and blood casts.
Mild case.

Had pneumonia a few months ago.   No headaches or oedema.

Heart - Apex 5th space in nipple line. All sounds pure.

Blood pressure - 118. 72.

Urine - Specimen 1. S.G. 1018. Acid. Trace of albumin. One or two pus cells. No casts seen.


Urea concentration 2.6%.

Remarks - Albuminuria. Renal and cardio vascular systems unaffected.
Case 27.

Girl 5½ years. S.N. 4 years ago.
124 days in Hospital. Albuminuria 24 days.
Much albumin (7 grs. per oz. up to 10 grs. per oz.).
No blood. Tonsils and adenoids removed. A septic scarlet.

No serious illness since discharge, but has a chronic cough summer and winter. Sweats at night.
Very thin but not losing weight. No edema or headaches. Otorrhea for 6 months after discharge.
Lordosis not abnormal.

Heart - Apex 5th space in nipple line. All sounds pure.

Blood pressure - 95. 75.


Urea concentration 2.0%.

Water Test - 570 cc. S.G. 1024 - 1004.
Case 27. (Contd).

Remarks - Possibly a tuberculous or pre-tuberculous child. Orthostatic albuminuria (delayed). Renal efficiency tests normal. Blood pressure within normal range.
Case 28.

Boy 15 years. S.N. 8 years ago.
43 days in Hospital. Albuminuria 9 days.

Has not been well since discharge, always very tired and mother says he is "dense" and stupid. No headaches. No oedema. No other serious illness.

Heart - Apex 5th space. 3 in from M.S.L. All sounds pure. Mitral area - second sound accentuated.
Aortic area - second sound accentuated and reduplicated.

Blood pressure - 125. 95.


Urea concentration 3.1%.

Remarks - Renal efficiency test normal. Systolic blood pressure within, but diastolic pressure just outside normal range.
Case 29.

Girl 7 years. S.N. 4 years ago.
85 days in Hospital. Albuminuria on admission (13th day) and for 20 days. Amount - 18 grs. per litre. Blood and granular casts. Oedema marked.

Always in good health, but still otorrhoea.
No oedema. Eats well. Never off school.

Heart - normal.

Blood pressure - 114. 66.

2. S.G. 1018. Albumin +
A few pus cells, and epithelial squames.

Urea concentration 1.8%.

Water Test/
Case 29. (Contd).

**Water Test**

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**Remarks** - Renal efficiency tests not normal, but blood pressure within normal range.
Case 30.

Boy 6 years. S.N. 2 years ago.
50 days in Hospital. Albuminuria 30 days.
Blood and granular casts.
Left border of heart in nipple line and a loud mitral systolic murmur.

Uneventful recovery but readmitted five months later with a rash and fever. Kept in 6 days. Not scarlet. Heart now normal.

General health good and never off school.
No oedema or headaches. Plays games.
Heart - normal.

Blood pressure - 112. 70.

Urine - 2nd hour specimen - Albumin present. A few isolated pus cells and some epithelial squames. A few yeasts.

Urea concentration 4.0%.

Remarks - Complete cardiac recovery. Albuminuria but renal and cardio vascular systems unaffected.
Case 31.

Boy 15 years.    S.N. 3 years ago.
72 days in Hospital.    Albuminuria 10 days.
Traces of blood in urine.    Mild case.

He has not been in good health. Still has syncopal attacks, which he also had before having scarlet. The attacks do not appear to be fits. Seen by Dr Guy and at Edinburgh Royal Infirmary - in both cases the mother was reassured.

Heart - normal.
Blood pressure - 90. 64.
Urine - All specimens albumin free.

Urea concentration 2.35%.

Remarks - No cause found for the syncopal attacks, which appear to be functional. Both renal and cardio vascular systems unaffected.
Case 32.

Boy 17 years. S.N. 3 years ago.
86 days in Hospital. Albuminuria 10 days.
Urine contained blood.

Has been well since discharge. No other illness. Plays games. No oedema.

Heart - normal.
Blood pressure - 128. 74.
Urine - Albumin free.

Urea concentration 3.65%.

Remarks - Renal and cardio vascular systems unaffected.
Case 33.

Boy 15 years. S. N. 7 years ago.
58 days in Hospital. Albuminuria 8 days.
On admission only 6 ozs. of urine in 24 hours.
Albumin +++. Blood. Oedema of face and legs.
Mitral systolic murmur.

Has been well since discharge, and is a
butcher assistant.

Heart - dilated to nipple line. Loud mitral
systolic murmur.

Blood pressure - 142. 80.

Urine - All specimens albumin free.
Cooperation for urea. Concentration
test refused.

Remarks - Cardiac enlargement and mitral systolic
murmur persist. No rheumatic history. Diastolic
blood pressure within normal limit, but systolic
abnormally high.
Case 34.

Boy 18 years. S.N. 10 years ago.
76 days in Hospital. Albuminuria 50 days.

Urine contained blood.

Well since. Never off work as a barman.

Appendicitis but no other illness.

Heart - normal.

Blood pressure - 138. 76.

Urine - 2nd hour specimen - S.G. 1022. Acid.
No albumin.

Urea concentration 2%.

Remarks - Renal and cardio vascular systems unaffected.
Case 35.

Boy 18 years. S.N. 10 years ago. 48 days in Hospital. Albuminuria on admission (25th day) and for 44 days. Slight presystolic murmur.

Healthy although troubled with chest. Pneumonia 7 years ago, and since then chronic bronchitis. No history of oedema.

Heart - Normal in size but still a mitral presystolic murmur.

Blood pressure - 120. 74.


Urea concentration 3.65%.

Case 36.

Boy 9 years. S.N. 6 years ago. 84 days in Hospital. Albuminuria 43 days. Urine contained blood. Heart normal. Gave a history of previous nephritis. Albuminuria continued until within a week of discharge.

Had measles and tuberculous glands in neck about one year later. Was coughing and losing weight. No headaches or oedema.

Heart – Apex 5th space just outside nipple line. Sounds pure.

Blood pressure – 95. 60.


2. S.G. 1006. Acid.

Urea concentration 0.6%.

Water Test/
Case 36. (Contd).

Water Test -

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Remarks - Renal efficiency tests abnormal, but history of nephritis prior to scarlet fever. Cardiac enlargement, but blood pressure within normal range.
Case 37.

Boy 14 years.  S.N. 8 years ago.

72 days in Hospital.  Albuminuria 21 days.

Never ill, but often severe headaches.  No History of oedema.

Heart  - normal.

Blood pressure  - 104.  70.


Urea concentration  2.8%.

Remarks  - Renal and cardio vascular systems unaffected.
Case 38.

Boy 7 years. S.N. 6 years ago.
92 days in Hospital. Albuminuria 17 days.
Blood present. Tonsils and adenoids removed.

Very easily tired. Takes "bad turns" of headaches. puffiness under eyes at times? No other serious illness, but often off school. A very pale undersized child.

Heart - Soft mitral systolic murmur.

Blood pressure - 94. 60.


2. S.G. 1020. Acid.

Urea concentration 2.6%.

Remarks - Albuminuria and a mitral systolic murmur of no ascertainable cause. No note of cardiac condition while in Hospital. Blood pressure within normal range, and renal efficiency test normal.
Case 39.

Girl 6 years. S.N. 1 year ago.
65 days in Hospital. Albuminuria 16 days.
Blood + and epithelial squames and granular casts.
Heart normal.

Has not been well since. Not eating.
Frequently abdominal pain. No oedema.

Heart - normal.
Blood pressure - 90. 60.
Urine - All specimens albumin free,

Urea concentration 2.35%.

Remarks - Renal and cardio vascular systems unaffected.
Case 40.

Boy 16 years. S.M. 9 years ago.

92 days in Hospital. Albuminuria 58 days.

Blood present.

Not in very good health. Ear still discharges off and on. No oedema. A pale boy with accentuated lordosis.

Heart - normal.

Blood pressure - 116. 88.


A few isolated pus cells, some epithelial squames and yeasts.

Urea concentration 2.9%.

Remarks - Orthostatic albuminuria with lordosis.

Renal and cardio vascular systems unaffected.
Case 41.

Woman 28 years. S.N. 1 year ago.

In Hospital 67 days. Still trace of albumin on discharge. In Hospital blood. Epithelial and granular casts.

Heart - Left border normal, but first sound roughened in mitral area.

Blood pressure - 142. 90.

Well since discharge. No other illness.

Heart - normal. First sound pure.

Blood pressure - 104. 66.

Urine - All specimens albumin free.

Urea concentration $3.15\%$.

Remarks - Renal and cardio vascular systems unaffected.
Case 42.

Girl 13 years. S.N. 8 years ago.
49 days in Hospital. Albuminuria 9 days.
Chicken pox.

Quite well since discharge. No other illness. Never off school. No history of oedema. No urinary symptoms.

Heart - normal.
Blood pressure - 120. 92.


Urea concentration 3.3%.

Remarks - Renal and cardio vascular systems unaffected.
Case 42.

Boy 14 years. S.N. 9 years ago.
50 days in Hospital. Albuminuria on admission (8th day) and for 45 days. Urine contained blood.

Has been well since. No other illness.

Is an apprentice printer.

Heart - normal.

Blood pressure - 120. 80.

Urine - Specimen 1. S.G. 1018. Albumin free,
        2. S.G. 1020. Albumin free,

Urea concentration 3.05%.

Remarks - Renal and cardio vascular systems unaffected.
Case 44.

Boy 20 years.  S.N. 8 years ago.
44 days in Hospital.  Albuminuria 10 days.
Very mild case.

Not in robust health. Has had jaundice.
Easily tired. Passed by doctor for admission to
a Bank. Is anaemic — for which he has had
treatment.

Heart — Normal size. Soft mitral systolic murmur.
No abnormal lordosis.

Blood pressure — 104. 80.


Urea concentration 2.90%.

Remarks — Mitral systolic murmur — probably
haemic. Orthostatic albuminuria associated with
anaemia. Diastolic blood pressure normal, the
systolic below the average for his age. Renal
efficiency test normal.
Case 45.

Boy 16 years. S.N. 4 years ago.
52 days in Hospital. Albuminuria 28 days.
Blood and casts present.

Is a baker. Has been in good health.
No other illness.

Heart - Normal.

Blood pressure - 130. 80.


Urea concentration 3.75%.

Remarks - Renal and cardiac vascular systems unaffected.
Case 46.

Boy 18 years. S.N. 8 years ago.
80 days in Hospital. Albuminuria 20 days.
Blood and epithelial casts.

In good health since. No other illness.
Eats well.

Heart - normal.

Blood pressure - 138, 86.

Urine - Albumin present in all specimens. A few granular casts seen.

Urea concentration 3.60%.

Remarks - The renal efficiency test is normal.
The diastolic blood pressure is within normal range, the systolic is raised.
Case 47.

Boy 12 years. S.N. 4 years ago.
16 weeks in Hospital. Albuminuria 40 days.
Blood and epithelial casts.

Has been well since. No other illness and never off school. Sometimes swollen under eyes and occasional headaches.

Heart - normal in size and action.

Blood pressure - 102. 68.

Urine - All specimens albumin free.  S.G. 1022.

Urea concentration 2.30%.

Remarks - Renal and cardio vascular systems unaffected.
Case 48.

Girl 15 years. S.N. 8 years ago.
52 days in Hospital. Albuminuria 14 days.
No oedema.

Good health since discharge. No other illness.

Heart - normal.

Blood pressure - 128. 80.

2. S.G. 1020. No albumin.

Urea concentration 3.7%.

Remarks - Renal and cardio vascular systems unaffected.
Case 49.

Boy 12 years. S.N. 8 years ago.
76 days in Hospital. Albuminuria 16 days.
Blood in urine.

Has never been well since discharge. Often off school for many minor complaints. General lassitude. Headaches but no oedema. Tonsillectomy two years ago. A thin pale boy.

Heart - normal.
Blood pressure - 122. 80.
Urine - S.G. 1020. Albumin free.

Urea concentration 2.25%.

Remarks - Renal and cardio vascular systems are unaffected.
Case 50.

Girl 7 years.  S.N. 2 years ago.
54 days in Hospital.  Albuminuria on admission (20th day) and for 43 days.  Blood.  Epithelial and granular casts.

Heart - Left border normal.  Mitral systolic murmur.  Rhythm regular.

