THE PROGNOSIS OF NEPHRITIS IN CHILDHOOD WITH REFERENCE TO THE ADDIS URINARY SEDIMENT COUNT

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by

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C O N T E N T S

PREFACE.

There has been much controversy about the prognosis in the different types of nephritis. In an attempt to throw further light on this question, the Addis method of counting the formed elements in the urinary sediment has been taken as the main subject of this thesis. The investigation was conducted in the wards and the biochemistry department of the Royal Hospital for Sick Children, Glasgow.

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A. REVIEW OF PREVIOUS WORK.

I. CLASSIFICATION.

Since Bright (1836) first studied nephritis, this condition has always been a subject for discussion, especially the classification of the different types. This was clarified by Volhard and Fahr (1914) and Volhard (1918), whose classification has achieved considerable popularity, being based on a combination of clinical and pathological findings. They described three main types of nephritis which were thought to be essentially different in etiology and pathology. (1) Glomerular nephritis due to glomerular inflammatory destruction; (2) Nephrosclerosis due to arteriosclerosis with thickening of the small renal arteries, and (3) Nephrosis due especially to degeneration of the tubules. Addis (1925 & 1928), agreeing with these three main types, named them (1) Haemorrhagic Bright's disease; (2) Arteriosclerotic Bright's disease, and (3) Degenerative Bright's disease, but modified their classification in various ways. For example, Volhard divided glomerular nephritis into diffuse, which was again subdivided, and focal types according to the blood pressure and renal function tests. This division was not accepted by Addis, who

separated haemorrhagic nephritis into four progressive stages according to the clinical and urinary findings. Both authors agreed on the varied and varying etiology of nephrosis or degenerative nephritis. Addis, however, stated that this condition may progress to renal failure with uraemia, but Volhard and Fahr did not accept this, although they had noticed nitrogen retention in some of their cases and found some glomerular alteration as well as tubular degeneration at postmortem examination. The degenerative type differed from the haemorrhagic in that there was no haematuria, hypertension or nitrogen retention. This form of nephritis was first described by Muller (1905), under the term 'nephrosis', as a kidney lesion where the changes were purely degenerative. In 1906 Munk suggested the name 'lipoid nephrosis', as the urines of these cases often contained lipoid bodies. In 1917, Epstein under the heading of 'nephrosis', included certain types of chronic diffuse nephritis, because the course of the disease and clinical findings were similar. He treated both types in the same way and suggested that nephrosis was due to some general metabolic upset.

Van Slyke et al (1930), accepting the clinical classification of Addis and the pathological findings of Volhard, divided nephritis into (1) Haemorrhagic nephritis and (2) Non-haemorrhagic nephritis. The latter was subdivided into

(a) arteriosclerotic and (b) degenerative types. These authors agreed with Addis that the degenerative, as well as the haemorrhagic type, may pass into renal failure with uraemia and death.

Other classifications have been given by different workers, e.g. Lyttle (1929) suggested (1) Glomerular nephritis, (2) Tubular nephritis which is similar to nephrosis, and (3) Diffuse glomerulo-tubular nephritis which is a mixture of the first two types. Aldrich (1930) classified his cases into the following types: (1) Acute post-infectious haemorrhagic nephritis; (2) Chronic nonspecific nephritis in which there is no history of previous infection, but haematuria and albuminuria occur and the course proceeds rapidly to renal failure and death, (3) Nephrosis and (4) Renal Infantilism, which has all the signs and symptoms of chronic nonspecific nephritis plus infantilism. Snoke (1937) suggested (1) Pure degenerative Bright's disease or Nephrosis and (2) Glomerular nephritis, which is similar to the main classification given by Volhard. More recently Ellis (1942), trying to simplify the classification of nephritis in both adults and children, suggested the following which is based on both clinical and pathological findings. (1) Type I nephritis which is the equivalent of haemorrhagic nephritis and glomerular nephritis. There is usually a sudden onset following an acute infection. Signs of

general upset may be present. The degree of haematuria, albuminuria, oedema, hypertension and nitrogen retention varies. Recovery is the rule. (2) Type II nephritis in which the onset is insidious and usually without any preceding infection. Oedema and massive albuminuria are the most prominent symptoms, haematuria being rare. There is no nitrogen retention or hypertension. Ellis included 'nephrosis' or degenerative nephritis in this group, as the symptoms and signs in that condition are identical with those already described, with the exception of haematuria. (3) Chronic Bright's disease, which is equivalent to chronic interstitial nephritis and is considered to be the end result of various renal disorders in which hypertension leads to renal failure with hypertensive retinitis and papilloedema. The renal lesions leading to this condition may be (a) chronic type I nephritis, (b) chronic type II nephritis, (c) essential hypertension, (d) malignant hypertension, (e) chronic pyelonephritis or (f) toxaemia of pregnancy etc. Ellis therefore agreed with Addis that both acute haemorrhagic nephritis (type I) and degenerative nephritis (type II) may lead to renal failure, but considered this stage of renal failure to be part of the chronic interstitial nephritis described by Addis as arteriosclerotic.

The chronic Bright's disease or chronic interstitial nephritis of Ellis was described in adults, but the etiology

of the condition and the clinical findings differ slightly in childhood. Under this heading are two forms of renal fibrosis; (1) chronic nephritis with hypertension and (2) 'renal dwarfism': Both these types are recognised by Ellis (1942), Sheldon (1941) and others.

Type (1), chronic nephritis with hypertension, is thought to be the end result of acute haemorrhagic nephritis, nephrosis, or a congenital abnormality leading to chronic pyelonephritis, i.e. an inflammatory destructive lesion associated with hypertension, which may or may not lead to cardiac enlargement and changes in the optic discs. Hypertension, essential or malignant, is not usually recognised as a primary cause of nephritis in childhood, although Ellis (1942) stated that he had seen at least one case. Longcope (1933 & 1937) showed that chronic pyelonephritis may, after a long course, give rise to a clinical and histological picture very similar to that obtained in 'chronic interstitial nephritis.' Kennedy et al (1941) reported a case of malignant hypertension with albuminuric retinitis in a girl aged 7 years, due to unilateral atrophic pyelonephritis which was caused by an obstruction in the urinary tract. On removal of the affected kidney, the blood pressure returned to normal and the retinitis cleared. On the other hand Benjamin & Ratner (1941) reported a similar case of atrophic pyelonephritis in a boy of 6 years, in which removal of the kidney

did not relieve the hypertension. Nye (1931) described 22 patients (young adults) with chronic interstitial nephritis, who had had severe plumbism in childhood. These patients were dwarfed, but differed from the usual type of renal dwarf in that there was hypertension, cardiac enlargement and the secondary sexual characters were fully developed. Weill-Hallé and Loewe-Lyon (1939) reported a case of chronic interstitial nephritis in a baby of 3 months old. The condition was thought to be due to antenatal lead poisoning caused by attempted abortion.

The second type (2), 'renal dwarfism', which is usually found in younger children, differs from type (1) in that there is not usually any hypertension, cardiac enlargement or eye changes and that there is associated infantilism. This condition is thought to be due in some cases to congenital hypoplasia of the kidneys but in others there may be dilatation of the urinary tract. This may be due to spasm of the vesico-urethral sphincter, its failure to relax or to definite urethral or ureteral obstruction. Chronic pyelonephritis or congenital cystic disease of the kidneys may also be the causal lesion. In 'renal dwarfism' there may be associated rickets. Lucas (1883) was the first to comment on the combination of bony changes with albuminuria. Fletcher (1911) described the definite association between chronic kidney disease and bony changes. Parsons (1927) divided the bony

changes of renal rickets into three types (1) atrophic (2) florid and (3) woolly. Schoenthal and Burpee (1930) described two causes of 'renal dwarfism', (1) congenital malformation of the renal tract and (2) chronic interstitial nephritis in older children. Ellis (1933) stated that 'renal dwarfism' was usually due to congenital kidney changes, for example, hypoplasia or congenital cystic disease, but reported two cases which appeared to result from acute haemorrhagic nephritis. Ellis & Evans (1933) reported 20 cases of 'renal dwarfism'. In 14 of the 17 cases examined postmortem, the kidneys were small and fibrotic with some dilatation of the urinary tract although no cause of obstruction could be found. They suggested that the cause of the hydronephrosis might be a disorder of the neuro-muscular mechanism at the neck of the bladder. Langmead (1933) reported a case of 'renal dwarfism' associated with parathyroid hyperplasia. Kaijser (1939) described a girl, aged 14 years, with 'renal dwarfism'. At postmortem examination there was hypoplasia of the right kidney and uretral obstruction on the left side. Albright et al (1940) reported a case of 'renal dwarfism' where there were massive deposits of calcium in the pyramids of the kidney. It may be concluded therefore that the causes of chronic interstitial nephritis including 'renal dwarfism' in childhood are many and varied.

It is suggested that a simple classification describing

the three main types of nephritis given by Volhard, Addis, Van Slyke and Ellis, should be used to avoid misunderstanding. In the present investigation, the cases have been placed into the following three groups according to the clinical and most prominent pathological findings although at postmortem examination all three kidney structures may be found to be involved:

1. Acute haemorrhagic nephritis.

This is synonymous with glomerular nephritis, haemorrhagic nephritis, type I nephritis and acute parenchymatous nephritis. The onset of the disease is sudden and is usually preceded by an acute infection. Albuminuria and haematuria vary in amount, and the urinary sediment contains casts of blood, granular and hyaline types. There may be no oedema, or the degree of oedema may vary from slight puffiness under the eyes to gross anasarca. There may be hypertension and nitrogen retention at the onset. At postmortem examination, the most outstanding lesions are in the glomeruli.

2. The Nephrotic Syndrome.

This type is similar to and includes non-haemorrhagic degenerative nephritis, nephrosis, tubular nephritis, type II nephritis, hydraemic nephritis, oedematous nephritis and exudative nephritis. The tubular lesion is the most prominent at postmortem examination. The onset is insidious without a history of preceding infection. The most outstanding symptom

is slowly progressive oedema which may be persistent or intermittent. Albuminuria is marked. Haematuria occurs only occasionally and may be microscopic or macroscopic. Hypertension and nitrogen retention are rare. The serum proteins are low and the blood cholesterol high. The renal function is good. In this nephrotic syndrome, are included cases of 'nephrosis', which is thought to be due to tubular degeneration only and runs a course similar to that already given, but haematuria is absent. In the series of cases to be reported, at least one case was diagnosed and treated as nephrosis for a period of three months before haematuria, at first microscopic but later macroscopic, appeared. In childhood these two conditions are very similar. Little attempt has been made to differentiate between the cases with and those without haematuria.

3. Chronic Interstitial Nephritis.

This type is similar to nephrosclerosis, arteriosclerotic nephritis, renal fibrosis, azotaemic nephritis and chronic Bright's disease. It has been divided into two groups:

(a) 'Chronic nephritis with hypertension'.

(b) 'Renal dwarfism'.

In group (a), 'chronic nephritis with hypertension', the onset is insidious with a history of failure to thrive, poor appetite, thirst and polyuria. There may be headache and vomiting.

There is nitrogen retention and hypertension which may be associated with enlargement of the heart and retinal changes. The urine is of low fixed specific gravity and contains a trace of albumin. The sediment contains casts, red cells and white cells. The etiology is often difficult to determine. There may or may not be a history of preceding infection, acute haemorrhagic nephritis or nephrosis. It may be possible to detect a congenital lesion of the urinary tract, e.g. urethral ur uretral obstruction causing hydronephrosis and chronic pyelonephritis.

Congenital hypoplasia of the kidneys or some other congenital abnormality may be the cause of group (b), 'renal dwarfism,' which is usually found in younger children. The history of insidious onset with failure of growth, thirst and polyuria is similar to that already given. There is dwarfism with renal insufficiency which may cause rickets, but the picture of hypertension with enlargement of the heart and retinal changes is not usually found.

II. PROGNOSIS.

Before describing the Addis count in detail, the previous work relating to the prognosis and the factors influencing it will be briefly reviewed in each type of nephritis.

1. ACUTE HAEMORRHAGIC NEPHRITIS.

Most workers agree that the prognosis of this type of

nephritis is good. Hill (1919) stated that the majority of cases recovered. James (1931), studying a series of 67 children from three months to fifteen years after the initial attack, found that only 13.3 per cent had become chronic. Allison (1925) followed 12 children from nine months to one year; all recovered. In a series of 50 patients followed from two to five years by Boyd (1927), 72 per cent recovered and 16 per cent were in the chronic stage. Greenwood (1927) stated that the prognosis in acute nephritis was good. Lyttle (1929) found that of 58 patients, 15.5 per cent were in the chronic stage and that 11.1 per cent had died. Only 6.2 per cent of the 129 cases examined by Aldrich (1930) died. Hutchison (1931) thought that the majority of cases recovered and that death was rare in the initial attack. Tallerman (1932) had a recovery rate of 66.6 per cent in the series of cases he followed. Thomson and Findlay (1933) found that 20 of 25 cases admitted in one year, had completely recovered. Thursfield and Paterson (1934) stated that, in mild cases of nephritis, recovery is always complete. Boyle et al (1937) found that 24 of 25 children had recovered completely. Recovery was observed in 72.5 per cent of a second series of 146 children examined by Snoke (1939). Cass (1939) found the recovery rate to be slightly lower - 64 per cent. In a series of 166 children reported by Gachet (1941) the mortality rate was 7.2 per cent. Of the surviving he was able

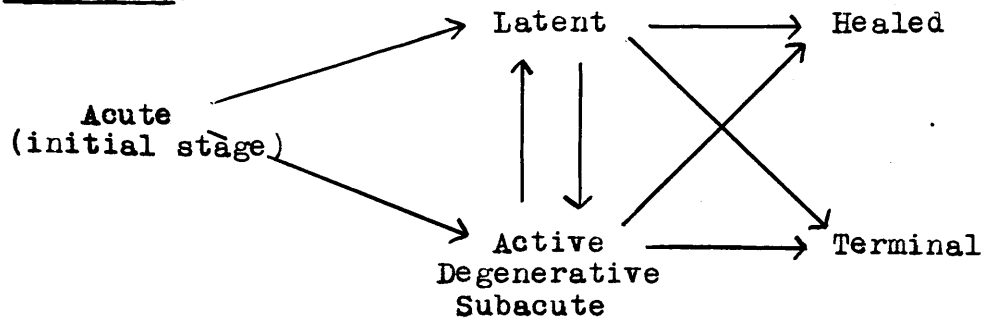
to trace 114, of whom 90.5 per cent had recovered. In a series of 225 adults and children, Ellis (1942) found that 82 per cent had recovered.

On the other hand, many workers have reported the recovery rate in acute nephritis to be much lower. Boyd (1922) in an earlier series of 26 cases had a recovery of only 50 per cent. Osman (1925) followed 56 cases from eighteen months to twenty-two years and found that 35.7 per cent had become chronic. Paterson and Wyllie (1926) stated that of 49 cases re-examined only 17 (34 per cent) had recovered. Smellie (1926), who examined 16 cases more than 10 years after the initial attack, reported that all were well clinically but that only in 21 per cent of the cases was the urine normal. Still (1927) found that only in the minority of cases, was recovery complete. Bell (1935) in a series of 72 cases (mostly adults) discovered that only 36 per cent recovered. In an earlier series of 110 patients examined by Snoke (1937), the recovery rate was 42.7 per cent. This differed from the 72.5 per cent recovery rate obtained in a later series (1939) in a different part of America by the same author, who suggested that climate and geographical distribution may play a part in the prognosis of nephritis. Of 150 patients examined by Murphy & Rastetter (1938) 49.3 per cent had recovered. Payne & Illingworth (1940) reported that at least two thirds of their cases remained in the

latent or active stages. Murphy & Peters (1942), finding that only 41 per cent had completely recovered, stated that the prognosis in acute nephritis is less favourable than was formerly believed.

As early as 1897, Holt suggested that acute and chronic (terminal) nephritis were the beginning and end of the same process but was unable to produce any conclusive proof. In 1925, Addis stated that by studying the urinary sediment, he had traced cases of acute haemorrhagic nephritis through a latent stage, which may last for many years, to a terminal stage which is similar to chronic interstitial nephritis and that one was the end result of the other. He suggested that cases of renal failure in adult life, which did not have any definite etiology, may be due to an attack of acute nephritis in childhood which had been forgotten or missed. By counting the casts and cells of the urinary sediment (by the method to be described later) Addis gave the following diagram to show the prognosis in cases of acute haemorrhagic nephritis.

Diagram 1.



It will be seen that from the initial stage, the lesion in the kidney may heal, become latent or active and heal, or pass from these stages into the terminal stage. There is considerable difference in the various phases.

(1) The latent stage contains patients who are clinically well and who give satisfactory results to routine tests but the Addis count shows an increase in the casts and red cells in the urinary sediment.

(2) In the active stage there is continuation of the symptoms from the initial stage with increased evidence of tubular damage. There may be anasarca and the raised Addis count may be the only means of differentiation from nephrosis.

(3) In the terminal stage are found the signs of renal insufficiency. The urine contains albumin and the Addis count is raised.

Thus Addis was able to show that in many patients, who are clinically well, the renal lesion is still active. Since Addis (1925) gave proof of the link between acute and chronic nephritis, others have worked out the prognosis in acute nephritis using the Addis count. The majority are in agreement with Addis. These include Van Slyke (1930), Snoke (1937), Cass (1939), Murphy & Rastetter (1938), Gachet (1941) and Murphy & Peters (1942), but Aldrich (1930) and Boyle et al (1930) could not find any evidence that the acute stage passed into the chronic stage and considered that acute

nephritis and chronic nephritis were separate entities. Ellis (1942), although agreeing with Addis that chronic nephritis may be the end result of acute nephritis, described the prognosis rather differently. He stated that the initial attack may (1) heal; (2) cause death in this stage; (3) undergo a rapidly progressive course over a few weeks or months to uraemia or intercurrent infection and death. This stage is probably equivalent to the active stage of Addis and to what Volhard calls subacute parenchymatous nephritis; (4) undergo a slowly progressive course over years to end in chronic interstitial nephritis, where albuminuria is found but at first the patients are well. This is similar to the latent period of Addis, except that in the latter stage the urine, although showing raised Addis counts, did not contain albumin. Ellis did not mention Addis counts in detail but it is possible that if these had been done, a greater number of patients would have been placed in this latter stage instead of in the recovered stage.

It is therefore seen that there is still much discrepancy in the results of investigations on acute nephritis. Payne & Illingworth (1940) suggested that this may be due to:-

(1) failure to examine the urinary sediment by the Addis count and thus miss the latent stage of nephritis,

(2) placing too much reliance on the clinical appearance of the patient or on the renal function tests alone,

(3) observation of the cases over too short a period and in this way missing exacerbations.

Factors influencing the prognosis in acute haemorrhagic nephritis.

Age. Griffith & Mitchell (1937) stated that the younger the child the worse the prognosis. Murphy & Rastetter (1938) considered that the prognosis was better in the younger age groups. Snoke (1937) and Payne & Illingworth (1940) decided that the age of the child was of no prognostic significance.

Sex. Most workers have found that sex does not influence the prognosis, but that more boys are affected than girls. Lyttle & Rosenberg (1929), Snoke (1937) and Ellis (1942) found that boys predominate over girls in the ratio of 3:2. On the other hand, Payne & Illingworth (1940) found that the sexes were equally affected.

Intensity of the initial attack. Lyttle (1929) stated that the less severe the initial attack the better the prognosis. Addis (1931) and Boyd (1922) agreed that the more severe attacks had a worse prognosis. Snoke (1937), Van Slyke (1930), Osman (1925) and Tallerman (1932) found, however, that there was no relationship between the intensity of the disease and the prognosis.

Duration of the initial attack. Boyd (1922), Moorhead (1928), Archibald (1937) and others considered that the longer the

initial attack the worse was the prognosis.

Removal of septic foci and infection. The effect of removal of septic foci is still disputed. Addis (1925) and Cass (1939) stated that the removal of septic foci had no permanent effect on the prognosis of nephritis, and that it was not proven that a persistent source of infection prevented the healing of the kidney lesion. Payne & Illingworth (1940) and others thought that exacerbations may occur without infection and that the removal of septic foci is of no benefit. Loeb et al (1938) found that 8 of 10 cases resisted streptococcal infection and that in no case did the nephritis become chronic. Seegal et al (1941), on the other hand, stated that no exacerbation occurred without a concomitant infection. Lyttle (1942), Platt (1932), Murphy & Rastetter (1938) and Lyttle & Rosenberg (1929) thought that removal of septic foci would be beneficial by erradicating the danger of infection. Bateman (1934) reported a case of acute mastoiditis with gross haematuria which disappeared in five days after operation. He advocated early removal of septic foci in such a case.

It has been found that several members of one family may be affected at the same time with acute nephritis. Tudor (1943) reported 3 children in a family of four, who had acute nephritis simultaneously. He suggested that the siblings of a case of acute haemorrhagic nephritis should be examined,

especially as the attack usually followed a respiratory infection. Ernstene & Robb (1931) reported an epidemic of acute nephritis in 6 of 8 children in one family following streptococcal tonsillitis. Rinkoff et al (1939) stated that 3 brothers (young adults) died of uraemia within four years. Kilpatrick (1945) reported 3 sisters, who developed acute nephritis one week after impetigo of the scalp had been noted.

Nitrogen retention. Snoke (1937), Lyttle & Rosenberg (1929), Tallerman (1932), Crawford (1924), Parsons (1926), Murphy & Peters (1942) and others considered that the level of the non-protein nitrogen in the initial stage had no effect on the prognosis, but Griffith and Mitchell (1937) found that nitrogen retention gave a bad prognosis.

Hypertension. Rubin & Rapoport (1939) and Lyttle (1929) thought that hypertension in the initial stage raised the mortality rate. Van Slyke (1930), Snoke (1937), Murphy & Rastetter (1938) and Ellis (1942) stated that if the blood pressure rose in the latent, active or terminal stages the prognosis was poor, but that hypertension in the initial stage was of no prognostic value. Hypertensive encephalopathy is thought by Lyon (1934) and Murphy & Peters (1942) to be due to cerebral oedema produced by a toxic factor, which is responsible for the general condition and that if the immediate response be favourable, there is no residual effect

on the prognosis. Rubin & Rapoport (1939) and Ellis (1942) considered that hypertensive encephalopathy is not due to cerebral oedema primarily, but to vasomotor spasm which can be relieved by magnesium sulphate therapy and that the condition is of no prognostic significance. Boyle et al (1937), in 25 cases examined, found that 10 were complicated by hypertensive encephalopathy and that all recovered. On the other hand, Aldrich (1930) and Lyttle & Rosenberg (1929) stated that this complication caused a higher mortality rate in the acute stage.

It will therefore be seen that there is still much discussion and disagreement about the prognosis and the factors affecting the prognosis in acute haemorrhagic nephritis.

2. THE NEPHROTIC SYNDROME.

It is generally agreed that the prognosis in this type of nephritis is poor. As already stated, Volhard and Fahr (1914) found that the main cause of death was infection and that cases did not result in renal failure. Addis (1925), however, said "The disease may pass through active and latent stages to complete recovery or may gradually progress to termination in uraemia." Van Slyke et al (1930) agreed with Addis that renal failure may develop in the course of nephrosis and that at postmortem examination, the glomeruli may be involved in the degenerative changes. Linder et al (1927),

describing nephrosis as a degenerative kidney lesion with very little inflammation, stated that, although the usual cause of death was infection, some cases may pass into renal failure and at postmortem examination show 'nephrotic contracted kidneys'. Aldrich (1930) found that of 20 cases of nephrosis, 40 per cent recovered, 25 per cent became chronic and 35 per cent died. Schwarz and Kohn (1935), following 36 children with lipoid nephrosis over a period of 15 years, found that 25 per cent had recovered and 50 per cent had died, usually of infection. The remaining 25 per cent were either in the active stage or had residual albuminuria although well clinically. In a further series, Schwarz, Kohn and Weiner (1943) followed 40 patients with nephrosis, and found that 22 had died. Of the 18 living, 8 cases were examined and it was found that the Addis count was raised in 7 of these. At postmortem examination some cases showed glomerular obliteration or capsular thickening as well as tubular changes. They stated that in classical lipoid nephrosis there is usually glomerular involvement which may differ from that found in chronic glomerular nephritis. Tappan (1935) gave the term 'nephrotic syndrome' to those cases similar to nephrosis with or without haematuria. In his series he found that 51.1 per cent died and 17.7 per cent recovered. He stated that haematuria was of grave significance, and that in those with haematuria the death rate rose to 75 per cent without one

recovered case, while in those without haematuria the death rate fell to 42 per cent with 24.2 per cent recovered. Ellis (1942) found that in Type II nephritis recovery is rare; that the majority of cases died of intercurrent infection, but that the remainder progressed to the terminal stage with renal failure, uraemia and death. Campbell (1930) followed 23 cases of 'subacute nephritis' in which decapsulation of the kidneys had been done. He found that 43.5 per cent recovered, 30.4 per cent died, 17.4 per cent had become chronic and 8.7 per cent could not be traced. It is generally agreed, therefore, that the outlook in this syndrome is poor.