Blood pressure - 116. 70.

Quite well since discharge.  Appetite good.  Active.

Heart - All sounds pure.  Left border in nipple line.

Blood pressure - 102. 70.

Urine - 2nd hour - S.G. 1022.  No albumin.

Urea concentration 3.15%.

Remarks - Renal and cardio vascular systems are unaffected.
Case 51.

Girl 6 years. S.N. 1 year ago.
73 days in Hospital. Albuminuria 11 days.
Urine - Albumin ½ gr. per oz. Cellular casts.
No blood.

Heart - normal on admission. Later a soft mitral systolic.

Has been well. Never off school. Still a nasal discharge.
Heart - Sounds closed. Not enlarged.

Blood pressure - 88. 54.

" No lordosis.

Urine - Specimen 1. Albumin free.

2. S.G. 1022. Albumin +

Urea concentration 2.75%

Water Test - 536 cc. S.G. 1027 - 1006.

Case 52.

Girl 17 years. S.N. 7 years ago.
68 days in Hospital. Albuminuria 22 days.

In good health and has had no other illness.

Heart - normal.

Blood pressure - 105. 80.

Urine - Specimen 1. S.G. 1018. No albumin.
2. S.G. 1018. No albumin.

Urea concentration 3.45%.

Remarks - Renal and cardio vascular systems normal.
Case 53.

Girl 10 years.  S.N. 2 years ago.
66 days in Hospital.  Albuminuria 23 days.  Blood, but no casts seen.

Heart - 7 days after admission left border in nipple line.  Mitral systolic murmur.  31 days after admission, left border 1/4 in outside nipple line.  Loud mitral systolic murmur.

Occasionally off school with headaches, but no serious illness.  Eats well.  No oedema.  Enuresis since discharge.

Heart - normal.

Blood pressure - 104. 74.

Urine - Specimen 1.  S.G. 1020.  Acid.  Albumin present.  A large number of urates.  No casts or pus.


Urea concentration 3.0%.

Remarks - Cardio vascular system unaffected.  Renal efficiency test normal but persistent albuminuria.
Case 54.

Boy 9 years. S.M. 2 years ago.
123 days in Hospital. Albuminuria 16 days.

Heart on admission normal. During nephritis a mitral systolic murmur. Nephritis began 4 days after tonsillectomy. Later otorrhoea and mastoid operation.

Has been well since. No history of oedema.
No other serious illness. Eats well and plays games at school.
Heart - Apex beat in nipple line. Sounds pure.
Blood pressure - 128. 80.

Urea concentration 2.2%.
Remarks - Slight cardiac enlargement with a systolic blood pressure above normal range, but a diastolic within normal range. Renal efficiency test normal.
Case 55.

Girl 15 years. S.N. 6 years ago.

Following this, occasional swelling of face and legs with dyspnoea and frequent syncopal attacks and abdominal pain. Admitted Sick Children's Hospital, May 1927. Discharged 28. 7. 27. She had been healthy until scarlet fever, but never since.

In Hospital albumin ++. Epithelial casts and renal epithelium. Pus. Trace of blood.

Blood pressure - 140. 90, 130. 100, 122. 95.

Diffuse pulsation in 4 - 5 space within nipple line.

Mitral systolic murmur and accentuated pulmonary second sound. Extra systoles. Moderate cyanosis.

Some clubbing fingers. 1. 7. 27. Blood urea 40 mgs. per 100 cc.. 3. 7. 27. Urea concentration 1.3.

Since then never in good health and has not attended school until a few months ago. No oedema except occasional puffiness under eyes when she gets cold. Typical nephritic appearance.

Heart - Apex beat diffuse and forcible. ½ in outside nipple line in 6th space. Sounds closed.

Blood pressure - 130. 95.
Case 55. (Contd).

Urine - Specimen 1. S.G. 1014. Acid. Albumin ++
Many pus cells and epithelial squames. No casts seen.

2. S.G. 1010. Acid. Albumin ++
Many pus cells. No casts.
Epithelial squames.

3. S.G. 1014. Acid. Albumin ++

Urea concentration 1.5%.

Water Test -

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179
Case 55. (Contd).

Blood Chemistry -

1. N.P.N. 78 mgs. per 100 cc..
2. Urea N. 50 mgs. per 100 cc..
3. Creatinine 4.2 mgs. per 100 cc..

The fundi are quite normal.

Remarks - Chronic parenchymatous nephritis, with grossly inefficient renal function. Abnormal blood contents, cardiac enlargement, and a blood pressure moderately raised.
Case 56.

Girl 8 years. S.M. 4 years ago.
53 days in Hospital. Albuminuria 41 days.
Urine contained blood and casts. Soft mitral systolic murmur. Subsequently contracted diphtheria.

Very well since operation for appendicitis and peritonitis 8 weeks after discharge. No headaches or oedema. Tonsils enlarged and unhealthy. Heart - no enlargement. Sounds pure.

Blood pressure - 112. 70.

Fair number of pus cells and some epithelial squames and amorphous urates. No casts, blood cells or crystals.

2. S.G. 1020. Acid. Albumin +
A few pus cells, oxalate crystals and epithelial squames. No casts or blood.

Urea concentration 3.3\%. 
Case 56. (Contd).

Remarks - Cardiac recovery. Albuminuria but renal and cardio vascular systems unaffected.
Case 57.

Boy 14 years.  S.N. 8 years ago.
97 days in Hospital.  Albuminuria 18 days.
No casts.

In perfect health since.  No oedema or any other illness.  Is a message boy.

Heart - normal.

Blood pressure - 116. 82.

Urine - All specimens albumin free,

Urea concentration 3.05%.

Remarks - Renal and cardio vascular systems are unaffected.
Case 58.

Boy 20 years.  S.N. 5 years ago.
63 days in Hospital.  Albuminuria on admission and for 41 days.  Urine contained blood, epithelial and granular casts.

Has been only fairly well since discharge. Frequent headaches of severe nature.  No oedema. Slight cough at present.  Eyesight better than it was before an operation for strabismus.

Heart - Apex 5th space in nipple line.  Sounds pure but apex beat forcible.  Aortic second sound accentuated.

Blood pressure - 170. 120.

A pale man, very thin.


Urea concentration 2.6%.

Water Test/
Case 56 (Contd).

Water Test.

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Remarks — No note of cardio vascular condition in Hospital, but now a grossly abnormal blood pressure, with no albumin, cardiac enlargement, and renal test normal.
Case 59.

Boy 16 years. S.N. 2 years ago.
52 days in Hospital. Albuminuria 13 days.
Albumin, blood for 3 days only. Granular casts.
Heart - Apex 4th space inside nipple line.
Sounds closed.
Blood pressure - 3rd day after onset of nephritis 170. 120.
Otorrhoea for 14 days.

General health now good. Plays rugby.
Heart - normal.
Blood pressure - 128. 85.
Urine - Specimen 1. S.G. 1010. Albumin free.
2. S.G. 1014. Albumin free.
Urea concentration 3.4%.
Remarks - Renal and cardio vascular systems are unaffected.
Case 60.

Girl 15 years. S.N. 4 years ago.
91 days in Hospital. Albuminuria 39 days.
Urine contained pus, blood, epithelial and blood casts.

Has not been in good health. Headaches and occasional vomiting. Frequency of micturition and sometimes pain on micturition. Eyesight good. History of oedema of ankles after standing, (she is a factory worker). History of cervical adenitis. No other serious illness.

A pale, thin girl.

Heart - normal.

Blood pressure - 106. 50.


2. S.G. 1012. Acid. Trace of albumin.

Urea concentration 1.6%.

Test repeated - Urea concentration 1.25%.
Case 60. (Contd).

**Water Test.**

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**Remarks** - Blood pressure just below normal range. Renal function impaired.
Case 61.

Man 23 years.  S.N. 10 years ago.
30 days in Hospital.  Albuminuria 10 days.
Blood in urine.

In good health.  No other illness.
Never off work.

Heart  - normal.

Blood pressure  - 124.  70.


Urea concentration  3.05%.

Remarks - Renal and cardio vascular systems are unaffected.
Case 62.

Boy 12 years. S.N. 6 years ago.

30 days in Hospital. Albuminuria on admission (23rd day) and for 34 days. Blood in urine.

Heart - Left border inside nipple line.

Mitr al systolic murmur.

Has been well since. No other illness.

No history of oedema.

Heart - normal.

Blood pressure - 112. 70.

Urine - all specimens albumin free.

Urea concentration 2.70%.

Remarks - Renal and cardio vascular systems normal.
Case 63.

Boy 17 years. S.N. 8 years ago.
53 days in Hospital. Albuminuria 15 days.
Urine contained blood and granular casts.

Heart - slightly irregular for a few days.

Has had no complaint since. Never off work as a slaughterman.

Heart - normal.

Blood pressure - 132. 84.

Urine - All specimens albumin free.

2nd hour - Urea concentration 2.30%.

Remarks - Renal and cardiovascular systems are unaffected.
Case 64.

Boy 14 years.    S. N. 9 years ago.
107 days in Hospital.    Albuminuria 37 days.
Urine contained blood.
    Heart - normal.

Has been fairly well - chronic dyspepsia.
No headaches or oedema.

Heart - Distinct prolongation and roughening of first sound.

Blood pressure - 110. 78.


Urea concentration 2.65%.

Remarks - Renal and cardio vascular systems unaffected.
Case 65.

Boy 16 years.        S.N. 3 years ago.
78 days in Hospital. Albuminuria 25 days.

Large quantity of blood.

Heart - mitral systolic murmur and accentuated pulmonary second sound.

Has been well. No other illness. No symptoms.

Heart - normal.

Blood pressure - 142. 50.


Urea concentration 3.10%.

Remarks - Renal system unaffected. Systolic blood pressure above normal range, diastolic within normal range.
Case 66.

Man 25 years.  S.N. 9 years ago.
55 days in Hospital.  Albuminuria 17 days.
Blood in urine.
Heart - normal.

Doing heavy work as a cooper, and is quite fit.  No other illness.

Heart - normal.

Blood pressure - 130. 80.

Urine - All specimens albumin free.
Urea concentration 2.45.

Remarks - Renal and cardio vascular systems normal.
Case 67.

Girl 19 years.  S. N. 9 years ago.
76 days in Hospital.  Albuminuria 31 days.
Blood in urine.  No complications.  Admitted to City Hospital 4 years ago with encephalitis lethargica. Was well until then, but only in fair health since. Easily tired but no headaches or oedema.

Heart - normal.

Blood pressure - 122. 80.

Urine - Urea concentration test could not be carried out as patient refused to co-operate.

All specimens albumin free.

Water Test.

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224

Remarks - Cardiovascular systems normal. On account of possible nervous sequelae of the enceph-
Case 67. (Contd).

...alitis, the water excretion is not considered abnormal especially as the variations in specific gravity are satisfactory.
Case 68.

Man 18 years. S.M. 8 years ago.

58 days in Hospital. Albuminuria on admission (11th day) and for 38 days.

Has not been ill since. No symptoms.

Heart - normal.

Blood pressure - 130. 90.

Urine - All specimens albumin free.

Urea concentration 3.25%.

Remarks - Renal system normal. Diastolic pressure above average.
Case 69.

Girl 9 years. S. N. 2 years ago.
52 days in Hospital. Albuminuria 14 days.

Blood in urine. No casts.

Heart - Apex 4th space in nipple line. Mitral systolic murmur.

History of oedema of ankles one month after discharge and again two months after. Never off school since. Enuresis before scarlet, but not since. Occasional headaches.

No lordosis.

Heart - normal.

Blood pressure - 78. 40.

Urine - Specimen 1. Albumin free.


Urea concentration 2.45%.

Remarks - Orthostatic albuminuria with a blood pressure much below normal range. History of
Case 69. (Contd).

Oedema suggests severe renal involvement originally. There has been complete cardiac recovery. Renal function normal.
Case 70.

Girl 11 years. S. N. 4 years ago.
34 days in Hospital. Albuminuria 47 days.

Since discharge, although she has increased in weight, her mother complains that she is frequently dull, listless, and "dreamy" for a day or two. She is clever at school and is in a class in advance of her years. Has had no other illness and no history of oedema.

Heart - normal.
Blood pressure - 118. 78.

Urine - Specimen 1. S. G. 1020. Albumin +
2. S. G. 1018. Albumin +
Few pus cells and several granular casts. No blood.