Factors influencing the prognosis in the nephrotic syndrome.

Age is not of much significance in the prognosis. Ellis (1942) found that nephrosis affects people of all ages. It is not, like acute haemorrhagic nephritis, a disease of children and young adults.

Sex. Smalley and Pinger (1944) found a preponderance of males but Ellis (1942) stated that the sexes were equally involved, although in females he found a tendency for the disease to become chronic more frequently.

Haematuria is of uncertain significance, but Tappan (1935) stated that the prognosis was poor when haematuria was present.

Infection. Although it is well-known that intercurrent infection is the most frequent cause of death in the nephrotic

syndrome, cases have been reported where marked improvement occurred after an acute complicating infection. Schwarz et al (1943) stated that acute infection in the oedematous stage may be beneficial. In their series, one attack of tonsillitis and two of measles were followed by diuresis with lessening of the oedema and albuminuria for several months. Thomas (1943) reported a case of nephrotic syndrome which, after a long stay in hospital without response to treatment, cleared up with marked diuresis and loss of oedema after cellulitis of abdomen and legs. Casaubon and Cassoy (1938) reported marked diminution in the anasarca and gradual general improvement in a girl aged 11 years, who developed an erysipeloid dermatitis six weeks after admission to hospital. Aldrich (1930) found that most of his cases which recovered, did so after an acute infection.

Serum proteins and oedema. It is understood that there is some relationship between the degree of albuminuria, the level of the serum proteins and the intensity of the oedema and that the persistence of albuminuria, low serum proteins or oedema is of poor prognostic significance. Albuminuria may be due to increased permeability of the renal epithelium. This loss of protein may be the cause of the fall in the serum proteins, especially the albumin fraction in the nephrotic syndrome. Peters et al (1931), however, found that in some cases with marked albuminuria the serum proteins were high and suggested

that proteinuria was not the sole factor in the serum protein deficit. The oedema in nephrosis is thought to be related to the hypoproteinuria (Starling). Epstein (1917) thought that the higher the level of the serum proteins and the smaller the degree of the oedema, the better was the prognosis. Peters et al (1931) stated that oedema was usually present if the total serum protein was less than 4 gm. per cent or if the albumin was less than 2 gm. per cent, but rarely present if the total protein was greater than 5 gm. per cent. They considered that a total protein of less than 4 gm. per cent was a sign of continued renal damage and, therefore, of poor prognostic value. Hartmann & Senn (1932) reported that oedema was usually present if the total serum protein was less than 5 gm. per cent or the albumin less than 2 gm. per cent and that the lower the total protein and the greater the oedema, the worse the prognosis. Moore and Van Slyke (1930) found that the critical levels for the appearance of oedema were 5.5 gm. per cent total protein and 2.5 gm. per cent albumin. The figures of Weech & Ling (1931) are similar, for example, 5 gm. per cent total protein and 2.5 gm. per cent albumin. Schwarz & Kohn (1935) stated that there was no constant relationship between the total protein and the oedema, but thought that a low protein level or persistent oedema was of poor prognostic significance.

Blood cholesterol. Thomas (1943) found that the cholesterol

level varied with the degree of oedema and the level of the total serum protein and that a high blood cholesterol indicated a poor prognosis. He suggested that the fat in the blood stream may not have been fully desaturated in the liver due to the upset of transportation and metabolism of food caused by the low plasma proteins. Smalley & Binger (1944) agreed that hypercholesterolaemia was a sign of continued renal damage and varied inversely with the serum protein level. Schwarz and Kohn (1935) and Linder (1927), on the other hand, found that although the cholesterol was usually high when the total protein was low, this was not a constant finding.

Diet. By special diets, the course of the attack may be influenced. In 1917 Epstein advocated a high protein diet, which, he claimed, would cause a rise in the serum protein and lead to a temporary or permanent disappearance of the oedema. Fishberg (1939), Bing (1936) and Casten & Bodenheimer (1941) found that it was difficult to alter the level of the serum proteins by a high protein diet. Peters et al (1931) stated that in nephrosis, a high protein diet may cause a slight rise in total protein with lessening of the oedema and improvement in the general condition, but doubted if this had any effect on the ultimate prognosis. Aldrich (1930) found no clinical benefit with a high protein diet and no effect upon the prognosis.

A diet poor in salt ('salt free') is widely used in the nephrotic syndrome. It is hoped that, by restricting the salt intake, the fluids in the tissues will be excreted with lessening or disappearance of oedema and with beneficial effect on the course and prognosis. Atchley et al (1932) found, that on giving salt to a normal and a nephrotic patient, both retained chloride and water, but the nephrotic to a greater extent, probably because of the difference in the serum protein concentration. Weech and Ling (1931) reported that when the total protein was low, the giving of salt caused an increase in the oedema. Moore and Van Slyke (1930) stated that by giving a 'salt-free diet', they could diminish the degree of oedema even when the serum proteins were below the critical level and thought that the diet alleviated the general condition. Peters et al (1931) advocated the restriction of salt to 2 grams or less daily, but only as a temporary measure for diuretic purposes. Linder et al (1926) reported a case which collapsed with dehydration and a fall in serum base after administration of a 'salt-free' diet and stated that this diet should not be given over long periods. Dieting, therefore, may or may not affect the course and prognosis of the nephrotic syndrome.

Plasma and serum transfusions. It having been shown in more recent years, that a high protein diet is not always effective, plasma or serum has been given intravenously in an

attempt to raise the serum protein level, diminish the oedema and improve the general condition. Aldrich et al (1938) stated that in 6 of 9 cases, the oedema cleared completely after transfusions of concentrated serum. They thought that the ultimate prognosis was better if the transfusions were given in the first six weeks of the attack. Casten & Bodenheimer (1941) thought that the temporary rise in serum protein following transfusion might be of value. Weech et al (1933) experimenting on dogs stated that although there might be a temporary rise in the albumin level of the serum after transfusion, the oedema was not significantly affected. Later in 1940, the same workers found that only one case in seven treated, responded and thought that transfusion of plasma had no effect on the course of the disease. Leutscher (1943) treated three nephrotic patients without any lasting clinical benefit. Madden and Whipple (1940) stated that there was no guarantee that protein given intravenously would remain in the blood stream. Brown et al (1942) gave quadruple strength serum to 11 patients and found that 2 became worse, 5 remained unaffected, 2 had slight reduction in oedema and 2 lost the oedema completely. Hartmann & Senn (1932) and Smalley & Binger (1944) used acacia in place of plasma with good effect on the prognosis.

Concentrated plasma transfusion, therefore, may have an adverse, a beneficial or no effect on the prognosis in the

nephrotic syndrome. There is still much controversy about the influence that treatment and other factors may have on the course of the disease.

3. CHRONIC INTERSTITIAL NEPHRITIS.

It is known that the prognosis in both 'chronic nephritis with hypertension' and 'renal dwarfism' is poor, all cases eventually progressing to renal failure with uraemia and death.

The factors which can influence the course of the disease are few, but the method of treatment may be of value in prolonging life. In 1931 Lyon et al suggested that the diet should be kept alkaline by giving alkaline ash foods and adequate amounts of alkaline salts to counter-act the latent if not the actual acidosis which is present in the terminal stages of nephritis. Parsons (1927) stated that as the kidneys were unable to excrete the acid products of metabolism including acid phosphate, there was retention of phosphorus in the blood with an upset of the calcium/phosphorus ratio, which caused the removal of calcium from the bones, resulting in rickets. Schoenthal & Burpee (1930) agreed with this cause of renal rickets and found that by giving calcium acetate orally there was a decrease in the blood phosphorus with a rise in the calcium. Orr et al (1942) found that by giving a diet rich in calcium, they could increase the retention of calcium with a rise in the

serum calcium and a lowering in the serum phosphorus, which was excreted as insoluble calcium phosphate in the stools. Karelitz and Kolomoyzeff (1932) reported a case of 'renal dwarfism' with a normal serum calcium which was treated with 494,000 rat units vitamin D over eighty-two days. This caused a fall in the serum phosphorus and a rise in the serum calcium. In 1938, Graham and Oakley treated two cases of renal dwarfism with large doses of alkali, calcium and vitamins A and D with marked improvement in the kidney function and the general condition. There was an increase in the height and weight and improvement in the bony changes. Sheldon (1943) treated a renal dwarf in this way and produced complete healing of the bones, although the serum phosphorus remained high and the boy died of uraemia. Freeman (1941) suggested giving a low phosphorus diet under observation in order to raise the calcium level and lower the phosphorus level in the blood.

By these methods it was hoped to influence the immediate prognosis by postponing the onset of uraemia, although there could be no effect on the ultimate prognosis.

THE ADDIS COUNT.

As already stated, in 1925 Addis introduced his method of counting the cellular constituents of the urinary sediment in an attempt to clarify the classification and prognosis in nephritis. He found that this test could detect renal

lesions which were not apparent by the more usual function tests. Since the urea clearance and concentration test results do not fall below the normal values until more than half the kidney tissue is destroyed, mild degrees of renal damage may not be detected. On routine examination of the urine, mild albuminuria and occasional casts or red cells on microscopic examination tend to be disregarded, whereas these findings may be proved to be of pathological significance by a quantitative estimation by the method of Addis.

In 1926, Addis estimated by his method the number of cellular elements and the amount of protein in the urine of normal healthy adults who were mainly out-patients. They were given written instructions about the method of collecting the specimen of urine used for the count.

1. Method. Each patient was instructed to obtain a twelve hour specimen of urine, e.g. from 6 or 8 p.m. until 6 or 8 a.m. During the day prior to and the night of collecting the urine, fluids were to be omitted. The bladder was emptied and the urine discarded at the start of the collection. For the next twelve hours, all urine was passed into a bottle which had been previously sterilised and dried. Female patients were catheterised. The urine was found to be acid and concentrated. The volume of the urine in the twelve hour specimen was then measured in cc. and thoroughly mixed. Into a graduated centrifuge tube, were placed 10 cc.

of the urine which was centrifuged for five minutes at 1800 revolutions a minute. The type and the amount of the deposit were then noted. The supernatant fluid was reduced by pipetting to a known volume, usually about 1 cc. This was mixed and contained all the cells and casts from the 10 cc. specimen of urine. With a haemocytometer, the number of casts and cells was counted over a known area, several drops of urine being used. By a simple calculation, the number of casts and cells in the twelve hour collection of urine was estimated. Addis estimated the amount of protein in the urine by the method of Shevky and Stafford (1923), in which a definite quantity of urine was centrifuged at 1800 revolutions a minute for fifteen minutes - after the addition of a solution of phosphotungstic acid in strongly acidified alcohol. The volume of the protein thus precipitated was packed by centrifuging. By calculation the amount of protein in milligrams for the twelve hour specimen of urine was estimated.

2. <u>The Addis count in normal adults and children</u>.

Addis gave the following upper limits of normality (Table 1) in adults for a twelve hour specimen of urine collected by the method given above and stated that counts over these values were of pathological significance.

Casts	5,000
Red cells	500,000
White cells + epithelial cells	1,000,000
Protein (mg)	30

Table 1. Upper normal limits of casts, red cells, white cells and protein in a 12 hour specimen of urine in adults.

As the counts done by Addis were in adults, Lyttle (1933) and Snoke (1937) examined the urines of healthy children to determine the normal upper limits of casts and cells in the urine in childhood. The method of collecting urine in small children was similar to that in adults, that is, the urine was collected over a twelve hour period but fluids were only restricted on the afternoon preceding and the night during which the urine was collected. An allowance of 200 cc. fluid was given at the evening meal. The count was done by the method described by Addis. Lyttle counted the urinary sediments of 74 children and Snoke had 202 children in his series. Their findings with those of Addis are given in Table 2.

Urine	Snoke (children)	Lyttle (children)	Addis (adults)	Proposed upper normal limits (Snoke)
Casts (R	0 - 29,000	0 - 12,916	0 - 4,270	10,000
(A	1,230	1,085	1,040	
Red cells (R	0 - 800,000	0 - 129,000	0 - 425,000	600,000
(A	81,000	15,181	65,750	
White cells + Epithelial cells (R	---	9,000 - 2,822,000	32,000 - 1,835,000	2,000,000
(A	---	322,484	322,000	
Protein (mg) (R	5 - 90	3 - 45	---	55
(A	28.5	18.5	30	

Table 2. Normal Addis counts. The range (R) and the average (A) counts of casts, cells and protein in the urinary sediment of normal adults and children and the proposed upper normal limits in children (Snoke).

It will be seen from Table 2. that the average findings in the three series are fairly similar although Addis did his counts on adults. In Snoke's series the average red cell count and the average protein content of the urine (28.5 mg. compared to 18.5 mg.) are higher than those found by Lyttle. The proposed upper limits of normal of Addis given in Table 1., although lower, agree fairly well with the results of Lyttle and

Snoke except in the upper limit of proteinuria. Lyttle suggested 35 mg. and Addis 30 mg. but in Snoke's series 55 mg. included 95 per cent of all the values obtained. In children, therefore, this figure is accepted as the normal upper limit of protein in a twelve hour collection of urine. It was found that there was a greater number of zero cast counts (64 per cent (Snoke) and 73 per cent (Lyttle)) and zero red cells counts (55 per cent (Snoke) and 67 per cent (Lyttle)) in children than in adults (40 per cent for casts and 51 per cent for red cells.) It has been suggested by Lyttle that the higher percentage of zero cast and red cell counts in children may be due to the fact that the fluid intake, during the collection of the twelve hour specimen of urine, is not so rigidly restricted as in adults. Another reason given is that children usually have a low salt intake and that if there is a low salt concentration in the urine the red cells tend to disappear. The difference in the percentage of zero counts may account for the slight variation between the counts in adults and children. The proposed normal limits given by Snoke (Table 2) are accepted by most workers.

3. <u>The Addis count in nephritis</u>.

Addis (1925) counted the constituents of the urinary sediment in the different types of nephritis.

Type	Stage	Casts	Red Cells (millions)	White + epithelial cells (millions)	Protein (mg)
I Haemorrhagic	1 Initial	2,300,000 (all types)	160 +	40	800
	2 Active	2,000,000 (esp.hyaline)	120 +	30	2,800
	3 Latent	1,100,000 (all types)	60	5	200 or less
	4 Terminal	1,100,000 (all types)	100	6	2,000
II Degenerative	Initial	3,750,000 (hyaline)	1 +	15	3,000
III Arteriosclerotic	---	1,100,000 (esp.hyaline)	2 +	1 +	100 or less

Table 3. The Addis counts in the different types of nephritis.

Using the Addis count, other workers have tried to link acute haemorrhagic and chronic nephritis. Van Slyke (1930), Snoke (1937), Cass (1939), Murphy & Rastetter (1938), Gachet (1941) and Murphy & Peters (1942) agreed with Addis that the acute haemorrhagic type could be divided into different stages and that the initial stage may progress to terminal nephritis. On the other hand, Aldrich (1930) followed 129 cases without finding any in the active or terminal stages and thought it

unlikely that acute nephritis passed into the chronic stage. Boyle et al (1937) agreed with Aldrich. They found that 24 of 25 children with acute nephritis made a complete recovery and that the remaining child had hydronephrosis.

The results of the Addis counts in the different stages of haemorrhagic nephritis (Table 3) are slightly higher than those of other workers, including Van Slyke (1930) and Snoke (1937) who gave lower counts especially in the latent and terminal stages.

There is little mention in the literature of the Addis count in degenerative nephritis. Addis stated that it is only by the increase in the red cells and the presence of blood casts that the active stage of haemorrhagic nephritis can be differentiated from 'nephrosis'. One of Snoke's cases (1937) in the same stage of haemorrhagic nephritis, gave for a short time counts similar to those found in degenerative nephritis, i.e. there was a marked increase in the cast and white cell counts with only a slight increase in the number of red cells.

In many cases, chronic interstitial nephritis in childhood is really similar to the terminal stage of acute nephritis and not to the arteriosclerotic nephritis of Addis. One would expect therefore that the urinary sediment counts would tend to conform to the results obtained in the terminal stage of acute nephritis. Ellis (1942) stated that in

chronic interstitial nephritis there was an excess of red cells and casts in the urinary sediment.

Rubin et al (1939), following 40 cases of acute haemorrhagic nephritis during the initial stages, did Addis urinary sediment counts and sedimentation rates every two weeks until they returned to normal. These workers found that an average of 37 days from the onset was required for the urine to become clear to routine tests. The average time for the red cell Addis count to reach the 10 million level was 76 days and 120 days were taken before the count fell below the upper limit of normality. The routine analysis of the urine may not detect the latent stage in which the renal lesion is still active and therefore is of little value in prognosis.

4. <u>The Addis count in other diseases</u>.

Goldring & Wycroff (1930) suggested that mild attacks of glomerular nephritis during some previous infection might have been missed and have led to chronic nephritis in adult life. They thought that the application of the Addis count in various acute infections might be of value by detecting subclinical attacks of nephritis. They found (1930) that in 16 cases of rheumatism, all had raised Addis counts which persisted for four to ten weeks after the acute rheumatism had subsided. Goldring (1931) reported that in 16 of 44 cases of lobar pneumonia, there was microscopic haematuria before the crisis. Two of these cases progressed to acute

haemorrhagic nephritis but the others cleared. Lyttle (1933) stated that of 14 boys with scarlet fever all had 'toxic albuminuria' with raised Addis counts in the first week and that raised counts were obtained at intervals from eight to forty-five days. He suggested that this subclinical nephritis was due to an allergic reaction to which most patients became adjusted. The kidney damage was usually slight, but in a few cases the condition progressed to true haemorrhagic nephritis. Wallgren (1939) found 24 cases of subclinical renal lesions with raised Addis counts in 64 cases of erythema nodosum and thought they were due to a febrile toxic-allergic reaction. Nathorst (1940), investigating 430 patients with acute rheumatism, discovered 8 cases of acute haemorrhagic nephritis. He examined 35 of these cases. The Addis count was raised in 50 per cent of them, thus showing subclinical irritation of the kidneys. This, however, passed off quickly and was thought to be allergic and similar to the polyarticular symptoms.

Mild or subclinical attacks of acute haemorrhagic nephritis in childhood may therefore be the cause of chronic interstitial nephritis in later life.

B. PRESENT INVESTIGATION.

1. INTRODUCTION. This investigation deals with the fate of 324 children who were admitted to the Royal Hospital for Sick Children, Glasgow with nephritis between 1933 and 1944. Between the years of 1938 and 1944, 251 had acute haemorrhagic nephritis; 60 had the nephrotic syndrome and 23 had chronic interstitial nephritis between 1933 and 1945. The 2 children (renal dwarfs) who were admitted in 1945 have been included to complete the investigation. In addition, before examining these children, it was decided to apply the Addis count to the urinary sediments of a small number (20) of normal children to confirm the results of Lyttle (1933) and Snoke (1937). The object of this thesis is to determine the prognosis of the three types of nephritis in childhood and to correlate the value of the Addis count with the other renal function tests e.g. urea clearance and concentration tests, in estimating the degree of kidney damage.

11. SCHEME OF INVESTIGATION. Each child was brought in for re-examination. On reporting to hospital a thorough general examination was carried out. The weight and height were recorded. The urine was examined by the routine tests and by the Addis count (two counts being made). Written instructions about Lyttle's modification of the method of collecting the twelve hour specimen of urine for the count,

were given to each parent. The blood pressure was taken. The non-protein nitrogen was estimated by the micro-method of Folin and Svedberg (1930).

In as many cases of acute haemorrhagic nephritis as possible, in all cases of the nephrotic syndrome (some of which were followed at weekly intervals throughout their stay in hospital) and of chronic nephritis, the serum proteins, total and fractional, were estimated by the micro-Kjeldahl method.

The blood cholesterol was determined colorimetrically by the method of Leiboff (1917) which depends on the reaction of the free cholesterol plus the ester cholesterol with acetic anhydride and sulphuric acid

In all cases of the nephrotic syndrome and chronic interstitial nephritis and in those cases of acute haemorrhagic nephritis, which, by the preceding tests, did not appear to have completely recovered, the renal function was determined by the urea concentration test of MacLean and the urea clearance test of Van Slyke.

The blood urea for the clearance tests was estimated by the urease-Nesslerisation method of Archer & Robb (1939).

111. RESULTS OF INVESTIGATION.

1. THE RANGE OF ADDIS COUNTS IN NORMAL CHILDREN.

The urines of twenty children, who did not have a history of previous nephritis, rheumatism or recent acute

infection but had been admitted for investigation or observation for some other condition, were examined by the Addis count. The results are given in Tables 4 and 5.

-	Casts	Red cells	White & epithelial cells.	Protein(mg)
1	1,400	438,000	58,000	18
2	0	0	48,000	18
3	0	0	9,000	3.6
4	0	0	292,000	27.5
5	0	36,000	262,000	18
6	0	0	384,000	18
7	1,800	252,000	24,000	18
8	0	19,800	330,000	18
9	0	0	10,000	9
10	2,600	53,500	714,000	45
11	1,200	17,800	178,250	36
12	0	0	472,000	18
13	4,650	94,500	2,032,500	36
14	0	126,000	378,000	36
15	0	0	962,000	18
16	0	0	524,000	18
17	2,150	42,600	254,000	18
18	0	0	11,000	3.6
19	3,200	52,000	360,000	36
20	6,350	436,500	94,500	18

Table 4. The number of casts, cells and the amount of protein in the total twelve hour collection of urine.- Addis count (20 cases)

Urinary sediment	Range of counts	Average count.
Casts	0- 6,300	1,175
Red cells	0- 438,000	61,325
White & epithelial cells.	9,000-2,032,500	366,710
Protein(mg)	3.6 - 45	22.25

Table 5. The range and average Addis counts in normal children (20 cases).

It will be seen from Tables 4 and 5 that the results obtained in this small series are very similar to those in normal children by Lyttle (1933) and Snoke (1937) (Table 2). In one case (number 13) the white cell count was above the upper limit of 2,000,000. The proposed upper limits of normal for the cellular content of the urinary sediment or Addis count suggested by Snoke (Table 2.) have been accepted and are used when the Addis count is applied to the cases of nephritis which follow.

2. ACUTE HAEMORRHAGIC NEPHRITIS.

(1) RESULTS OF ALL CASES. Of the 251 cases in this group, 27 could not be traced owing to war time conditions, 5 were omitted as the specimens of urine were unsatisfactory and one case was discarded because the child, who had made

an apparent recovery from the initial stage, had been killed in a street accident. This reduces the number of cases followed to 218. They were classified according to the stages in the plan laid down by Addis (see page 14).

Stage at present.	Duration of the disease.	Number of cases.	Percentage of total.
(1)Recovered		159	72.9
(2)Latent.	under 2 yrs. over 2 yrs.	6) 35) 41	2.2) 15.6) 18.8
(3)Active		none	-
(4)Terminal		3	1.4
(5)Died		15	6.9
		Total.218	

Table 6. Stage of nephritis at last examination (218cases).

On the first examination, the results obtained differed somewhat from those given in Table 6. It was found that 156 cases had recovered and that 44 were in the latent stage. The condition of those in the terminal stage, and the number of deaths remained the same. Of the 44 patients in the latent stage, 16 had been followed for less than two years and 28 for more than two years since the initial attack. During subsequent examinations, 10 of the 16

patients in the under two years group, passed into the over two years group which was therefore increased to 38 patients. Of those 10 patients 3 were found to have recovered, while the remaining 7 patients could be definitely placed in the latent stage. The results were finally arranged as shown in Table 6, that is, of the 218 cases, 159 (72.9 per cent) were found to have recovered, 41 (18.8 per cent) were in the latent stage and of these 35 (15.6 per cent) had been followed for more than two years after the initial attack and were therefore unlikely to heal. The remaining 6 cases, which had been followed for less than two years, may heal or remain in the latent stage. Not one patient was found to be in the degenerative (active or subacute) stage. In the terminal stage there were 3 (1.4 per cent) patients, and 15 (6.9 per cent) had died. The probable eventual mortality rate will be the sum of the cases in the terminal stage, those who have been in the latent stage for over two years and those who have died, that is, 35+ 3 + 15 = 53 cases which is 24.3 per cent of the total number of cases. This does not include the future of the 6 cases in the latent stage which have been followed for less than two years. Some of these may pass into the terminal stage. Therefore 24.3 per cent is probably a low estimate of the eventual mortality rate.