Urea concentration 1.70%.
Repeated Urea concentration 2%.

Water Test/
Case 70. (Contd).

**Water Test**

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**Remarks** - Normal cardio vascular system. Renal function slightly impaired.
Case 71.

Girl 9 years. S. N. 4 years ago.
85 days in Hospital. Extent of albuminuria not recorded.

This case was under the author's care before and after S. N.. The following is an extract of her case card.

20. 10. 25. Rash fading.
29. 10. 26. Enuresis almost nightly since scarlet. Pain left lumbar region. Urine has a trace of albumin.

1928. Heart - in nipple line 5th space. Sounds closed.
Blood pressure - 96. 50.
Case 71. (Contd).

**Urine**

- Specimen 1. S.G. 1018. No albumin.
- Specimen 2. S.G. 1020. No albumin.

Urea concentration 2.80%.  

**Water Test.**

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538

**Remarks** - Slight cardiac enlargement, but blood pressure and renal function normal.
Case 72.

Girl 9 years. S. N. 4 years ago.

112 days in Hospital.

Since discharge under author's care. Has been well since except on 5:10:27. Swelling of face and eyes with frequency of micturition the day before. Urine had a trace of albumin, but the condition appeared to be due to urticarial condition.

9. 4. 28. Diphtheria.

She has had no other illness. Is active and eats well. The tonsils are still large and unhealthy.

Heart - normal.

Blood pressure - 108. 60.


Urea concentration 3.5%

Specimen 2. S.G. 1018. Albumin +.

Urea concentration 2.95%
Case 72. (Contd).

A few granular casts are present and some pus cells.

Remarks - Albuminuria but cardiovascular and renal function normal.
Case 73.

Girl 16 years. S. N. 5 years ago.
44 days in Hospital. Albuminuria 8 days.
No Blood or casts. A mild case.

Has been well since. No other illness.
Very pale. No oedema.

Heart - normal.

Blood pressure - 110. 88.

Urine - Specimen 1. Albumin +.
2. Albumin +.
3. Albumin +.

Urea concentration 3.2%. 
A good many epithelial squames and 
triple phosphates. No casts or pus.

Remarks - Albuminuria but renal function and cardio 
vascular systems normal.
Case 74.

Boy 8 years. S. N. 3 years ago.

64 days in Hospital. Albuminuria on admission (8th day) and for 52 days.

Much blood and granular and epithelial casts. Had a fit after admission.

No other illness since scarlet, but has never been well. Very thin and pale and is said to be losing weight. History of swelling of face. Easily tired. Morning headaches.

Heart - normal.

Blood pressure - 125. 90.

Urine - Specimen 1. Albumin +.


3. Albumin +.

Urea concentration 1.4%.

Water Test/
Case 74. (Cont'd).

Water Test -

1. 41 1018
2.  7 1012
3.  9 1012
4. 18 1010
5. 22 1010
6. 49 1006
7. 52 1006
8. 45 1006

243

Remarks - Blood pressure above normal range.
Albuminuria. Renal function impaired.
Case 75.

Girl 10 years. S. N. 2 years ago.
56 days in Hospital. Albuminuria 22 days.
Granular casts. Apex 4th space, internal to nipple line. Mitral systolic murmur.

Well since discharge. No symptoms.

Heart - Apex 6th space inside nipple line. Rough blowing systolic murmur at mitral area. 2nd sound closed.

Blood pressure - 100. 70.


Urea concentration 2.7%.

Remarks - Renal and cardio vascular systems unaffected.
Case 76.

Girl 7 years. S. N. 3 years ago.
66 days in Hospital. Albuminuria 36 days.

Well since discharge. No oedema or headaches.

Heart - Apex 5th space in nipple line. Sounds pure.
Blood pressure - 125. 90.
Urea concentration 2.6%.
Some isolated pus cells and epithelial squames. No casts, blood, or crystals.

Remarks - Blood pressure above normal range with cardiac enlargement. Slight albuminuria but renal test normal.
Case 77.

Girl 13 years. S. N. 3 years ago.
90 days in Hospital.

General health good. No oedema and no other illness. No lordosis.

Heart - normal.

Blood pressure - 110. 86.


This child was delivering milk between specimens 1 and 2. The urea concentration was 1.9%.

Repeated, child kept in.

No. 2. Urea concentration 3%.
No. 3. Urea concentration 3.3%.

Microscopically a fair number of pus cells, and a few transitional epithelial cells, and oxalate crystals. No casts or red blood cells.

Case 78.

Boy 13 years. S. N. 4 years ago. 59 days in Hospital. Albuminuria 16 days.

Pleurisy 2 months after discharge. Is well now except for attacks of blueness of the face. Attacks of pain in left side simulating renal colic and he complains of pain in the back. Headaches during these attacks of pain. He passes a large quantity of urine. ? Renal calculus.

Heart - Apex beat very forcible in 6th space in nipple line. Sounds pure, but 2nd sound accentuated in all areas.

Blood pressure - 140. 100.

Urine - Specimen 1. Acid. Albumin+.
   Microscopically a few pus cells and epithelial squames.

Urea concentration 3.4%. 
Case 78. (Cont'd).

Remarks - Cardiac enlargement with blood pressure above normal range. Albuminuria but renal function normal.
Case 79.

Girl 7 years.  S. N. 2 years ago.
55 days in Hospital.  Albuminuria 10 days.

Urine - No blood, but a few granular casts.
Heart - Sounds closed. First mitral sound rough. Apex inside nipple line.

Health only fair. Has had rheumatic fever, in which ankles were swollen. Never off school.
Heart - normal.
Blood pressure - 98. 62.


Urea concentration 3%. 

Remarks - Renal and cardio vascular systems are unaffected.
Case 80.

Girl 12 years. S. N. 7 years ago.
35 days in Hospital. Albuminuria 15 days.
No blood or casts.

Well since discharge. No oedema. No headaches.

Heart - Apex 5th space in nipple line. Mitral presystolic murmur. All sounds closed.

No lordosis.

Blood pressure - 122. 85.


2. S.G. 1016. Trace of albumin.

Urea concentration 2.5%.

Microscopically a fair number of pus cells. Some epithelial squames and transitional epithelial cells.

No casts or red blood cells seen.
Case 80. (Contd).

Case 81.

Girl 16 years.  S. N. 5 years ago.
65 days in Hospital.  Albuminuria 30 days.
Urine contained blood, granular casts and pus.

Heart - On admission a systolic mitral murmur, propagated to the axilla. Other sounds closed.

Has been well since discharge. No oedema, or headaches. Occasional precordial pain unassociated with exertion.

Heart - Apex beat forcible, inside nipple line.

Harsh mitral systolic murmur, propagated to the axilla. Pulmonary second sound accentuated. No evidence of stenosis. Other sounds closed.

Blood pressure - 120. 84.
Case 81. (Contd).

Urine - Specimen 1. S.G. 1025. Acid. Trace of albumin. A few pus cells. No casts or red blood cells seen.


Urea concentration 3%.

Remarks - Mitral systolic murmur persisting. No history of rheumatism. Renal function and blood pressure normal.
Case 82.

Girl 13 years. S. M. 9 years ago.
39 days in Hospital. Albuminuria on admission and for 13 days.

Has been well since. Never off school and no other illness.

Heart - normal.

Blood pressure - 110. 75.


Urea concentration 4%.

Remarks - Renal and cardio vascular systems normal.
Case 83.

Boy 14 years. S. N. 10 years ago.
74 days in Hospital. Albuminuria 20 days.
Urine contained blood.
Heart - soft mitral systolic murmur, but no cardiac enlargement.

Has been well since. Is a message boy.
No other illness.

Heart - normal.
Blood pressure - 110. 70.

Urine - Specimen 1. S.G. 1014. Albumin free.
2. S.G. 1010. Albumin free.

Urea concentration 3.0%.

Remarks - Renal and cardio vascular systems are unaffected.
Case 84.

Girl 12 years. S. N. 7 years ago.
84 days in Hospital. Albuminuria 26 days. No blood.
Arthritis wrists.

Never off school and no other illness.

Heart - normal.

Blood pressure - 114. 74.

Urine - Specimen 1. S.G. 1024. Albumin free.

Urea concentration 2.85%.

Remarks - Renal and cardio vascular systems normal.
The Most Important Facts are Summarized as Follows:

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<th>Days in Alb.</th>
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Table 1. (Contd).

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<tr>
<td>77</td>
<td>13</td>
<td>3</td>
<td>90</td>
<td>?</td>
<td></td>
<td>3.9</td>
<td>110.86</td>
<td>B.P. normal.</td>
</tr>
<tr>
<td>78</td>
<td>13</td>
<td>4</td>
<td>59</td>
<td>16</td>
<td>+</td>
<td>3.4</td>
<td>140.100</td>
<td>Renal calculus?</td>
</tr>
<tr>
<td>79</td>
<td>7</td>
<td>2</td>
<td>55</td>
<td>10</td>
<td>-</td>
<td>3.1</td>
<td>98.82</td>
<td>No abnormality.</td>
</tr>
<tr>
<td>80</td>
<td>12</td>
<td>7</td>
<td>35</td>
<td>15</td>
<td>0.A.</td>
<td>2.5</td>
<td>122.85</td>
<td>B.P. normal.</td>
</tr>
<tr>
<td>Case</td>
<td>Age</td>
<td>Years since S.N.</td>
<td>Days in Hosp.</td>
<td>Days Alb.</td>
<td>Alb.</td>
<td>Urea Conc.</td>
<td>B. P.</td>
<td>Remarks</td>
</tr>
<tr>
<td>------</td>
<td>-----</td>
<td>------------------</td>
<td>---------------</td>
<td>-----------</td>
<td>------</td>
<td>------------</td>
<td>-------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>81.</td>
<td>16</td>
<td>5</td>
<td>65</td>
<td>30</td>
<td>+</td>
<td>3</td>
<td>120.84</td>
<td>persistant mitral systolic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>murmur.</td>
</tr>
<tr>
<td>82.</td>
<td>13</td>
<td>9</td>
<td>39</td>
<td>13+</td>
<td>-</td>
<td>4</td>
<td>110.75</td>
<td>No abnormality.</td>
</tr>
<tr>
<td>83.</td>
<td>14</td>
<td>10</td>
<td>74</td>
<td>20</td>
<td>-</td>
<td>3.05</td>
<td>110.70</td>
<td>Cardiac recovery.</td>
</tr>
<tr>
<td>84.</td>
<td>12</td>
<td>7</td>
<td>84</td>
<td>26</td>
<td>-</td>
<td>2.85</td>
<td>114.75</td>
<td>No abnormality.</td>
</tr>
</tbody>
</table>
DISCUSSION.
Chapter VI.

DISCUSSION.

The Incidence and Death Rate of Scarletinal Nephritis for the Last Nine Years, Compared with the Incidence of Late Effects.

The incidence of nephritis as a sequel of scarlet fever, varies in different years and in different epidemics. It is usually very much higher on the Continent and in Denmark than in Great Britain. Koch 72 quotes incidence up to as high as 60%. The incidence also appears on the whole to be somewhat higher in Scotland than in England. In a series
of 4,436 cases of scarlet fever admitted to the Edinburgh City Hospital, the incidence of nephritis and late albuminuria taken together was 11.02%, although in the next series of 3,172 cases it had fallen to 5.64%. In England, of 7,209 M.A.B. cases between 1900-1909 there was an incidence of 4.68%.

The incidence and death rates for the years covered by this investigation is low and is as follows:

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence</th>
<th>Hospital D.R. from</th>
<th>scarlet fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1919</td>
<td>1.4</td>
<td>2.4%</td>
<td></td>
</tr>
<tr>
<td>1920</td>
<td>1.6</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>1921</td>
<td>1.3</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>1922</td>
<td>2.1</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>1923</td>
<td>4.6</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td>1924</td>
<td>4.9</td>
<td>4.18</td>
<td></td>
</tr>
<tr>
<td>1925</td>
<td>4.5</td>
<td>3.14</td>
<td></td>
</tr>
<tr>
<td>1926</td>
<td>3.2</td>
<td>1.99</td>
<td></td>
</tr>
<tr>
<td>1927</td>
<td>1.8</td>
<td>1.14</td>
<td></td>
</tr>
</tbody>
</table>

It is of interest that the severity of the original attack of scarlet fever appears to play little, if any, part in determining the occurrence of nephritis.
Indeed a study of a large number of cases shows that the most fatal cases are often those which follow an attack of scarlet fever, so apparently mild that it was overlooked. Nor, once the nephritis is established, has the amount or duration of albumin and blood present in the urine, as much influence on the prognosis as might be expected.