(2) RESULTS IN THE DIFFERENT STAGES.

(2) RESULTS IN THE DIFFERENT STAGES.

On re-examination, the cases in the recovered and latent stages were found to be well clinically. In the terminal stage, the mothers stated that the children were not thriving and one child had definite symptoms, in the form of polyuria, thirst and occasional headache.

The state of nutrition (Table 7.) of the children in recovered and latent stages was fairly good in comparison with that of the average child admitted to hospital, although the nutrition in the latent stage was slightly less satisfactory than that in the recovered stage. The three children in the terminal stage were under average weight and height and poorly nourished. One of these three had a dry wrinkled skin and all had pale sallow complexions.

Stage at present.	Number of cases.	Percentage of Children Over	Average	Under.
Recovered	159	15.9	47.6	36.5
Latent	41	9.8	34.1	56.1
Terminal	3	-	-	3.

Table 7. The percentage of children in each stage over, under and of average weight and height.

It will be seen (Table 8.) that there is little association between acute infections and exacerbations of nephritis after the initial attack. In the recovered stage, 14 children had acute infections, that is, diphtheria (4 cases) scarlet fever (3 cases), pneumonia (3 cases), measles (2 cases), tonsillitis (1 case) and herpes zoster (1 case). In only one case (pneumonia) was there a concomitant exacerbation of nephritis. In four other cases there were relapses without obvious associated infection. In the latent stage, there were 7 cases of acute infection, comprising, tonsillitis, rheumatic fever, scarlett fever, influenza (2 cases) and diphtheria (2 cases). Only with the two cases of influenza was there mild haematuria lasting for a few days. Three other cases had relapses without evidence of infection. In the terminal stage, one child had measles with relapse, and another child had a relapse without an associated infection.

In assessing the relationship between infection and relapse, the probability of subclinical nephritis with an infection, or mild unnoticed upper respiratory infection with a relapse has to be remembered.

Stage at present.	Number of infections.	Number of relapses.	Number of infections + relapses.
Recovered	14	4	1
Latent	7	3	2
Terminal	1	1	-

Table 8. The number of acute infections and relapses taken separately and together after dismissal from hospital.

THE NON-PROTEIN NITROGEN.(N.P.N.), was estimated in all cases and the results are given in (Table 9.)

Stage at present.	Number of cases.	N.P.N. results mg.% Range.	Average.
Recovered	159.	16.5 - 38	25.6
Latent. under 2 yrs.	6)	22.7 - 36.1)	
Latent. over 2 yrs.	35) 41.	22.7 - 30.7)	30.3.
Terminal.	3.	41.7 - 55.5	51.6.

Table 9. Non-protein nitrogen (N.P.N.) results. The range of and the average non-protein nitrogen readings in each stage.

The non-protein nitrogen readings (range and average) were, therefore, within the normal limits (20-40 mg.per cent) in

the recovered and latent stages, although the readings of those in the latent stage were higher. In the terminal stage, all the readings were above normal and a mild degree of nitrogen retention was present.

HYPERTENSION. All the blood pressure readings in the recovered and latent stages were within normal limits. In the terminal stage, only one case (F.G.) gave a reading of 120/80, therefore even in this stage, hypertension was not a prominent finding. There was no cardiac enlargement and the optic discs showed no abnormality on examination.

THE URINE AND ADDIS COUNTS. In each of the 159 cases in the recovered stage, the urine was clear to routine tests and on microscopic examination. The Addis counts were normal.

In 25 of the 41 patients in the latent stage, routine tests showed the urine to be clear but the Addis count was raised; 15 had a trace to a cloud of albumin with raised Addis counts and one case had only a faint trace of albumin in the urine with a normal count.

In the terminal stage, the three cases had abundant albumin in the urine, with occasional red cells, white cells or casts on microscopic examination. The Addis counts were all raised. The albuminuria in the latent and terminal stages was not orthostatic.

The range and average Addis counts in each stage are given in Table 10.

Stage.	No.	Casts.	Red Cells.	White + epithelial cells.	Protein (mg.)
Recovered.	159.	R.0- 8,650.	0- 552,000	0-7,695,000	3- 36
		A. 842.	75,445	486,325	19.79
Latent.	41.	R.0- 22,600	517,000- 6,324,000	0-2,360,000	36-90
		A. 6,725	1,386,000	654,510	72.
Terminal.	3.	R. 0-58,000	960,000- 3,670,000	45,000- 4,860,000	320- 1230
		A. 16,940	2,071,330	1,625,000	735

Table 10. Addis counts. The range (R.) and average (A.) Addis counts in each stage.

From Table 10, the average counts for casts, cells and protein in the recovered stage were seen to be within normal limits. In the latent stage many of the cast and white cell counts and all except one of the red cell counts were above normal, the average red cell count, therefore, was higher than the normal upper limit and the cast and white cell counts were high, although not above the upper limit of normality.

In the terminal stage the average counts were well above the upper normal limits.

The amount of protein in the urine is within normal

limits in the recovered stage but is high in the latent and terminal stages, although lower than the results given by Addis. (Table 3.)

The Addis counts in the three different stages will now be considered.

(a) In the recovered stage, the 159 patients were divided into two groups.

Group 1. 120 patients who had been admitted to the wards between 1938 and May 1943. Three of this group had at first been in the latent stage, On subsequent examination, the Addis counts, which had been raised, returned to normal and have remained so for more than one year.

Group 11. 39 patients who were admitted from May 1943 to December 1944 and who were examined at regular intervals after dismissal. The final Addis counts of these 39 patients have been taken with the 120 counts from Group 1 to give the average Addis counts of the total 159 cases in the recovered stage. The results are shown in Table 11.

Number of patients.	Casts.	Red Cells.	White + epithelial cells.	Protein (mg.)
(1) 120 (R	0-4,250	0- 552,000	0- 7,695,000	3-36
(A	755	67,960	601,800	20.5
(11) 39 (R	0-8,650	0-584,000	0- 1,640,000	3.6-36
(A	930	82,930	370,850	19.08
Total (R	0- 8,650	0-552,000	0-7,695,000	3- 36
159 (A	842	75,445.	486,325	19-79

Table 11. The Addis counts in the recovered stage (159 cases). The range (R) and average (A) counts for all elements are given in Group 1- 120 cases, and Group 11- 39 cases and for the total 159 cases.

From Table 11, it is seen, as already stated, that the sediment counts in the recovered stage are within the normal limits suggested by Snoke (Table 2). The average cast count was rather less than that in normal children although the zero counts were also low- (52 per cent.). The average red cell count was very similar to that of Snoke but rather higher than that of Lyttle (Table 2). The zero red cell counts in Group 11. were only 30.75 per cent which is less than the findings of either Snoke (55 per cent) or

Lyttle (67 per cent). The lower percentage of zero cell counts in this group may be due to the fact that these children have only recently entered the recovered stage, and the red cells may diminish when recovery is prolonged. The white and epithelial cell counts are very similar to those of normal children. The range of protein levels and the average level of 19.79 mg. were in close agreement with the values of other workers. In the 39 patients in Group 11 an attempt was made to estimate the time taken for the Addis count to return to normal after the initial attack. On dismissal from hospital, the urines of 36 of the 39 patients were clear to routine chemical and microscopic tests, but in the other 3 cases the urine contained a faint trace of albumin and on microscopic examination an occasional red cell was seen. The Addis counts were done on dismissal and in all cases the urinary sediment contained an excess of casts, cells and protein. Addis counts were repeated at intervals after dismissal in those 39 cases and in 5 others, who remained in the latent stage and will be discussed in that stage.

Table 12 gives the range and average counts for red cells on dismissal.

Duration of disease, in weeks.	Number of cases.	Red Cells. Range.	Average
3	3	1,765,000- 6,782,000	4,472,000
4 - 6	19	1,262,000- 24,676,000	9,161,400
6 - 8	7	1,260,000- 14,210,000	3,717,400
8 - 10	4	1,324,000- 11,200,000	3,889,000
10 - 12	3	2,300,000- 3,845,000	2,541,600
12 - 14	2	1,945,000- 1,962,000	1,953,000
14- 16	-	- -	-
16 - 18	1	- -	1,720,000

Table 12. The red cell Addis counts on dismissal (39 cases) with the duration of the disease in weeks.

The results are all well above the normal upper limit of 600,000. It is difficult to correlate the average red cell counts with the duration of the disease. The highest average count was obtained in the 4 - 6 weeks group but as the time interval lengthened the average count tended to fall. All but one of the 39 cases were dismissed within 14 weeks of the onset of the initial attack.

The Addis counts for casts and white and epithelial cells were also done, but have not been tabulated in detail, the red cell levels being considered more important as an aid to prognosis. The cast counts were all above the upper

limit of 10,000 and were of blood, granular amd hyaline types. Similarly the white cell counts were higher than 2,000,000 in most cases. The range of cast and white cell counts, together with the average results, are tabulated with the red cell counts in Table 13.

Casts.	(R)	11,300 - 89,000,000
	(A)	24,6000.
Red cells.	(R)	1,260,000 - 24,576.000
	(A)	3,927,500.
White cells + epithelial cells.	(R)	480,000 - 10,650,000
	(A)	2,938,940.

Table 13. Total Addis counts on dismissal (39 cases). The range (R) and average (A) cast, red cell and white cell counts are shown.

Many cases on dismissal had Addis counts of red cells well below the 10 million level. Within 11 weeks from the onset, 36 of the 39 patients had been dismissed and of this number, 25 had red cell counts less than 10 million. Of the remaining 11 cases, in which the red cell count was greater than 10 million, 9 had been dismissed within 5 weeks and the other 2 within 7 weeks of the onset. In 3

of these 11 cases, the counts had fallen to below the 10 million level by the end of 7 weeks, in 5 cases by 9 weeks, in 2 by 10 weeks and in the last case by 11 weeks, from the onset. The average time taken therefore, for the majority of the 39 cases to reach the 10 million red cell level is 9 weeks, with 3 weeks as the shortest time and 11 weeks as the longest time.

The interval from the onset of the initial attack to the return of the red cell Addis count to normal levels is shown in Table 14.

Time in weeks.	Number of cases	Percentage of total.
12 or less	3	7.7
13 -16	19	48.7
17- 20	11	28.3
21- 24	4	10.2
25- 28	-	-
29- 32	1	2.55
52	1	2.55

Table 14. Time (in weeks) taken for Addis red cell counts to return to normal i.e. below the level of 600,000.)

From the above results, 48.7 per cent and 7.7 per cent that is, 56.4 per cent (22 cases) of the red cell counts

had returned to below the upper normal limit (600,000) by 16 weeks, 84.7 per cent (33 cases) by 20 weeks and 94.4 per cent (37 cases) by 24 weeks. In the remaining 5 per cent (2 cases) the time taken was longer, in the first, 29 weeks and in the second 52 weeks. The details of these 2 cases are given;-

(1) M.W. 6 yrs. female. On dismissal from hospital on 12.9.44 after a mild attack of nephritis, the urine was clear by routine tests and the Addis red cell count was 1,262,000. The urine was examined at four weekly intervals after dismissal, but the Addis red cell count remained raised, that is, 1,074,000 to 914,000 until 14.3.45, when the count was 252,000. Since that date, that is, for more than nine months, the count has remained normal.

(2) M.McM. 7yrs. female, was dismissed from hospital on 10.4.44 as a measles contact, three weeks after the onset of the initial attack. The urine at this time, contained a trace of albumin and on microscopic examination, showed red cells. The Addis count on dismissal was; Casts 148,000, red cells: 168,000,000 and white cells 4,600,000. The child had intermittent haematuria at home for a few weeks but this cleared. She went on holiday and was not seen at hospital again until 21.9.44 when she was re-admitted with mild haematuria. In the interval, the Addis count was not known. She was dismissed four weeks later on 20.10.44 7 and a half months after the onset of the initial attack.

At this time the Addis count was: Casts 12,600, red cells 3,480,000 and white cells 1,284,000. The red cell count remained elevated until 16.4.45, that is, 24 weeks after re-admission and 52 weeks after onset of the initial attack. For more than eight months the count has remained within normal limits.

The shortest time taken, therefore, for the Addis red cell count to become normal is 12 weeks from the onset of the initial attack, and the longest time is 52 weeks. If the two reported cases (M.W and M.McM.) are omitted, the average time taken for the red cell count to become normal is 16 weeks (110 days). Each of the 39 patients had normal counts by the end of one year and with one exception by the end of 29 weeks.

In the present series, it has been accepted that recovery is not complete unless the Addis counts have been normal on numerous occasions for more than one year. The duration of the normal counts in the 159 children in the recovered stage is shown in Table 15.

Time in years.		½-1	1-1½	1½-2	2-3	3-4	4-5	5-6	6-7	7+
Number of patients. Group 1.	120.	-	-	27	34	14	15	20	9	1
Group 11.	39.	6	4	15	14	-	-	-	-	-
Total.	159.	6	4	42	48	14	15	20	9	1

Table 15. Duration of normal Addis counts in Groups 1. and 11. of the recovered stage. (159 cases).

From the above figures it can be seen that 153 cases have had normal Addis counts for one year or more. Indeed 106 have had normal counts for more than two years. Therefore 153 cases are in the definitely recovered stage. Of the remaining 6 cases, 5 have normal counts for almost one year and the last case for eight months. These cases will probably heal completely and have been included for the present in the recovered stage.

(b) In the latent stage, repeated Addis counts were done on the urinary sediments of the 41 patients, 5 of whom were followed from the time of dismissal. The results of the final counts are given in Table 16.

Number of patients.		Casts.	Red cells.	White Cells	Protein (mg)
(1)under 2yrs.	(R	0- 15,600	690,000- 1,056,000	84,600- 720,000	11.4-25.2
6	(A	9,990	860,150	305,800	18.
(2)over-2yrs.	(R	0- 22,600	517,000- 6,324,000	0-2,360,000	10.8-44
35	(A	6,163	1,419,370	712,130	27.72.
Total.41	(R	0- 22,600	517,000- 6,324,000	0-2,360,000	10.8-44
	(A	6,725	1,386,570.	654,510	26.64.

Table 16. Final Addis counts (R-range)and(A- average) in the latent stage (41 patients).

The counts are given for Group 1.those in the latent stage for under 2 years and for Group 11. those who have been in this stage over 2 years.

From Table 16, it is seen that the average counts in Groups 1. and 11.are higher than those obtained in normal children or in children in the recovered stage, although only the red cell count in all cases is above the upper normal limit (600,000). There were no zero counts for red cells but 50 per cent of the cast counts were zero. This may account for the low average figure, since the majority of the counts in which casts were present, were found to be above the upper limit of normal. The Addis counts of the 5 cases followed after dismissal from hospital and remaining

in the latent stage, are given in detail at the end of this section.

In Group 1. are the 6 cases who have been followed for under two years. Three of them, however, have been followed for more than one year and the other 3 for more than one and a half years. These 6 cases give Addis counts for red cells, white cells and protein of lower readings than do the 35 cases in Group 11 which have been followed for more than two years, and may therefore heal within the two year period.

The time from the onset of the initial attack to the final examination in each case is given in Table 17.

Time from onset in years.	1-1½	1½-2	2-3	3-4	4-5	5-6	6-7	7 +
Number of cases.	3	3	2	7	7	8	7	4

Table 17. Interval between the onset of initial attack and the final Addis count in the latent group (41 cases).

(c) In the 3 cases in the terminal stage, the Addis count was done at each examination. The results of the repeated counts are given in Table 18.

Number of cases	casts.	red cells	White + epithelial cells.	Protein (mg.)
3 (R)	0- 58,000	960,000- 3,670,000	45,000- 4,860,000	320-1230
(A)	16,940	2,071,330	1,625,500	735.

Table 18. The Addis counts in the terminal stage (3 cases).

R-range. A- average.

From Table 18, it may be noted that the average counts in the terminal stage were above the normal upper limits and higher than the average counts in the recovered and latent stages. There were no zero counts for casts, which were of granular and hyaline types. The broad renal-failure casts, described by Addis in this terminal stage, were not prominent. The amount of protein in the urine was also high, but rather less than in the results given by Addis (Table 3.)

As already stated, when a child did not give normal results to all the preceding tests, the serum proteins and cholesterol were estimated and the renal function tested further by the urea clearance and concentration tests. The total serum proteins and blood cholesterol were estimated in 20 of the patients in the latent stage and in one of the 3 cases in the terminal stage. The results are

shown in Table 19.

Stage	No.	Total protein gm. %	Albumin gm. %	Globulin gm. %	Whole blood cholesterol mg. %
Latent	20.	R 5.04-8.18.	2.67-4.93	1.90-3.79	54-157.2
		A 7.02	4.08	3.02	78.4
Terminal	1.	R -	-	-	-
		A 6.1	3.4	2.7	98.4

Table 19. Serum protein and blood cholesterol levels in latent and terminal stages.

R- range and A- average.

In the latent stage, the average total protein, albumin and globulin estimations were within normal limits. Only two of the total protein estimations were less than 6 gm. per cent and in these cases the albumin was also low but greater than 2.5 gm. per cent.

In the terminal stage, both the total protein and the albumin fraction levels were rather low.

The blood cholesterol values in both the latent and terminal stages were within the normal limits.

The urea concentration and clearance tests were estimated in 25 of the 41 patients in the latent stage and in the 3 cases in the terminal stage.

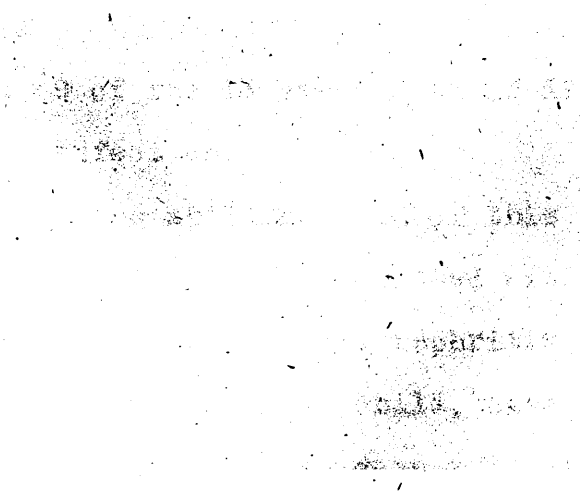
Stage	No.	Urea Conc. gm.% urea.	Urea clearance in % of normal	
			before urea.	after urea.
Latent	25	(R 1.625- 4.28	47 - 170	45- 150
		(A 3.425	107.8	91.3.
Terminal	3	(R 1.2 -2.1	42 - 85	34 - 54
		(A 1.51	56.	45.6

Table 20. Urea concentration (conc.) and clearance tests in the latent and terminal stages.

In the urea concentration test of MacLean, the lower limit of normality is a concentration in the urine of 2 grams urea per cent two hours after 15 grams of urea have been given. In two of the above 25 cases in the latent stage, the concentration was less than 2 grams per cent. The only other abnormal finding was the raised Addis count. In each case the urea clearance test was normal, as were the non-protein nitrogen and blood pressure readings. Similarly three cases gave clearances of less than the accepted lowest limit of 60 per cent of normal. In two of these cases, the clearances, before urea was given, were below normal but after urea had been given, were over 60 per cent of normal. The third case showed a fall in the urea clearance after urea had been given. In each of these cases, the urea concentration was normal. These 5 cases have been

included in the latent stage at present but may soon pass into the terminal stage. The other cases in the latent stage had urea concentration and clearance tests well above the lower limits of normality.

In the terminal stage, the urea concentration and clearance tests were found to be below the lower normal limits, although in one case, the urea concentration was just above normal - 2.19 per cent, with a urea clearance of 85 per cent of normal (before urea) but falling to 49 per cent of normal (after urea).



(3) CAUSES OF DEATH IN CASES FIRST SEEN IN THE INITIAL STAGE.

Of the 251 cases of acute haemorrhagic nephritis, 18 had died, but 3 of these were discarded. One had been killed in a street accident; another had died of tuberculous meningitis and the third child, who had Banti's disease, died at home three years after dismissal apparently of that disease.

The remaining 15 cases have been divided into 2 groups:

(A) 13 cases who died in the acute stage;

(B) 2 cases who were first seen in the initial stage before 1938 and had been followed to the terminal stage.

(A) Of the 13 cases in this group the cause of death was

I. Infection

II. Uraemia

I. Infection. 9 of the 13 cases died of different types of infection.

(a) Pneumonia. Three children died of this infection. Two, aged 4 years and 5 years, were admitted with bronchopneumonia and coincident acute haemorrhagic nephritis. They died shortly afterwards. The third child, aged 7 years, developed lobar pneumonia seven days after admission and died. In none of these cases were the sulphonamide drugs used.

(b) Peritonitis. One child, aged 5 years, died of

peritonitis, which developed eight days after admission to hospital. The nephritis had shown no sign of healing.

(c) Gastro-enteritis. One child, aged 2 years, was admitted to hospital with acute nephritis, vomiting and diarrhoea of several days duration. These symptoms did not clear up and the child died twelve days later.

(d) Suppurative pericarditis. A child, aged 8 years, with a history of right otitis media and haematuria of four days duration, collapsed and died soon after admission and at post-mortem examination suppurative pericarditis was found.

(e) Meningitis. Two cases, aged 3 years and 4 years respectively died of pneumococcal meningitis, developing one day and seven days after admission. The first case, after one dose of sulphapyridine, was transferred to a fever hospital where he died. The other child was given full doses of soluseptasine without avail.

(f) Diphtheria. At the height of the initial stage of acute nephritis, one child developed diphtheria and died later in a fever hospital

11. 'Uraemia' which is divided into 2 groups:

(a) Acute hypertensive encephalopathy. Two cases with acute haemorrhagic nephritis had purpuric spots at the onset of the attack. One case also had swollen joints, while the other had abdominal pain and melaena suggestive of anaphylactoid purpura. In both cases there was persistent

hypertension and nitrogen retention. Ten to fourteen days later, convulsions started and papilloedema was noted. Coma and death resulted, in spite of treatment.

(b) True Uraemia. Two cases (J.A. and J.R.) were admitted with acute nephritis and progressed through a comparatively rapid course, lasting six to twelve weeks, to death.

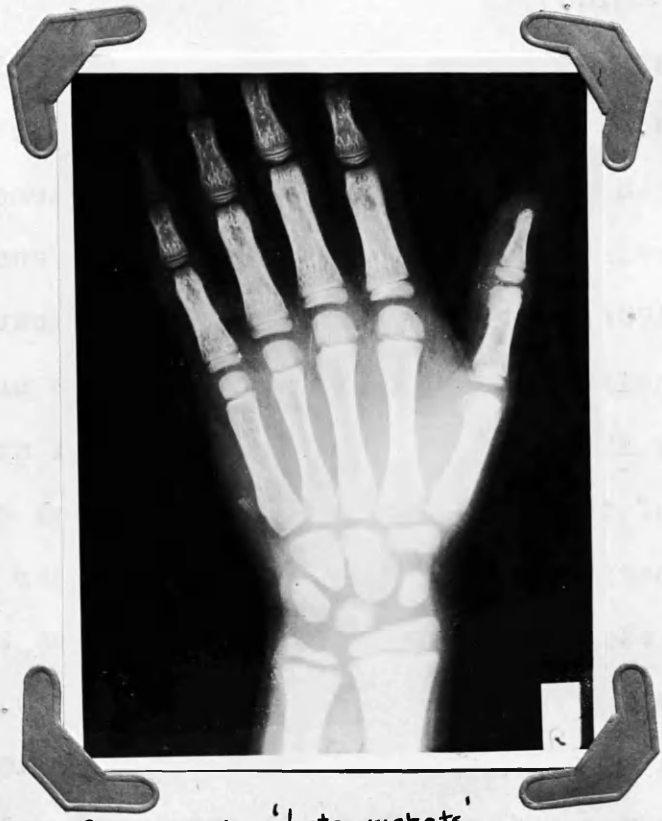
(1) J.A. (female) aged 7 years, was admitted on 17.9.44 with generalised anasarca, albuminuria and haematuria following tonsillitis. There was no hypertension but the non-protein nitrogen was 69.4 mg. per cent. During the next six weeks there was little change apart from occasional vomiting and a rise in the non-protein nitrogen level to 200 mg. per cent. Treatment had no effect and at the end of this time, there was marked epistaxis and slight vaginal bleeding. The child became anaemic and a blood transfusion of 300 cc. was given, but the condition deteriorated with a rise in blood pressure and increased nitrogen retention. Septic skin lesions developed. She became very drowsy and comatose and died on 29.11.44. At post mortem examination, there was terminal bronchopneumonia and right otitis media. The kidneys were large and oedematous with a broad yellow-red cortex. The capsules stripped easily.