Ker 73 has seen patients die who at no time had more than a trace of albumin in the urine, while on the other hand patients recovered even when their urine solidified on boiling. And in his experience some of the worst cases showed no blood in the urine.

Price 74 and Osler and McCrae 75 both consider on the other hand that the more severe the attack, the more probability there is of kidney injury.

Weaver 76 says that nephritis with uraemia is most apt to occur in the less severe cases, and often in the mildest.

If in this series one takes the duration of albuminuria during the nephritis, one finds that the
average for cases showing later no cardiovascular or renal abnormality is twenty-one days. Whereas the average for those showing some abnormality is only twenty-six days.

Those cases admitted comatose and taking fits, and the cases with prolonged pyrexia and other evidence of severe infection do not show a higher incidence of late effects.

A comparison of the incidence of abnormalities with the yearly death rate from scarlet fever is as follows:

<table>
<thead>
<tr>
<th>Year</th>
<th>Death rate</th>
<th>Cases showing any abnormality</th>
<th>Albumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1919</td>
<td>2.4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>1920</td>
<td>0.8</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>1921</td>
<td>2.1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>1922</td>
<td>1.9</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>1923</td>
<td>5.2</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>1924</td>
<td>4.13</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>1925</td>
<td>3.14</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>1926</td>
<td>1.99</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1927</td>
<td>1.14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A study of these cases therefore confirms the view that there is no relation between the severity of the attack of nephritis and the incidence of subsequent abnormalities.
The eighty-four cases are reviewed by being placed into the following groups.

**GROUP I.**

**Cardiac Lesions.**

This Group consists of sixteen cases showing either cardiac enlargement, or murmurs, or both. Six cases Nos. 16, 26, 27, 55, 58, 76, show simply a slight cardiac enlargement without any valvular lesion, and of these, four have blood pressures above the normal range.

Ten cases, Nos. 33, 35, 75, 1, 2, 15, 17, 38, 44, 80, have various valvular lesions. Three have mitral presystolic murmurs, with a history of rheumatic joint pains in one. And seven have systolic mitral murmurs.

A consideration of a possible relation between these findings and the scarletinal infection
is rendered difficult and almost impossible by several factors. The great majority of these children are at the age when slight relative mitral incompetence is not uncommon. They are not of the social class in which any reliance can be placed on the absence of a history of mild rheumatic infections, and in most cases, there is no note of the cardiac condition during the attack of scarlet fever, although this does not exclude the possibility of a minor lesion having been present. In seventeen cases, however, there is a note of the cardiac condition during the scarlet fever. One had a presystolic mitral murmur which has persisted. Sixteen had had mitral systolic murmurs during scarlet fever. In twelve there is now complete recovery, but in four the murmur has persisted.

Simple endocarditis is of course not uncommon in acute nephritis and it is not easy to say whether the apical systolic murmur so often heard signifies a valvular lesion or not. The knowledge that it was absent before the nephritis, and of its
persistence after convalescence with signs of cardiac enlargement, may alone decide that the murmur indicated an organic lesion.

We agree with Wells who finds no support for the view that scarlet fever is a frequent cause of valvular disease. As he points out, scarlet fever is not infrequently followed by a fever bearing a close resemblance to rheumatic fever.

**GROUP II.**

Consists of four cases, Nos. 20, 36, 67, and 78.

Number 20 died six months after discharge from hospital.

Number 36 has a history of nephritis before scarlet fever.

Number 67 had encephalitis lethargica after being discharged.

Number 78 gives a history suggesting the presence of a renal calculus.

On account of the various factors present
in these cases, they have been excluded from the discussion. This leaves eighty cases.

**GROUP III.**

Thirty-eight cases showing no abnormality of urinary contents, of renal efficiency, of the blood pressure, or of cardiac abnormality.

Cases - 5, 7, 9, 10, 18, 21, 22, 31, 32, 34, 35, 37, 39, 41, 42, 43, 45, 47, 48, 49, 50, 52, 54, 57, 59, 61, 62, 63, 64, 65, 66, 67, 71, 75, 79, 82, 83, 84.

Several cases are included in this Group, which present either some cardiac abnormality known to be antecedent to the scarletinal nephritis, or a slight cardiac enlargement not uncommon in individuals of this age, and therefore probably having no relation to the nephritis.

A consideration of this Group raises only one question — whether a nephritis can exist without
albuminuria.

Chronic parenchymatous nephritis without albuminuria is said to have been met with, but if this is so, it is so rare that it need not be considered; and other quite definite symptoms are always present.

In chronic interstitial nephritis, however, there is frequently a temporary absence of albuminuria, but here again easily recognisable symptoms are always present after the condition has existed for any length of time.

About this Group, showing no signs of renal or cardiovascular abnormality, one can say that they are clinically healthy, and in view of the length of time since the original infection, we conclude that they run no further risk of renal or cardiovascular changes occurring.

GROUP IV.

Cases with Albuminuria.

Of the eighty cases, all of whom except
one, were discharged from hospital albumin free, twenty-one are now passing albumin.

Cases - 4, 11, 12, 14, 16, 26, 29, 30, 38, 46, 53, 55, 56, 60, 70, 72, 73, 74, 76, 78, and 81.

This number does not include those with albuminuria of an orthostatic nature. Table 4 shows the numbers falling in each yearly period since the scarletinal nephritis.

<table>
<thead>
<tr>
<th>Years after S.N.</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

The term albumin includes a group of substances related to each other though differing
in constitution and properties. A number of proteins may be found in the urine among which are serum albumin, serum globulin, nucleo albumin, haemoglobin and others, but the chief clinical interest centres around serum albumin, which is frequently combined with serum globulin, and by the term albuminuria is usually meant the presence of these bodies in the urine without regard to the possibility of the presence of other proteins.

The presence of albumin in any appreciable amount must always be regarded as a pathological phenomenon, although it does not necessarily mean the presence of renal trouble. Even a comparatively large amount may exist without any kidney lesion whatever, and it is a grave mistake, which is now fully realised, to conclude that a nephritis must exist because albumin has been found. In 1876, Cormack wrote "It is to be regretted that albuminuric urine is still so much spoken of as specially diagnostic of renal disease, as it leads to errors in practice".
McLean found in 50,000 healthy soldiers albumin in the morning urine of 6%, and casts in 2%.

On the other hand a nephritis may exist and yet albumin be found in such minute quantities as often to escape detection entirely. This is sometimes the case in cirrhosis of the kidney where a large amount of albumin is rarely seen, and may be entirely absent. Hartman found that in cases of nephritis experimentally produced in dogs by X-ray applications, the urine may be free of albumin and casts, while all other tests indicate severe kidney insufficiency. And MacNider found that the amount of albumin in the urine gave no index to the severity of the disease or to the degree of functional disturbance.

Barringer examined twenty men who had been found to have albuminuria ten years before when examined for life insurance. None of them had a chronic nephritis as far as could be judged from the condition of the heart, blood pressure and urine.
Eight were still passing albumin, and four had, in addition, casts.

Of thirty men who ten years before had both albumin and casts in the urine, one had a chronic interstitial nephritis, while two were doubtful. In eighteen the urine had become normal, and nine were still passing albumin and casts. The investigator concluded that it is the exception for albuminuria without casts to be a symptom of incipient chronic nephritis.

In trying to assess the significance of the presence of albumin in the urine, we should consider what is the change, if any, which the glomerular endothelium and the capsular epithelium undergo that they allow a portion of the plasma proteins to filter through. In actual inflammatory conditions such as in nephritis, the capsular and glomerular epithelium is either directly damaged by bacteria or their toxins, and in the diffuse nephritis there is in addition an obstruction to the blood flow. Insufficient blood supply results in insufficient oxygen supply to the glomerular and capsular
epithelium causing deficient cellular respiration. In passive congestion and in cirrhosis of the kidney, insufficient blood supply is also the cause of injury to the glomerular, and capsular epithelium.

In cachectic states and in anaemia the diminished oxygen supply is probably the chief cause of injury. In febrile albuminuria there may be several factors such as the toxin of the primary disease, the temperature itself, and probably also a deficiency in the oxygen supply. In general convulsions, a sudden temporary cessation of respiration is sufficient to cause a temporary deficiency in the supply of oxygen to the glomerular and capsular epithelium.

Albuminuria can be induced experimentally by compressing the renal artery or vein, and in this case the protein is first seen in the capsule. On the way down in the lumen of the tubules, as the urine becomes concentrated, and increasingly acid, some of the protein is solidified as hyaline and granular casts.
Clinically, this passive congestion of the kidney is seen in disease of the lungs and heart, and the trace of albumin, and the occasional cast may be of great importance as an expression of the cardiovascular disease, but not as an indication of renal inefficiency. In none of the investigated cases could the albuminuria be due to any cardiac disease.

Changes in the composition of the blood, such as is seen in extreme anaemia, tuberculosis, malaria, leukaemia, pyaemia, etc., when no lesions of the kidney can be discovered, will cause the appearance of albumin.

Another type of albuminuria, the so-called orthostatic or postural albuminuria is not infrequently the cause of albumin being found in the urine. As it is most frequently seen in young persons, it is of special importance in this series of cases and is therefore discussed separately.

It is thought that the albuminous escape through the kidneys is via the glomeruli. It would be expected therefore that there would be some parallelism between the occurrence of albuminuria and
the presence of glomerular disease. Batty Shaw however found no such parallelism. In cases which were free from such a complication as valvular disease of the heart which might be considered to be the cause of the albuminuria, the percentage of functioning glomeruli was found post mortem to range from 85 to 98; whereas in cases who had only intermittent albuminuria the percentage of functioning glomeruli was much lower.

It is doubtful therefore whether the physical state of the glomeruli as determined by the microscope gives any clue which may be relied upon in the explanation of the passage or not of albumin during life. It may be objected that the glomeruli may look normal and yet be in such a state of functional disturbance as to allow albumin to pass. If this is so, it cannot be claimed that if albumin escapes through the glomeruli, the objective condition of these bodies is necessarily such as to account for the abnormality. It seems reasonable to suppose that in all cases of true, renal, albuminuria,
the causal fault is a substance, which may allow the glomeruli to appear to be normal, or to be gravely damaged, such substances being brought to the glomeruli in sufficient strength and quantity to be capable of exerting a temporary and functional, or permanent and objective effect.

The manner in which albuminuria is produced is therefore essentially the same in every case, namely by disturbances in cellular respiration possibly with a relatively acid state in the cells of the kidney. The importance of the acid state of the kidney cells has been pointed out by Fischer. It has been assumed that in orthostatic albuminuria, the lordosis of the lumbar spine results in the venous stasis responsible for the albuminuria.

If any of the factors referred to operate for a sufficiently long period, then changes in the tubules may occur. These changes consist of swelling, fatty and hyaline degeneration and desquamation of cells forming casts. It was thought that casts were produced simply by the coagulation
of the albumin filtered through the capsule, the
supposition being based upon the fact that the pres-
ence of casts in the urine depends on the admixture
of albumin, and the more abundant the albumin, the
more likely it is that casts are present. They
probably are the products of the albuminous exudation
from the blood vessels with the addition of the
swollen and destroyed epithelia.

Having excluded the possibility of the
albuminuria in these cases being an extra renal or
accidental albuminuria, we divide this group into
the following four sub-groups.

Sub-group 1. Cases with albuminuria but with no
  cardio vascular change, and with renal
efficiency tests normal.
Cases – 14, 30, 53, 72, 81, 73, 26, 38, 46, 4.
  (11 cases).

Sub-group 2. Cases with albuminuria, with an abnor-
  mal condition of the cardio vascular
  system, but with normal renal efficiency
tests.
Cases – 78, 11, 16, 76, 12. (5 cases).
Sub-group 3. Cases with albuminuria. With the cardio vascular system normal, but with abnormal renal efficiency tests.

Cases - 29, 70. (2 cases).

Sub-group 4. Cases with albuminuria and both cardio vascular and renal function abnormalities.

Cases - 55, 60, 74. (3 cases).

**SUB-GROUP I.**

Eleven cases with albuminuria, but with no cardio vascular change, and with the renal efficiency tests normal. Of these five were passing traces of pus (3 girls and 2 boys), one urine contained casts, and one both casts and pus.

The existence of non-functional albumin or casts, or both, in a urine, merely indicates that the renal parenchyma has been damaged. Although it is probable that a diminished oxygen supply is
the cause of albumin reaching the tubules, we certainly have no knowledge as to what anatomical condition of the kidney corresponds to this albuminuria. And if the amount excreted remains stationary, one can only presume that any alteration is also stationary, and not progressive. There is no logical reason why even an early interstitial nephritis may not remain stationary - that is, that complete healing may not occur and end in fibrosis, just as any other inflammatory process does. The persistence of an albuminuria after an attack of acute nephritis is not even necessarily an indication that the disease has become chronic. Most patients recover completely from the acute lesion and enjoy perfect health, yet they may pass albumin for the rest of their lives.

Ernberg 85 says, "If there are no signs of progressive nephritis, these cases of continuance of albuminuria, are benign".

v. Noorden 86 considers these albuminurias when unaccompanied by signs of a progressive nephritis/
nephritis to be of good prognosis. "They are the expression of a stationary process".

Our conception of these cases is that when for years, even decades, they enjoy perfect health, and when above all, they show no trace of cardiovascular abnormality of any kind, one is not justified in regarding them with grave suspicion.

In accordance with the general law, that an organ which is not completely normal, is more exposed to the risk of subsequent infection than the normal organ, one might consider whether the normal degenerative processes incident to old age, may not first manifest themselves in the organs damaged in youth. That this is not an idle speculation is shown by the fact that individuals passing even only small quantities of albumin are not first class lives from a Life Insurance actuarial standpoint.

In our opinion, the most we are prepared to say regarding this Group is that they probably have a less amount of healthy parenchyma left. That they have in other words lost a fraction of the very large safety factor, but as regards an eventual
termination in chronic nephritis they are "not proven".

SUB-GROUP II.

Five cases with albuminuria, with some abnormal condition of the cardio vascular system, but with normal renal efficiency tests.

Of these, one has a blood pressure below the normal range. (Case 11 — a girl of 13 with a systolic reading of 82 and a diastolic of 48). Four have blood pressures above normal, varying in degree from Case 12, with a systolic blood pressure within normal range and a diastolic just above normal, to Case 16; (a girl of 14 with a reading 145. 110.), and Case 78; ( boy of 13 with 140. 100).

Of these four cases, three have cardiac enlargement; only Case 12, — with the least variation from normal blood pressure — has the left border of the heart inside the nipple line.
On account of the definite cardio vascular abnormalities, this Group of cases is to be less favourably regarded than those in Sub-group I, and the possible explanation of the hypertension is discussed later, when the cases are reviewed from the standpoint of abnormalities of blood pressure.

SUB-GROUP III.

Two cases with albuminuria, with the cardio vascular system normal, but with abnormal renal efficiency tests.

Case 29; has a urea concentration and a water test, both of which are below normal, and of doubtful significance. The variability of specific gravity (from 1002 - 1022) is normal, but the amount excreted is if anything, low, while the urea concentration is only 1.8%.

Case 70 has a still less normal water test, the quantity being only 285, with a specific gravity varying from 1012-1022 and a urea concentration of
In view of the normal cardiovascular conditions it is difficult to assess the findings. They are definitely under suspicion, but only a progression of the abnormalities after a further period of years would justify us in considering them as cases of chronic nephritis.

**SUB-GROUP IV.**

Three cases with albuminuria and both cardiovascular and renal function abnormal.

Case 55 is a typical chronic parenchymatous nephritis, with both urea concentration and water tests abnormal, with a slightly raised blood pressure, and with raised retention products in the blood.

Case 74 has never been well since discharge from hospital, has a history of oedema, has a raised blood pressure, and impaired renal function, and is also an early chronic parenchymatous nephritis.
Case 60 - a girl of 15, with a fairly normal water excretion, but with a urea concentration test of 1.6% and repeated 1.25%. The blood pressure is slightly below the normal, but she gives a definite history of oedema. We regard this case as an incipient chronic parenchymatous nephritis.

We regard Cases 60, and 74 as being early, and Case 55 as being an advanced case of chronic parenchymatous nephritis.
Of the thirty-six cases passing albumin of all kinds, nineteen also were passing pus in varying amount. Of the nineteen, six were boys and thirteen girls. Five of the orthostatics contained pus, three girls and two boys.

Whenever pus corpuscles are present in the urine even in small numbers, an abnormal condition exists somewhere in the genito-urinary tract. If they are very scanty this condition is not necessarily an inflammation though there is undoubtedly an irritation in some portion of the tract.

It is not possible to assess the significance of pus in the thirteen girls except in Cases 55 and 70. Both have a definite chronic parenchymatous nephritis.

Of the boys, No. 78 appears to have a renal calculus, and No. 36 has a history of previous nephritis. In the case of the other four boys
we interpret the presence of pus as indicating a continuance of an irritation, probably in the pelvis of the kidney, originating with the original infection.

Functional tests do not show the kidney function to be impaired, but it is assumed that these kidneys are more exposed to attack from other sources of infection, than healthy kidneys.
Orthostatic Albuminuria.

As fifteen patients of those examined showed this phenomenon, its nature and significance must be considered, and in particular the relationship, if any, between it and scarletinal nephritis. It is of particular importance to understand the significance of this condition as the great majority of the examined individuals were of the age when it is most likely to be present.

The facts regarding the condition are well known. The albumin is only to be found when the patient is up and about. So long as he remains in bed, or even lying down, it is absent. In most cases it appears immediately on rising, but in some its appearance is delayed, and the amount of albumin is not influenced by taking food or by exercises. If
If exercise has any effect, it would appear rather to diminish the loss of albumin. (Weise 87). Weise treated forty-nine children with orthostatic albuminuria by means of crawling exercises daily — by which means the lumbar lordosis was reduced — and claimed a cure for the condition in 89.9%.

Clinical observation shows that the condition is most often seen in young individuals of rather a distinctive type. Their general physique is below par and they are pale, narrow chested, and of poor musculature — in other words, the asthenic type. They complain in many instances of lassitude, headaches, attacks of giddiness and even of mild syncopal attacks, and of such circulatory disturbances as "dead fingers", etc. The pulse is usually markedly labile, and systolic apical murmurs are frequently present.

The incidence of the condition varies widely according to age. Steiskal 88 found that normally 77% of his cases occurred in children under ten.
Hansborg found it present in 8.8% of 114 boys and 11.6% in 112 girls and he quotes Svensson whose figures are 10.2% in 928 boys and 11.5% in 165 girls between the ages of six and twenty. He also quotes Petterson and Martius who found it in 25 and 28% respectively.

Jehle examined 223 children up to the age of fourteen years and found the incidence to be as high as 39% - 41% for boys and 37.4% for girls. He found the incidence for the age period 0 - 6 years 2.8%, 7 - 10 years 19.8% and 11 - 14 years 64.2%.

He also refers to several cases in which a familial tendency seemed apparent.

Weiss Eder also records a familial tendency. In twenty-three cases of orthostatic albuminuria, she found four pairs of brothers and sisters.

Reyher found an average percentage of twelve, but he adds that if one includes children with latent tuberculosis, the incidence rises to 60%.
Norman 96 examined the urines of 1787 boys between the ages of seven and fifteen, and found albumin present in 22.6% at the age of twelve, and 33.7% at fourteen years.

Bashford 97 found albumin which disappeared in an after rest specimen in about 1 in every 20 young male adolescents.

Although none of the authors quoted make any reference to it, it is obvious that unless one is certain that the bladder was emptied before the child went to bed, there exists the possibility of a fallacy occurring. If an orthostatic albuminuria is present, and the bladder not emptied last thing at night, then the morning urine taken before the child rises, will contain traces of albumin. It will rather than almost certainly be regarded as being a true albuminuria than a postural one.

Provision was made in our printed instructions that the possibility of this fallacy should not occur.

A great variety of views regarding the
aetiology of this condition has been promulgated. Some authors regard it simply as an exaggeration of the physiological albuminuria, while others consider it a definitely pathological state either with or without a lesion of the kidneys.

**Heubner**\(^98\) considers it in many cases a pretuberculous condition — partly on account of the general appearance of the patients, and partly from the few cases which have been examined post mortem, in which active tuberculous foci have been found.

**Fischer**\(^99\) says that many of these cases are undiagnosed cases of cardiac insufficiency — that although when at rest they may not show any urinary abnormality, albumin immediately appears as a result of the increased work incident to mere maintenance of the up-right position. It is also suggested that the blood of an anaemic individual may supply his kidneys when at rest in bed with enough oxygen to keep his urine albumin free, and prove
inadequate when he assumes the erect posture with its increased need for oxygen.

Engel 100 considers that neither the circulation, the blood pressure nor purely hydrostatic changes play any part in the condition, but that the "vital forces" of the parenchyma cells are not equal to the strain of performing normal excretion. That is due to a "Juvenilität der Nierenzellen" which are only able to function normally in the resting state.

v. Noorden 101 adheres to his original view, that the albuminuria is due to a metabolic anomaly, causing a degenerative alteration of the blood proteins and suggests the name of "diabetes albuminosus". He adds that an additional factor may be local circulatory changes in the kidney.

Porges and Pribram 102 say that in all probability the cause is constriction or spasm of the renal arteries, and refer to the fact that experimentally constriction of the blood supply results in albuminuria. They definitely disagree
with the view that an abnormally low blood pressure is a causal factor.

The most exhaustive study on the question of the etiology of orthostatic albuminuria is that of Jehle. He found that no alteration in blood pressure had any effect on the excretion of the albumin, but that the condition was due to an exaggeration of the normal degree of lumbar lordosis. He demonstrated that the children with this marked lordosis excreted albumin only when standing, but in lesser amounts or not at all when walking or running. The largest amount of albumin was while kneeling, in which position the lordosis is accentuated, and albumin ceased to appear, if while kneeling, the child sat on its heels, in which position the lordosis is less marked.

He also succeeded in making healthy persons pass albumin by producing an artificial lordosis, and concludes that this mechanical factor, with the consequent disturbance in renal circulation, is the cause of the albuminuria. That the lordosis in
such children is the main, if not only factor, appeared to him conclusive from the fact that if such a child was immobilised in plaster, he would continue to pass albumin whether he stood or lay down.

These experiments have been verified by Nothmann, Bingel, Faludi, Langstein and others.

Norman after investigating 1787 cases concluded that no single factor will explain the aetiology of the condition but that vaso-motor insufficiency, posture, exertion, lordosis, and asthenia, seem to be the prevailing causes.

Bashford says that it is not definitely associated with any particular type of youth such as with a so-called nervous disposition, nor with lordosis, oxaluria or a history of scarlet fever.

As a point of interest in view of Jehle's reference to cases where a familial tendency was observed, he noted that his group of adolescent albuminurics produced between them fourteen sons who
had attained puberty. Two of these present the same condition as their fathers.

Bass and Wessler say that in a series of cases, it will be found that a considerable number show evidence of relative cardiovascular insufficiency. These symptoms are usually not associated with any hypertrophy or dilatation, but on the contrary the heart is in most cases smaller than usual. After making a fluoroscopic examination of the hearts of children after running up and down 150 steps they found that although the heart did not dilate after the exercise, a considerable number of them failed to become smaller — as should occur. They suggest that this failure to contract may perhaps be looked upon as a restriction of the cardiac response. In 30% of their cases they found hearts of the "Trophherz" type, with other stigmata of maldevelopment.

Steiskal says that the aetiology is multiple and includes, an anatomical inferiority of the kidneys, circulatory causes, prolapsed kidney,
metabolic abnormalities, and lordosis.

Russel 113 disagrees with the mechanical and anatomical explanation, and also with the view that the responsibility is primarily on the circulation—whether through cardiac weakness or abnormality or through some vaso-motor disturbance. He maintains that some undue renal permeability must be invoked before an adequate explanation can be arrived at. By the presence of a renal pathology, he does not suppose necessarily an established nephritis such as would be recognised post mortem, but he imagines something far short of that—some small and recoverable toxic assault on the kidney.