(2) J.R. (male) aged 2 years 9 months, was admitted on 11.5.42 with generalised oedema, albuminuria and haematuria following otitis media. He passed through a course similar to that of J.A. and died six weeks later with nitrogen

retention, and uraemia.

(B) The 2 remaining cases are included here, because although well clinically after the acute initial attack they passed from the latent to the terminal stage over a period of years and died of uraemia.

The first patient was followed during the latter part of illness. (1) A.A. (male) was first admitted in June 1936, aged 3 years 3 months, with acute haemorrhagic nephritis following tonsillitis. This attack soon cleared and in August 1936, the urine was said to be clear. In April 1937, tonsillectomy was performed and the urine was clear. In May 1940 (4 years after the initial attack), he complained of tiredness, thirst and nocturnal eneuresis but did not report back to the hospital until May 1943, aged 10 years. In addition to the previous symptoms he was drowsy at times. He was a small thin sallow boy. The urine contained abundant albumin and a few granular casts. The Addis count was raised- casts 61,000: red cells 28,000,000 and white cells 3,500,000. There was hypertension and cardiac enlargement but no changes in the optic discs. The non-protein nitrogen was 142.9 mg. per cent and the blood CO2 was 45.8 vols. per cent. The urea concentration was 1.13 gm. per cent after 2 hours and the urea clearance was only 4.6 per cent of normal. The serum calcium was 9.7 mg. per cent, phosphorus 3.1 mg. per cent and the phosphatase 10.0 units. He was markedly anaemic with a haemoglobin of



Skiagram 1. 'Late rickets'
taken 22.5.43.

65 per cent. A skiagram of the wrist showed 'late rickets' - skiagram 1. On 23.5.43, in view of the acidosis and the rickets, it was decided to give him sodium bicarbonate and calcium lactate gr. 30 of each three times daily and adexolin m.10 thrice daily (21,6000 units vitamin A + 3,600 units vitamin D.) He remained fairly well on this treatment and was discharged on 21.6.43, but on 10.7.43 he was re-admitted having had a generalised convulsion lasting one minute. He was drowsy and complained of headache. The non-protein nitrogen was 200 mg. per cent and the blood pressure 160/130. On 22.8.43 he was again drowsy and vomited. The nitrogen retention increased and there was bleeding from the gums. The serum calcium had fallen to 8.8 mg. per cent and the phosphorus had risen to 8.1 mg. per cent before death which occurred on 9.9.43. Postmortem examination showed that the kidneys were small and fibrotic with the capsule adherent to the granular surface of the kidney. Section showed a pale surface with complete obliteration of all normal markings.

(b) J.M. (male) aged 7 years, was first admitted on 26.12.34 with oedema and haematuria following tonsillitis. This attack cleared up, but in January, 1938 (3 years later) he complained of listlessness and drowsiness. Albuminuria, hypertension, nitrogen retention and acidosis were found. He ran a similar course to the boy A.A. and died on 26.5.38.

At postmortem examination the kidneys were secondarily contracted. The glomeruli were not differentiated and there was an increase in the perivascular tissue.

(4.) FACTORS INFLUENCING THE PROGNOSIS OF ACUTE NEPHRITIS.

Various factors may play a part in influencing the prognosis, that is, age, sex, intensity and duration of the initial attack, type of preceding infection, nitrogen retention, and hypertension.

(1) Age. The relationship between the age at the onset of the initial attack and the prognosis is shown in Table 21.

Age in years	Number of cases	Recovered stage	Latent stage	Terminal stage	Dead
0 - 4	55	38 (69%)	10 (18.2%)	---	7 (12.8%)
4 - 8	98	76 (77.5%)	14 (14.3%)	3 (3.1%)	5 (5.1%)
8 - 13	65	45 (69.2%)	17 (26.2%)	---	3 (4.6%)
Total.	218	159	41	3	15

Table 21. Age at onset in relation to the prognosis of the initial attack.

From Table 21, it is seen that of the total 218 patients, 55 are in the 0 - 4 years group and of these 69

per cent have recovered and 12.8 per cent died. In the 4 - 8 years group are 98 patients, of whom 77.5 per cent recovered and 5.1 per cent died. In the last age group are 65 patients and of these 69.2 per cent recovered and 4.6 per cent died. The recovery rate is fairly equal in each age group, but the death rate is highest in the youngest group. In the younger children, therefore, there is a greater chance of death in the initial stage but the oldest group tend more to pass into the latent and terminal stages. Thus the ultimate mortality rate does not differ very greatly in each age group.

(2) Sex. Of the 218 patients, 131 were boys and 87 girls. The boys therefore are more frequent in the ratio of 3.2 approximately.

Sex	Number of cases	Recovered stage	Latent stage	Terminal stage	Dead
Male	131	99 (75.5%)	20 (15.3%)	1 (0.8%)	11 (8.4%)
Female	87	60 (68.9%)	21 (24.2%)	2 (2.3%)	4 (4.6%)
Total.	218	159	41	3	15

Table 22. The relation between the sex of the patient and the prognosis of the initial attack.

Table 22 shows that 75.5 per cent of the 131 boys have re-

covered and 8.4 per cent died. Of the 87 girls, 68.9 per cent recovered and 4.6 per cent died. The recovery rate is fairly similar in boys and girls. The death rate in the initial stage is higher in boys, but more girls pass into the latent and terminal stages. The ultimate prognosis, therefore, is very similar in both sexes.

(3) Duration of the initial attack. It was thought that the length of the initial attack might have some influence on the prognosis.

Duration in weeks	Number of cases	Recovered stage	Latent stage	Terminal stage	Dead
less than 6	66	43 (65.2%)	14 (21.2%)	---	9 (13.6%)
6 -12	98	85 (86.7%)	10 (10.2%)	---	3 (3.1%)
12 - 18	41	24 (58.6%)	11 (26.8%)	3 (7.3%)	3 (7.3%)
18 - 24	8	4 (50%)	4 (50%)	---	---
More than 24	5	3 (60%)	2 (40%)	---	---
Total	218	159	41	3	15

Table 23. Duration of the initial attack in weeks in relation to the prognosis.

From Table 23, it will be seen that the duration of the initial attack was less than 6 weeks in 66 patients, of whom 65.2 per cent recovered and 13.6 per cent died. Of the 98 patients in the 6 12 weeks group, 86.7 per cent recovered and only 3.1 per cent died. In the 12 - 18 weeks group are 41 patients, of whom 58.6 per cent recovered and 7.3 per cent died. Of the 8 patients in the 18 - 24 weeks group, there are 50 per cent in each of the recovered and latent stages. In the last group, 60 per cent recovered and 40 per cent were in the latent stage.

The recovery rate was higher in the attacks of shorter duration, especially in the 6 - 12 weeks group, in which only 3.1 per cent died and 10. 2 per cent became latent. The groups of longer duration had very similar recovery and chronicity rates. The number of deaths in the initial stage was highest, (13.6 per cent), in the under 6 weeks group, but more of the cases of over 18 weeks duration passed into the latent stage. It would appear that the optimum duration of the initial attack is 6 - 12 weeks, and that if the attack lasts longer, the prognosis becomes less favourable.

(4) The intensity of the initial attack has been divided into (a) mild (b) moderate and (c) severe, according to the condition of the patient at the onset and during the attack.

The results are shown on Table 24.

Intensity of initial attack	Number of cases	Recovered stage	Latent stage	Terminal stage	Dead
Mild	106	86 (81.1%)	18 (17%)	---	2 (1.9%)
Moderate	96	68 (70.8%)	18 (18.9%)	3 (3.1%)	7 (7.2%)
Severe	16	5 (31.25%)	5 (31.25%)	-	6 (37.5%)
Total	218	159	41	3	15

Table 24. Intensity of the initial attack in relation to the prognosis.

Of the total number of patients, 106 were in the mild group and 81 per cent recovered with 1.9 per cent dead. In the moderate group were 96 cases of which 70.8 per cent recovered and 7.2 per cent died. There were 16 patients in the severe group, 31.25 per cent of whom were in each of the recovered and latent stages and 37.5 per cent died. The rate of recovery therefore was in direct proportion to the severity of the initial attack. The death rate also rose from 1.9 per cent in the mild group to 37.5 per cent in the severe group.

(5) Preceding infection. It is commonly believed that a large proportion of the cases of acute haemorrhagic nephritis are preceded by an acute infection, especially of the upper respiratory tract and due, in many cases, to the haemolytic streptococcus. In the present series, the number and types of infection together with the interval between the onset of the infection and the onset of the initial attack are given in Table 25.

Present condition.	No.of cases	Without infection	With infect -ion	Infection Type	No.	Interval in days. R	A.
Recovered	159	58 (36.4%)	101 (63.6%)	Upper resp.	74 (73.3%)	0-35	11.6
				Pneumonia	8		
				Miscellan -eous	20		
Latent	41	15	26	Upper resp.	18 (69.2%)	0-21	13
				Miscellan -eous			
Terminal	3	3 (100%)	-	-	-	-	-
Dead	15	1 (6.7%)	14 (93.3%)	Upper resp.	9 (64.3%)	0-21	9.7
				Miscellan -eous	5		
Total	218	87 (39.9%)	131 (60.1%)				

Table 25. The types of preceding infections in relation to prognosis of the initial attack. R-range. A- average. resp.- respiratory.

From Table 25 we see that 131 (60.1 per cent) of the 218 patients gave a history of a preceding acute infection. In the recovered stage 63.6 per cent had a preceding infection, 63.4 per cent in the latent stage but in the terminal stage none of the 3 cases had a preceding infection. Of the 15 patients who died 93.3 per cent had a preceding infection. Therefore the percentage of cases with an associated infection was similar in the recovered and latent stages but much higher in those who died.

In each stage, upper respiratory infection, which included 'cold', tonsillitis and otitis media, was the most frequent type, accounting for 64.3 to 73.3 per cent of the infections in each stage. The miscellaneous group of infections were relatively uncommon, that is, scarlet fever, diphtheria, rheumatic fever, impetigo, ringworm, septic vaccination, abscesses, etc.

In all stages the interval in days between the infection and the onset of the clinical nephritis was calculated in each case. The range and the average intervals are shown in Table 25, and were found to be very similar in each stage.

It is shown, therefore, that the majority of the patients in each stage, apart from the terminal stage, had a preceding infection, especially of the upper respiratory tract, about ten to fourteen days before the onset of the nephritic symtoms, but that the type of infection played

no definite part in the prognosis of the initial attack.

(6) Effect of removal of septic foci. It has been suggested that recurrent or persistent infection may be a cause of the continued activity of the renal lesion in the latent stage.

Septic foci	Recovered stage.	Latent stage	Terminal stage
Total numbers	69	18	2
Foci removed initial attack.	46 (66.6%)	12 (66.6%)	-
Foci removed since dismissal.	3 (4.4%)	4 (22.2%)	-
Total removed.	49 (71%)	16 (88.8%)	-

Table 26. Removal of septic foci in relation to the prognosis of the initial attack.

In 89 of the 205 cases (excluding those who died), there were definite septic foci as shown in Table 26. In each of the recovered and latent stages, 66 per cent of the cases had septic foci removed in the initial attack. In the latent stage 88.8 per cent of the septic foci were removed, and 71 per cent in the recovered stage. The two children in the terminal stage did not have septic foci

removed. It is suggested that the removal of septic foci does not necessarily have any influence on the course of the initial attack.

(7) Season of the year. It has been found by many writers that the seasonal incidence of acute nephritis tends to correspond with that of the respiratory infection, especially streptococcal, that is, during the months of December to May.