Fischl 114 agrees with Jehle in considering the lordosis of great importance, but he believes there is still another factor in the shape of a peculiar weakness of the kidney which permits the lordosis to cause albuminuria. Heubner 115 believes that a case may be classified as orthostatic albuminuria only if the presence of albuminuria conforms strictly to the posture of the child and if
formed elements are continuously absent. Other authors adhere to the belief that the appearance of casts signify the existence of a nephritis, and that therefore Jehle's contention that formed elements appear after artificial lordosis is true only because he was dealing with kidneys, the seat of previous inflammation.

Hooker 116 says, "There can be no doubt that this form of albuminuria may exist without the consequent assumption of pathological conditions in the kidney". He quotes Senator who says he is strongly convinced that a slight irritation or inflammatory condition which may progress towards recovery or towards a diffuse chronic nephritis is responsible for most, if not all the cases of ortho-static albuminuria. Hooker suggests that variations in the magnitude of the pulse pressure might influence the oxygen supply to the renal epithelium and so alter its functioning normally.

Pincherle 117 finds that although lordosis is an important factor, it will only cause albuminuria
in individuals predisposed to it by nephritis, recent infective disease and tuberculosis. He considers that lumbar lordosis is an efficient mechanical factor in the genesis of some forms of albuminuria, but that it does not as a rule act alone, nor in a purely physical manner, but requires to be associated with another important cause, namely the lessened resistance in the urinary apparatus.

Saito 118 found that orthostatic albuminurics have an asthenic constitution. About half of them show lordosis. Renal function as measured by the phenolsulphphthalein test is generally normal. Despite anaemia a vast majority of them have normal haemoglobin content of the blood. He thinks that the direct cause of the albuminuria may be lordosis of the lumbar spine. Albuminuria, however, does not occur merely with a lordosis, and vaso-motor instability is also thought to be a factor.

Bass 119 gives a very extensive literature from which it appears that every proposed causal factor has its adherents.
Broadly there are three main views on the aetiology of the condition. According to one group of writers, the explanation is mechanical or anatomical - usually to a lordosis or some other spinal deformity (such as lateral curvature causing the condition to exist in one kidney), which brings about a condition of circulatory stasis in the kidney in the upright position. The second group of writers maintain that whether or no lordosis or other anatomical peculiarity is immediately responsible for the appearance of the albuminuria, some undue renal permeability must be present. The third group places the responsibility primarily on the circulation, either cardiac weakness or abnormality or through some vaso-motor disturbance. But it is generally agreed that spinal position with its circulatory consequences is a factor in the production of the albuminuria.
The Relation of Orthostatic Albuminuria to Scarletinal Nephritis.

Views on the possibility of such a relationship vary in accordance with the authors' views on aetiology. Russell establishes the point that the postural phenomenon is common both to the supposedly functional cases and also to most, if not all, cases of nephritis. In other words, that orthostatic albuminuria is the mildest extreme of a nephritis. He brings forward evidence that many cases of purely orthostatic albuminuria are the result of infection, and suggests that in some cases it may be the outcome of a past scarletinal nephritis. He describes two cases of scarlet fever discharged with normal urine, who later developed an orthostatic albuminuria, and two cases of patients with orthostatic albuminuria, who had previously had scarletinal
nephritis.

He concludes not only that a scarletinal nephritis may eventually be represented by an orthostatic albuminuria, but that it may occur after an attack of scarlet fever in which the kidneys had not been affected.

Bashford 121 considers the persistence of the condition consistent with prospects of a perfectly normal life and physical efficiency. Of forty-one cases there was a history of scarlet fever in only three — and apparently no history of scarletinal nephritis in any. Thirty of these were re-examined after periods of from seven to fourteen years. All of them were in good health and only one had subsequently had scarlet fever.

Nothmann 122 found that orthostatic albuminuria sometimes occurred during convalescence from scarlet fever. These cases showed a quickly disappearing albuminuria which was orthostatic in character, and he presumes the condition was due to a very slight post scarletinal renal damage.
Arnberg 123 thinks there is no relation between scarletinal nephritis and orthostatic albuminuria, which he considers a condition sui generis. In thirty-two cases of scarletinal nephritis, none had orthostatic albuminuria and he concludes that the former does not predispose to the latter.

v. Noorden 124 points out that a chronic interstitial nephritis may sometimes begin with an albuminuria which is orthostatic in character.

Hansborg 125 found orthostatic albuminuria present in twenty-three out of 284 children who had had scarletinal nephritis. The condition seemed to bear no relation to the severity of the scarletinal nephritis as of the twenty-three, eighteen had a mild nephritis and only five a severe nephritis. Nineteen of the twenty-three were albumin free on discharge.

Examination of the twenty-three cases showed that ten showed nothing pathological except the albuminuria. They were all healthy, fresh
looking children and none had any marked accentuation of the lumbar lordosis. Seven were pale and thin and the general health was not good. One of these had symptoms of cardiac trouble.

He states that although his investigations do not help to solve the cause of the condition, they do show that there is no connection between it and scarlet fever.

Batty Shaw considers that the albuminuria of adolescence seems to be another example of how albuminuria depends on toxic bodies brought to the kidney in the blood stream, and not necessarily from the organic changes in the kidney. The glomerulo-tubular arrangement "leaks" albumin because the glomeruli are destroyed or damaged temporarily by the toxic action of the contents of the abnormal blood.

Weiss Eder is one of the few investigators who has studied the question of relationship between orthostatic albuminuria and scarlet fever.
She produced an artificial lordosis in children suffering from scarlet fever, continuing the lordosis for from ten to twenty-five minutes, and repeating the procedure at intervals of from two to seven days. Only those children were used, who in the non lordotic position showed no albuminuria.

Of forty children examined thus, twenty-three showed albuminuria and seventeen none. In none of the twenty-three cases did a nephritis follow. She concluded that children, who while convalescing from scarlet fever have orthostatic albuminuria, are not more disposed to nephritis than other children. That children who have recovered from scarlet fever often show a temporary orthostatic albuminuria which may be due to weakness of the back muscles, and that the condition can be produced in 57.5% of children convalescent from scarlet fever.
We would therefore classify albuminuria in apparently healthy young individuals into three classes.

1. Those who show albuminuria only during the day—strictly orthostatic albuminuria and including the greater number.

2. Those who show small amounts of albumin occasionally.

3. Those who show albuminuria in all specimens, day and night.

It is our belief that so-called orthostatic albuminuria is really a subhead of the albuminuria of adolescence, and that these types represent different grades of the same disturbance. At the mildest extreme is the typical orthostatic condition, where, either associated with or without lordosis, the strain involved by standing up is sufficient to cause albuminuria.

In two cases a slightly greater strain was necessary in that albumin appeared not one hour after
rising, but only in the second hour specimen.

Other healthy individuals only pass albumin after having been up some hours or after having walked a mile or two. Others again only pass albumin after strenuous exercise. We consider all these as mild conditions of the same renal defect.

At the other extreme is the person in good health and with normally functioning kidneys who passes a trace of albumin constantly.

This group is also divided into the following sub-groups.

**Sub-group 1.**

Cases with orthostatic albuminuria but with no abnormalities of the cardio vascular system or with renal function.

Cases - 6, 8, 19, 24, 40, 51, 77. (7 cases).

**Sub-group 2.**

Cases with orthostatic albuminuria but with some abnormality of the cardio vascular system, but with normal renal function.
Sub-group 3.

Cases with orthostatic albuminuria with cardiovascular system normal, but with impaired renal function.

Cases - none.

Sub-group 4.

Cases with orthostatic albuminuria and both cardiovascular and renal abnormalities.

Cases - none.

Of the seven cases of Sub-group 1, two showed definite accentuation of the lumbar lordosis, and only two were pale, badly developed children. One (Case 6), is a congenital syphilitic under treatment, and we suggest that this may constitute the "small, recoverable assault" on the kidney and be the cause of the condition. In two cases (24 and 31), the blood pressures, while within normal limits are below the average.
Of Sub-group 2. —

Two cases (2 and 30), had mitral presystolic murmurs.
Two cases (13 and 27), had slight cardiac enlargement.
Two cases (17 and 69), have definite hypotension while two (Cases 2 and 23), have blood pressure above the normal range.

Only one (Case 17) had an abnormal lordosis.
Two (Cases 17, and 44), were anaemic with haemic cardiac murmurs.

It will be noted that in Case 17, the three possible factors, anaemia, hypotension, and lordosis are present.

Case 27 is almost certainly a tuberculous child, and in this case the albumin appeared not in the first hour after rising, but only in the second.

The occurrence of orthostatic albuminuria in this Group of fifteen cases may have several explanations.

Its occurrence may be a coincidence — all these cases may have had orthostatic albuminuria before contracting scarletinal nephritis. We have
117 children of similar ages, and of the same social status with the test carried out in the same manner in our own practice and find the condition present in %.

In this series the percentage is 10%. We conclude therefore that although the condition may have been present in an unknown number of these cases, mere coincidence does not explain such a high incidence.

It may be argued that any children after an illness in bed may show the condition for some time as a protect of the kidneys resuming work under harder conditions. But our cases show that the condition has persisted for periods up to nine years.

All factors such as anaemia, slight cardiac lesions, lordosis, hypotension and hypertension, enter into these cases, either singly or in conjunction, but none predominantly. Cases No. 6 having antisyphilitic treatment, No. 27 - possibly tuberculous, Nos. 13 and 69 both with a history of oedema suggesting extensive original renal involvement, all fulfill
the "recoverable assault on the kidney" as postulated by Russell.

The incidence of scarlatinal nephritis over the period in which our cases occurred, was highest in 1924 and 1925 (4.9% and 4.5%). Thirty-three and one third per cent of our cases of orthostatic albuminuria are in children who had nephritis in those years.

This investigation therefore, throws no new light on the aetiology of orthostatic albuminuria, but we suggest in view of our findings, that many of these cases may be directly attributable to the original kidney infection — which would now probably show nothing abnormal post mortem.
Blood Pressure.

In considering the blood pressures shown by these children, the literature was consulted so that a normal for children of various ages might be arrived at. Dally,128.

Has drawn up the following table to represent standard arterial pressure at various ages for males of Medium physique.

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>up to 2</td>
<td>81</td>
<td>45</td>
</tr>
<tr>
<td>5</td>
<td>86</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>95</td>
<td>55</td>
</tr>
<tr>
<td>15</td>
<td>110</td>
<td>67</td>
</tr>
<tr>
<td>20</td>
<td>123</td>
<td>80</td>
</tr>
<tr>
<td>25</td>
<td>125</td>
<td>81</td>
</tr>
<tr>
<td>30</td>
<td>126</td>
<td>82</td>
</tr>
</tbody>
</table>

Judson and Nicholson,129, give the following standard.

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>91.8</td>
<td>65.6</td>
</tr>
<tr>
<td>4</td>
<td>91.6</td>
<td>64.9</td>
</tr>
<tr>
<td>5</td>
<td>91.3</td>
<td>64.4</td>
</tr>
<tr>
<td>6</td>
<td>92.6</td>
<td>67.3</td>
</tr>
<tr>
<td>7</td>
<td>94.0</td>
<td>66.3</td>
</tr>
<tr>
<td>8</td>
<td>93.6</td>
<td>64.7</td>
</tr>
<tr>
<td>9</td>
<td>94.3</td>
<td>71.0</td>
</tr>
<tr>
<td>10</td>
<td>99.2</td>
<td>67.1</td>
</tr>
<tr>
<td>11</td>
<td>97.1</td>
<td>65.5</td>
</tr>
<tr>
<td>12</td>
<td>102.3</td>
<td>65.2</td>
</tr>
<tr>
<td>13</td>
<td>103.6</td>
<td>70.5</td>
</tr>
<tr>
<td>14</td>
<td>106.1</td>
<td>67.4</td>
</tr>
<tr>
<td>15</td>
<td>105.6</td>
<td>67.5</td>
</tr>
<tr>
<td>16</td>
<td>117</td>
<td>74</td>
</tr>
<tr>
<td>17</td>
<td>118</td>
<td>75</td>
</tr>
<tr>
<td>18</td>
<td>119</td>
<td>76</td>
</tr>
<tr>
<td>19</td>
<td>120</td>
<td>76</td>
</tr>
</tbody>
</table>
Gundobin, 130, gives the average systolic figures of 600 children.

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>82.7</td>
</tr>
<tr>
<td>3</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>84.5</td>
</tr>
<tr>
<td>9</td>
<td>95.4</td>
</tr>
<tr>
<td>10</td>
<td>86.5</td>
</tr>
<tr>
<td>11</td>
<td>90.9</td>
</tr>
<tr>
<td>12</td>
<td>104.8</td>
</tr>
<tr>
<td>13</td>
<td>108.5</td>
</tr>
<tr>
<td>14</td>
<td>108.8</td>
</tr>
<tr>
<td>15</td>
<td>116</td>
</tr>
</tbody>
</table>

Still, 131, 1927 gives the normal systolic pressure at 84 for 7 years and about 100 for 12 years. Melvin and Murray give the following average readings from children with no evidence of circulatory disease.

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>112</td>
<td>75</td>
</tr>
<tr>
<td>10</td>
<td>108</td>
<td>80</td>
</tr>
<tr>
<td>12</td>
<td>102</td>
<td>78</td>
</tr>
<tr>
<td>14</td>
<td>108</td>
<td>78</td>
</tr>
</tbody>
</table>

Salle, 132. In referring to the variations due to age, sex and size says that there are considerable variations in the normal for each age but that there is no appreciable difference between the figures for boys and girls. Although abnormally large children generally give higher readings, yet this is not always the case. He found the Blood pressure in all cases of orthostatic albuminuria to be normal.

Alvarez, 133.

Found that hypertension is not a disease of old
Age alone. Taking 140 as the highest limit of normality, he found in College students between 17 and 21, that 18-26% of males had a Systolic Blood pressure above 140, and from 35-57% above 130.

Alvarez's figures are 127 at 16 years and 118 at 30 for Males, and 118 at 16 years and 111 at 24 for Females.

A consideration of these figures shows that there is not yet a suitable and reliable standard which will define with any accuracy the limits of normal tension and of pathological hypotension or hypertension. Many authors supply us with averages but averages are of little value unless they are supplemented by standards of normal deviation from the average.

Measurement of blood pressure will always deviate to some extent from the average, and although there are a number of figures given as being of "normal range", it is very difficult to find any two clinicians to agree on the exact limits.

There is of course no difficulty in classifying as normal those readings which are near the average, or as abnormal those which deviate widely from the normal. Our difficulty lies in assessing the significance of the intermediate zone of pressures, between the certainly normal, and the certainly abnormal.

We have therefore adopted the Method of Faber & James, which has the advantage of easy applicabil-
ility and appears to give the best indication of what may be considered definitely normal or definitely abnormal. They point out that if the blood pressure of a large series of normal cases are taken, the majority will be found to occur at as near the average pressure of the whole group, and that at levels of pressure more distant from the average, a smaller number of cases occur. And that if the distribution of such a series is plotted, the curve will approximate in form to a curve of Mathematical probability.

Clinically, it is clear that the nearer a patient's pressure is to the average of all normal individuals, the greater are the chances that his pressure is normal, and conversely, the greater his deviations from the average, the greater the chances that his pressure is abnormal, and the smaller the chances that his pressure is normal.

In the mathematical statistical method used by them, the proportions and chances referred to are determined by the use of a Measure of deviation from the average, known as the Standard Deviation.

By dividing the deviation of a given measurement from the average, by the standard deviation, a quotient is obtained - the deviation index. The deviation index bears a definite relation to the normal and appears to have an important clinical value in defining the significance of individual variations from the average and also in determining the normal and
abnormal range. It is stated that a deviation index of less than 1 is certainly normal, while deviations of more than 3 are almost certainly abnormal, while between these two limits there is a doubtful zone where measurements may occur in both normal and abnormal cases.

Table 5 gives the average, and the standard deviation for the ages of 4 to 16 for the Systolic pressure, and Table 6 for the diastolic.

Table 5. Systolic.

<table>
<thead>
<tr>
<th>Age</th>
<th>Boys &amp; Girls Average</th>
<th>Standard Deviation.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Boys</td>
</tr>
<tr>
<td>4</td>
<td>89</td>
<td>5.5</td>
</tr>
<tr>
<td>5</td>
<td>92</td>
<td>6.0</td>
</tr>
<tr>
<td>6</td>
<td>94</td>
<td>6.5</td>
</tr>
<tr>
<td>7</td>
<td>97</td>
<td>6.5</td>
</tr>
<tr>
<td>8</td>
<td>100</td>
<td>6.5</td>
</tr>
<tr>
<td>9</td>
<td>101</td>
<td>6.5</td>
</tr>
<tr>
<td>10</td>
<td>103</td>
<td>6.5</td>
</tr>
<tr>
<td>11</td>
<td>104</td>
<td>6.5</td>
</tr>
<tr>
<td>12</td>
<td>106</td>
<td>6.5</td>
</tr>
<tr>
<td>13</td>
<td>108</td>
<td>6.5</td>
</tr>
<tr>
<td>14</td>
<td>110</td>
<td>6.5</td>
</tr>
<tr>
<td>15</td>
<td>112</td>
<td>7.0</td>
</tr>
<tr>
<td>16</td>
<td>115</td>
<td>7.0</td>
</tr>
</tbody>
</table>
Table 6. Diastolic.

<table>
<thead>
<tr>
<th>Age</th>
<th>Boys &amp; Girls Average</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Boys.</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>7.0</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>7.5</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>7.5</td>
</tr>
<tr>
<td>7</td>
<td>65</td>
<td>7.5</td>
</tr>
<tr>
<td>8</td>
<td>67</td>
<td>7.0</td>
</tr>
<tr>
<td>9</td>
<td>68</td>
<td>6.5</td>
</tr>
<tr>
<td>10</td>
<td>69</td>
<td>6.0</td>
</tr>
<tr>
<td>11</td>
<td>70</td>
<td>5.5</td>
</tr>
<tr>
<td>12</td>
<td>71</td>
<td>5.0</td>
</tr>
<tr>
<td>13</td>
<td>72</td>
<td>5.0</td>
</tr>
<tr>
<td>14</td>
<td>73</td>
<td>5.0</td>
</tr>
<tr>
<td>15</td>
<td>75</td>
<td>5.5</td>
</tr>
<tr>
<td>16</td>
<td>76</td>
<td>6.0</td>
</tr>
</tbody>
</table>

These tables are used in the following manner.

Ex.1. A boy of 10 with a systolic pressure of 125.

\[
\frac{\text{Deviation from average}}{\text{Standard Deviation}} = \text{Deviation Index.}
\]

i.e. \[\frac{125-103}{6.5} = \frac{22}{6.5} = +3.3 \text{ D.I.}\]

It has been calculated that:

(a) Out of 1,000 normal cases more than 999 will have a smaller index.

(b) That less than 0.1% of normal cases have an index as large.

(c) That the chances that a given individual, if normal, will have an index as large are less than 1 in 2070.

By the definitions of the three zones, an index of 3 or over places the individual in the abnormal zone. So that this boy has a pathological hypertension.
Ex. 2. A boy of 10 with a systolic pressure 116.

\[
\frac{116 - 103}{6.5} = \frac{13}{6.5} = 2
\]

Which falls in the doubtful zone as only 2.3% of normal cases have an index less than this. It is not definitely pathological, unless so determined by other tests or symptoms.

Ex. 3. A girl of 10 with systolic pressure 96.

\[
\frac{103 - 96}{7} = 1
\]

Being within the normal limit.

We have applied this method to our cases. It will be seen that in some cases the systolic pressures appear to be abnormal while the diastolic readings fall within normal limits. As the diastolic pressure is the measure of the load which throughout life the arterial walls have continuously to support, we consider those cases which show a diastolic reading as being within normal limits, to be normal.

The blood pressures of our cases are tabulated in Table 7.
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>118.90</td>
<td>+2.7</td>
<td>+3.2</td>
<td>Abnormal</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
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<td>+3.2</td>
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This table may conveniently be divided as follows:

**Group (6).**

Cases with normal blood pressures:

4. 5. 6. 7. 8. 9. 10. 13. 14. 18. 19. 21. 22. 24. 26. 27. 29. 30. 31. 32. 33. 34. 35. 37. 38. 39. 40. 41. 42. 43. 44. 45. 46. 47. 48. 49. 50. 51. 52. 53. 54.
Subgroup (1) Cases with normal blood pressure and no urinary or renal abnormality. 38 Cases.

Subgroup (2) Cases with normal blood pressure and some urinary or renal abnormality. 25 Cases.

In 11 of these the only abnormality is an orthostatic albuminuria.

Group (7)
Cases with abnormal blood pressures.
Nos. 1. 2. 3. 11. 12. 15. 17. 23. 25. 28. 55. 58. 68. 69. 74. 76. 78. 17 Cases.

Subgroup (1). Cases of hypotension.
Nos. 11. 17. 25. 69. 4 Cases.

Subgroup (2). Cases of hypertension with some urinary or renal abnormality.
Cases 2. 12. 16. 23. 55. 74. 76. 7 Cases.

In 2 of these the only abnormality is an orthostatic albuminuria.

Subgroup (3). Cases of hypertension with no urinary or renal abnormality.
Cases 1. 3. 15. 28. 58. 68. 6 Cases.

Group 6.
The 38 cases showing no urinary or renal abnormality have already been discussed under the section dealing with albuminuria and are dismissed as
being normal in every respect.

Of the 25 cases, with normal blood pressure, but with some renal or urinary abnormality, in 11 this abnormality was simply an orthostatic albuminuria. This tends to confirm the view that orthostatic albuminuria is not always associated with hypotension.

Of the 14 cases with true albuminuria, 11 were merely passing small amounts of albumin, but were otherwise quite normal.

Two of these cases, however, need individual mention. Cases No. 29 and 70 had normal blood pressures, were passing albumin, pus, and casts and in addition showed varying degrees of renal function impairment.

These two cases certainly indicate, that impaired ability to concentrate is not necessarily accompanied by any changes of blood pressure.


Of the 4 cases of hypotension, two had orthostatic albuminuria, one a true albuminuria, and the other showed no other abnormality. Only one appeared to be robust and in perfect health. The others were pale, anaemic, badly developed children. The low arterial pressure in these cases is probably an "essential" or primary condition associated with a low vitality, and is in our opinion unrelated to any previous renal condition.
Cases showing hypertension pressures.

Much confusion of terminology occurs whenever the relations of renal to cardiovascular and cardiovascular to renal changes are discussed. Many different names are employed by numerous authors to describe conditions which are identical, or which overlap, some attacking the problem from biological and clinical stand-points, while others endeavour to solve it from a groundwork of morbid anatomy and pathology. Hartman, 135. As a result of nephritis experimentally produced in dogs, found that the kidney may be directly responsible for a certain group of hypertensives. Kylin, 136, says that all attempts to explain any hypertension secondary to kidney insufficiency are failures. Allbutt, 137, Lee, 138, and Von Monakow, 139, agree with this view, as they all find a large group of so called essential hypertensives, in which no kidney changes are found. Moschowitz, 140, and many others point out that when sclerosis of the renal vessels is found, it is only a part of a general arterial sclerosis. Romberg, 141, says "in every case where the maximum pressure is 160 or higher, kidney disease may be the cause, irrespective of the diastolic pressure." O'Hare, 142. "Rarely indeed is an individual beyond middle life can one attribute a hypertension to a
previous acute nephritis.

The primary cause or causes of pathologically high arterial pressures are not yet definitely established, although many theories have been advanced.

It was long held that the heart has a selective action enabling it to overcome a general or local resistance due to arterial occlusion, and that hyperpiesis is due to arteriosclerosis. Many blood pressure readings have however established the presence of hyperpiesis in the absence of any evidence of arterial narrowing, and conversely the absence of hyperpiesis in elderly men who appear to have hardened arteries. The author's experience is that a great many miners past middle age have definitely hardened palpable radial arteries, associated with blood pressures falling within normal limits, and these findings are in accord with those of Sawada, ¹⁴³, and Romberg, ¹⁴⁴.

Experimentally neither ligation of the renal vessels, nor embolization with paraffin increases the blood pressure. Strouse and Kelman,¹⁴⁵, point out that the fact that patients with hypertension may later in life develop cardio renal complications, affords no justification for the conclusion that the primary cause of the high blood pressure lies in the organ or organs which secondarily show evidence of disease. "Study of histories of patients and careful continuous clinical
observation will reveal many patients with hypertension of fairly high grade and yet with no evidence of myocardial degeneration, arterial change or disturbance in kidney function."

On the other hand Bansi, has reported a number of cases of marked sclerosis of the kidneys with normal blood pressures.

It may therefore be taken as amply proved that arteriosclerosis without high arterial pressure is a clinical entity, and that there is no support for the mechanical view originally put forward by Traube, and subsequently by Loeb and others.

It is well known that the activity of the endocrines may permanently affect the blood pressure, but although certain clinical facts are well established, there is little knowledge of the relation between endocrine activity and chronic hypertension.

That increased secretion of the adrenals is the cause of hypertension has served for a large amount of research, but none of the results can in any way be called conclusive. All deductions based clinically or experimentally upon qualitative or quantitative analysis of adrenalin in the serum appear to be at variance, and there is no constant relation between the degree or even the presence of hypertension and the anatomical structure of the glands.

Experimental evidence has been invoked to prove that a pressor substance renin is formed in the kidney.
which when injected into animals causes a rise of blood pressure. Batty Shaw, believes it not unreasonable to think that in the large number of cases in man in which hyperpiesis is present, it may be directly due to the escape into the circulation of renin from the diseased kidneys. There appears as yet however to be no direct proof of autolysis of the renal cortex and the discharge of renin into the blood.

As acute urinary suppression is followed by a rise in blood pressure, a search has frequently been made for some metabolic whose defective elimination might result in hypertension. Martenson, in a recent study has emphasised this factor and points out that primary hypertension is not entirely a disease of the aged; and he quotes similar observations by Osler and O'Hare. Martenson suggests "an inherited inability to metabolize protein," which may be endocrine in origin or to abnormal function of liver cells. He bases his conclusions on uric acid studies. Evidence suggestive of this is also found in Majors. He showed a diminished urinary excretion of quanidine in these cases, and experimentally Croftan, found that the injection of the alloxuric bases, xanthin, hypoxanthin and quanin caused a marked rise of blood pressure, and endarteritic changes in the arteries. He concludes that where hypertension is primary it usually con-
constitutes a senile change. In all other forms it will be found that some kidney lesion coexists, and that we are dealing with a condition which is the result of parenchymatous nephritis - in which case the nephritis is primary and the hypertension secondary - or that the same toxins may simultaneously produce both the nephritis and the arterial changes.

The common findings in this class of cardiovascular disease may therefore possibly be explained in the following manner. In individuals with hypertension, if this is due to an inherited inability to metabolize protein, there may be a constant excess of guanidine or other pressor substance in the blood.

Hypertension following nephritis could then be explained as being due to the retention of such pressor substances, produced at a normal rate, but imperfectly excreted.

In a subject so confused as that of hypertension in its relation to nephritis it is impossible to formulate any definite hypothesis and this investigation throws no light on the question. We suggest however in a general way, that organic change in the kidneys and vessels may arise in diverse ways, the least indefinite of these being through intoxications of infections origin. It is also suggested that intoxications resulting from abnormal metabolism may have a similar effect.

These intoxications produce early only functional disorders, but when persistent they induce organic
changes affecting the blood vessels and kidneys. In other words that a nephritis is not primarily the cause of the hypertension, nor the hypertension the nephritis, but that both are caused by toxic products possibly different, possibly identical in character.

So that, as we are dealing here with cardiovascular - renal disease in its early stage, it appears reasonable to deduce that the cardiovascular cases may be in a group by themselves. Hypertension is the first symptom noted. They have no albuminuria at this stage, and their kidneys are functioning normally.

The primarily renal cases, may or may not, have hypertension, but show some renal abnormality, either albuminuria or impaired function, or both,

Cases with Hypertension may therefore be divided into two great groups, those with, and those without any evidence of renal abnormality. We consider that impaired renal function as shown by the tests employed, or the persistance of albuminuria or the presence of casts, either singly or in combination, constitutes an abnormal renal condition.

The cases showing hypertension are therefore placed in two sub groups.

(2) Cases of hypertension with some renal abnormality.
(3) Cases of hypertension without renal abnormality.

In Subgroup (2) are 7 Cases.
In Subgroup (3) are 6 Cases.
Subgroup (2).

Nephritic Hypertension occurs characteristically if glomerular lesions preponderate in the renal pathology.

It has been seen under "The Pathology of Scarletinal nephritis" that a marked elevation of blood pressure often, but not always occurs. The mean average pressure is not as high as in chronic nephritis and during the height of the infection the blood pressure rise entailed by the nephritis may be more or less counterbalanced by the hypotensive effect of the toxaemia. It has also been referred to, that the rise of pressure may precede the onset of scarletinal nephritis.

Although nephritic hypertension is usually found during middle life, many cases have been reported of it occurring in children and young adults. Magniel,¹⁵³

As a general rule both systolic and diastolic pressures are elevated, but occasionally only the systolic pressure is affected. As Foster,¹⁵⁴ suggests this may occur only in the early stages of the pathological process.

Increase of the diastolic pressure is generally construed as due to Vascular spasm, and when disproportionately present probably indicates a high degree of pressor effect.

Of these 7 cases, two (Nos. 23 and 2) had an orthostatic albuminuria, with normal urea concentration
tests. We consider this relation to be purely accidental.

Three (Nos.12, 16, 76) were passing albumin but in each case the urea concentration test was normal, but in Nos. 16 and 76 there was slight cardiac enlargement.

No. 74 has a urea concentration test of 1.4% with a doubtfully normal water test, and No. 55 is the typical chronic parenchymatous nephritis with a slightly raised blood pressure, impaired renal function, and abnormal blood chemistry.

We consider the outlook for the 2 orthostatic albuminuries to be less favourable than in other cases only in that there is the associated hypertension - the importance of which is very difficult to assess.

Nos. 12, 16, and 76, are less favourable than others simply passing albumin, for the same reason. The combination of albuminuria and hypertension makes them "Bad lives" for Insurance, and they may at a future date begin to show evidence of impaired renal function - having reached the stage of No. 74. No. 55 has reached the final stage and the prognosis in this case is of necessity, grave.
Subgroup (3).

Six Cases with abnormal blood pressure, but with no renal abnormality.

For lack of etiological knowledge, Vascular or essential hypertension is the term applied to a chronically increased blood pressure which is definitely non nephritic. It is also variously described as pre-albuminuric Brights' Disease, latent arteriosclerosis, primary hypertensive vascular disease, and hyperpiesis. It may exist for years without producing symptoms.

Hereditity appears to be an important factor as certain families have been shown to possess a liability, and develop cardio-vascular disease, and for its members to die of heart failure, apoplexy or uraemia. Schmidt, 155. studied 133 cases of essential hypertension in which the hereditary factor was marked and found disturbances of carbohydrate metabolism a frequent accompaniment.

Weitz, 156. investigated the families of 82 hypertensives and found that they showed a much greater and earlier mortality from apoplexy and cardiac disease than people with normal pressure. It was also found that brothers and sisters of hypertensive people showed a marked tendency to high pressure.

O'Hare, 157. found that 76% of his hypertensives showed a definite family history of vascular disease. He considers that the vast majority of patients with a
so called chronic nephritis are primary hypertensives in whom the sclerosis of the small renal vessels has produced secondary destruction of the kidneys. Kisch, 158. found that none of his cases of essential hypertension showed any abnormal renal function, but that after the condition has lasted some years, renal impairment did occur.

In these cases with normally functioning kidneys, some extra renal cause, as are suggested by Rosenberg 159. must be sought. If toxic in origin, the pressor effects must probably be looked for in the splitting up of proteins by bacteria, either in the course of some other infective process, or during the disintegration of protein food-stuffs in the alimentary canal.

Under the influence of infections proteinogenous substances may be formed in the blood, capable of inducing spasm. Under ordinary circumstances they are dealt with by the liver, but when the liver suffers as a result of the infection, these substances accumulate in the blood, and high blood pressure results from spasm of the arterioles. The effect of the chronic toxaemia are most apparent in the kidneys, but this is probably only one symptom of the general poisoning.

The extraneous material is believed to be a protein or a protein derivative from ordinary food or from the bodies of bacteria to which the cells of the patient may have become sensitive. Such sensitive-
ness usually appears to date from some acute illness of the nature of gall stones, appendicitis, typhoid, malaria, etc.

Strickland Goodall, who examined 2,000 cases under the age of 40, found that the most frequent antecedent of hyperpiesis was scarlet fever.

Hence although in this group, we cannot point to any one factor or to the definite source of origin of supernormal arterial pressure - and more than one source probably exists - we suggest that these findings may be due to some form of toxaemia arising from infective or autogenous sources, and that the previous attack of scarlet fever may be an etiological factor. We do not suggest that high arterial pressure, with normal kidney excretion determined by functional tests, and urine examinations, justifies a diagnosis of chronic nephritis, but we cannot exclude the possibility that renal changes may not appear after a long period of years.
SUMMARY.
Chapter VII.

SUMMARY.

Eighty-four children and young adults, having had nephritis complicating scarlet fever were investigated after periods varying from one to ten years. The cases were examined in particular as regards the condition of the cardiovascular system, the urinary findings, and the renal efficiency.

1. There appeared to be no relation between the severity of the attack as measured by the duration of the albuminuria, and the incidence of late effects.

2. Of sixteen cases in which cardiac abnormalities were noted during scarlet fever, and
which may or may not have been antecedent to that condition, complete recovery had occurred in twelve. It is concluded that scarlet fever and scarletinal nephritis cannot be considered as being common causes of valvular disease.

3. Of eighty cases reviewed, thirty-eight, presenting no abnormality of urinary contents, of renal efficiency or of the cardiovascular system, may be considered as having made a complete recovery.

4. Of seventy-nine cases discharged albumin free after scarletinal nephritis, twenty-one, or 26%, are, after periods varying from one to ten years again passing albumin.

Of these twenty-one with persistent true albuminuria —

(a) Eleven have albuminuria with no cardiovascular changes and with renal efficiency tests normal. These albuminuria are considered to be benign in character, representing a stationary process, but as being directly attributable to the original nephritis. From the standpoint of Life
Insurance, they are not first class lives, and the kidneys are impaired in as much as they are to be considered more liable to be affected by any focal infection.

(b) Five have albuminuria with abnormal blood pressure but with normal renal efficiency tests, and are therefore less favourably regarded than those with albuminuria alone.

(c) Two have albuminuria with normal blood pressure, but with abnormal renal efficiency tests. These cases are not regarded as being early chronic nephritics, but are also less favourably regarded than those with albuminuria alone.

(d) Three have albuminuria with both abnormal blood pressure and impaired renal function, and are considered to be suffering from chronic parenchymatous nephritis.

5. In addition to the cases of true albuminuria, fifteen, or 18½% have orthostatic albuminuria. The investigation throws no light on the aetiology of
the condition, but in view of the high incidence, it is suggested that in an unknown proportion of these cases there is a direct relationship between it and scarletinal nephritis.

6. Of the eighty cases, the blood pressure was within normal range in sixty-three. Of the sixty-three, thirty-eight were normal also as regards urinary constituents and renal efficiency, and twenty-five have an abnormality of urinary constituents or renal efficiency. In eleven the only abnormality was an orthostatic albuminuria, while fourteen have true albuminuria. Of the fourteen, three show varying degrees of renal function impairment.

7. Seventeen cases have abnormal blood pressures - four hypotension and thirteen hypertension.

Of the thirteen hypertensives, seven have some abnormal urinary constituent or impaired renal function or both. In two of this group of seven,
the only abnormality is an orthostatic albuminuria. Three have true albuminuria, and are regarded as being possibly early chronic nephritics, and two have definite signs of chronic parenchymatous nephritis.

Of the thirteen hypertensives, six have no abnormality of the urine or renal function. No conclusion could be formed regarding the cause of this hypertension, but the suggestion is made that the scarletinal nephritis may be an etiological factor.

8. The answers to the questions formulated in the introduction are therefore, first, that the acute scarletinal nephritis of childhood, may manifest itself in later years as a chronic nephritis, and that such a termination, although infrequent, occurs more often than has been stated by many authorities.

Second, that although the relationship of the cardiovascular changes, to the scarletinal
nephritis, is a debatable question, the incidence of these changes justify one in suggesting that they are in some cases attributable to the original renal infection, and that a large proportion show after long periods of time, evidence of renal damage, in the form of a persistent albuminuria.
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