Season	Total number of cases	Recovered stage	Latent stage	Terminal stage	Dead
(1)Jan-Mar	47 (21.5%)	33 (70.2%)	10 (21.3%)	-	4 (8.5%)
(11)April--June	47 (21.5%)	37 (78.8%)	7 (14.9%)	1 (2.1%)	2 (4.2%)
(111)July-Sept.	60 (27.4%)	37 (61.7%)	18 (30%)	-	5 (8.3%)
(1V) Oct--Dec	64 (29.6%)	52 (81.3%)	6 (9.3%)	2 (3.1%)	4 (6.3%)
Total	218	159	41	3	15

Table 27. The seasonal incidence of the onset in relation to the prognosis.

It will be seen that the evidence of the onset of the initial attack is fairly evenly divided throughout the year, with a slightly higher incidence in the early winter months

from October to December. The recovery rate was 61.7 per cent in the July-September period- but was fairly similar (70.2 - 81.3 per cent) in the other three quarters. The death rate was lowest (4.2 per cent) in the April-June period, but in fairly good agreement (6.2 - 8.5 per cent) in the other groups.

It would appear from Table 27. that the best prognosis is in the October-December group. the worst in the July-September group and that in the other months the ultimate prognosis does not differ very greatly.

(8) Nitrogen retention. The degree of nitrogen retention in each case was noted by the non-protein nitrogen levels which are shown in Table 28.

N.P.N. (mg.%)	Number of cases	Recovered stage	Latent stage	Terminal stage	Dead
under 40	114 (52.3%)	90 (78.9%)	22 (19.3%)	1 (0.9%)	1 (0.9%)
over 40	83 (38.1%)	57 (68.7%)	15 (18.1%)	2 (2.4%)	9 (10.8%)
not done	21 (9.6%)	12	4	-	5
Total	218	159	41	3	15

Table 28. The non-protein nitrogen (N.P.N.) results in the initial attack in relation to the prognosis.

Of the 218 patients, 114 (52.3 per cent) had normal non-

protein nitrogen values, 83 (38.1 per cent) had readings of more than 40 mg. per cent and in 21 (9.6 per cent) there was no record of the non-protein nitrogen results. Of the 114 patients with normal levels, 78.9 per cent recovered and 0.9 per cent died, and of the 83 cases with raised non-protein nitrogen, 68.7 per cent recovered and 10.8 per cent died. There is a slightly higher recovery rate and a lower immediate mortality rate in those cases with normal results; but there is no greater tendency for those cases with nitrogen retention at the onset of the initial attack to pass into the latent and terminal stage.

(9) Hypertension. The blood pressure readings were divided into three groups: Group (a) less than 110 systolic pressure; Group (b) more than 110 systolic pressure and Group (c) not done, that is, no record could be found. The findings are given in Table 29.

B.P. (systolic)	Number of cases.	Recovered stage	Latent stage	Terminal stage	Dead
under 110	77 (35.3%)	56 (72.7%)	15 (19.5%)	2 (2.6%)	4 (5.2%)
over 110	116 (53.2%)	83 (71.5%)	23 (19.8%)	1 (0.9%)	9 (7.8%)
not done	25 (11.5%)	20	3	-	2
Total.	218	159	41	3	15

Table 29. The blood pressure (B.P.) readings in the initial attack and the prognosis.

From Table 29 it may be seen that 77 (35.3 per cent) of the 218 patients had normal readings, 116 (53.2 per cent) had raised readings and in 25 (11.5 per cent) there was no record of the blood pressure having been taken. Of those with normal blood pressure, 72 per cent recovered and 5.2 per cent died and in those with higher blood pressure 71.5 per cent recovered with 7.8 per cent dead. The level of the blood pressure, therefore, at the onset of the initial attack is of little importance, but if the blood pressure remains elevated or rises in the latent stage the outlook is poor.

(10) Complications occurred in 3 groups (1) Hypertensive Encephalopathy; (11), Infections of various types (Table 30);

Upper respiratory infection includes 'cold', tonsillitis, cellulities, impetigo, retropharyngeal abscess, cervical abscess etc. The 'others' consist of peritonitis, gastro-enteritis and suppurative pericarditis and(111) Miscellaneous group which includes anaemia and epistaxis.

Complications	Number of cases	Recovered (159 cases)	Latent (41) (cases)	Terminal (3 cases)	Dead (15 cases)
1.Hypertensive encephalopathy	15	7	5	1	2
Uraemia	14	-	-	-	4
11.Respiratory infection	15	13	2	-	-
Pneumonia	10	7	-	-	3
Pulmonary Tuberculosis	5	4	2	-	-
Infectious fevers	10	8	2	-	-
Pneumococcal meningitis	2	-	-	-	2
Septic foci	7	5	2	-	-
'Others'	4	-	-	-	4
Total.	54.	37.	8.	-	9
111.Miscellaneous.	8.	6	2	-	-
Total.	81.	50 (31.4%)	15 (36.6%)	1 (33.3%)	15 (100%)

Table 30. Complications in the initial attack with relation to the prognosis.

The incidence of complications (Table 30) is very similar

in the recovered, latent and terminal stages (31.4, 33.3 and 36.6 per cent of the total number of cases in each stage), but is 100 per cent in those who died.

The commonest complications were hypertensive encephalopathy and upper respiratory infections. Hypertensive encephalopathy occurred in 15 cases, of which 13 (86.6 per cent) recovered and 2 (13.3 per cent) died, and of those 13 who survived the hypertensive attack, 7 recovered completely, 5 became latent and one passed into the terminal stage: 8 cases (53.3 per cent) therefore will most probably die. It would appear that hypertensive encephalopathy tends to affect the ultimate prognosis of the initial attack adversely. Of the 15 cases with upper respiratory infectious complications- 13 recovered and 2 became latent. Seven of the 10 cases which had pneumonia recovered and 3 died. Those cases which recovered had been treated with sulphonamides. In both cases of pneumococcal meningitis, sulphonamide treatment had been started before death, but the others had not been given this treatment.

From Table 30, it is seen that, if a child recovers from a complication other than hypertensive encephalopathy, then the ultimate prognosis does not tend to be affected by that complication,

(11) Oedema. The relationship of the degree of oedema in the initial attack to the prognosis is shown in Table 31.

Oedema	Number of cases	Recovered stage	Latent stage	Terminal stage	Dead
none	75	53 (70.6%)	15 (20%)	2 (2.7%)	5 (6.7%)
slight	55	45 (81.8%)	7 (12.8%)	1 (1.8%)	2 (3.6%)
moderate	34	27 (79.4%)	5 (14.7%)	- -	2 (5.9%)
marked	54	34 (63%)	14 (25.9%)	-	6 (11.1%)
Total.	218	159	41	3	15

Table 31. The degree of oedema in the initial attack in relation to the prognosis.

From these results it is seen that 75 of the 218 patients had no oedema; 70.6 per cent recovered and 6.7per cent died. Of the 55 patients with slight oedema, 81.8 per cent recovered and only 3.6 per cent died. There were 34 patients with moderate oedema, 79.4 per cent of whom recovered and 5.9 per cent died. In the group with marked oedema, were 54 patients of whom 63 per cent recovered and 11.1 per cent died. There is some relation, therefore, between the degree of the oedema and the prognosis of the initial attack, those with slight or moderate oedema having the best prognosis.

(12) Rest in bed and diet in the initial attack. In the present series of cases, both the duration of rest in bed and the variation in the diet were related to and depended upon the severity of the initial attack. Therefore there is no evidence that either, as a single factor, has any influence on the prognosis of the initial attack.

(5) CASE HISTORIES AND ADDIS COUNTS IN EACH STAGE.

The course of 8 cases with repeated Addis counts is given The first 6 cases were followed after dismissal until the Addis counts returned to normal and the last 2 cases were followed from the latent to the recovered stage, but not from the time of dismissal from hospital.

1. Recovered stage.

(1) R.C.(male) aged 6 years-dismissed on 28.12.44 four weeks after onset with urine clear to routine tests and has remained well.

Date	Casts	Red cells	White + epithelial cells
28.12.44.	89,000	14,131,000	6,495,000
19. 1.45	12,000	2,650,000	2,360,000
14. 2.45	6,420	882,000	680,000
27. 3.45	-	540,000	634,000
17. 4.45	-	395,000	485,000
12. 5.45	-	-	326,000
20.12.45	-	126,000	324,000

(2) E.T.(male) aged 7 years-dismissed on 11.2.44 four weeks after onset with urine clear and remains well.

Date.	Casts	Red cells	White + epithelial cells
11.2 .44	35,000	5,075,000	4,640,000
9.3 .44	11,000	1,481,500	1,865,000
8.4 .44	4,200	925,000	768,000
6.5 .44	-	498,000	526,000
18.8 .44	-	522,000	196,000
27.12.44	-	48,600	126,000
19.4 .45	1,200	54,300	286,000
14.11.45	-	-	48,000

(3) P.F. (male) 10 years - dismissed on 25.11.43, twelve from onset with urine clear. He had a relapse at six weeks, but was well on dismissal and remains well.

Date.	Casts.	Red cells.	White + epithelial cells
25.11.43	11,500	1,945,000	935,000
10. 1.44	1,200	586,000	428,000
6. 4.44	-	438,000	126,000
11. 7.44	-	386,000	424,000
5.10.45	1,400	126,000	234,000
14. 3.45	-	45,000	-
7. 6.45	-	-	-
9. 8.45	-	-	-
10. 1.46	-	124,000	84,000

(4) A.F. (male) 4 years- dismissed on 27.1.44 after five weeks from onset with urine clear and clinically well.

Date.	Casts	Red cells	White + epithelial cells
27. 1.44	15,500	11,053,000	3,159,000
9. 2.44	2,500	1,643,000	856,000
8. 3.44	-	432,000	540,000
31. 5.44	-	356,000	420,000
10.10.44	-	52,000	363,000
3. 3.45	-	-	520,000
3. 10.45	-	-	86,000

(5) E.K. (female) 7 years - dismissed on 22.12.44, five weeks after onset with urine clear. She has remained well

Date.	Casts	Red cells.	White + epithelial cells
22.12.44	57,000	13,848,000	10,650,000
4. 1.45	10,600	938,000	2,640,000
8. 2.45	3,600	520,000	468,000
5. 4.45	-	43,800	394,000
6. 9.45	-	-	96,000
10.12.45	-	-	126,000

(6) R.McC. (male) 12 years- dismissed on 9.12.44, five weeks after onset. Urine contained a faint trace of albumin but the microscopic examination was negative. On re-examination on 21.12.44 there was no albumin in the urine, which has since remained clear.

Date.	Casts	Red cells	White - epithelial cells
9.12.44	34,100	24,567,000	2,364,000
21.12.44	12,500	3,196,000	1,384,000
4. 1.45	4,640	936,000	258.400
7. 2.45	-	465,000	482,000
15. 3.45	-	125,000	132,000
19. 4.45	-	456,000	294,000
21. 6.45	-	-	184,000
23. 8.45	-	80,000	-
22.11.45	-	-	264,000

(7) F.G. (male) 10 years, had a mild attack of nephritis from 16.10.42 - 24.11.42 and was dismissed well.

7. 1.43. - urine clear
6. 3.43. - urine alb.faint trace.

		Casts.	Red cells.	White cells.
17.7.43.	- urine clear	4,400	726,000	792,000
18.4.44.	- urine clear	-	918,000	642,000
15.4.44.	- urine clear			
	Urea concentration = 3.5 gm.%			-
	Urea clearance - - -90% normal			
15.10.45	Urine clear	Casts -	Red cells 35,000	White cells. - -

Tests were satisfactory.

(8) C.R. (female) aged 3½ years had nephritis from 23.1.43 to 3.2.43 and was dismissed well.

		Casts	Red cells	White cells
18.5.44.	Urine - alb. trace	7,250	1,430,000	+++
	Tests satisfactory.			
8.6.45.	Urine clear	1,200	170,000	869,000
6.11.45	Urine clear	-	-	48,500
	Tests satisfactory.			

2. Latent Stage. A short summary is given of the 5 cases, followed from dismissal with repeated Addis counts, who remained in the latent stage.

(1) E.L. (male) 12 years- was dismissed on 11.3.44 with urine clear to routine tests and good renal function. This has not changed but the Addis red cell count remains raised.

Date.	Casts.	Red cells.	White cells
10.3.44	24,600	5,544,000	1,320,000
9.4.44	14,400	2,680,000	1,260,000
7.6.44	4,100	987,000	432,000
9.10.44	8,600	1,080,000	842,000
16. 4.44	-	780,000	250,000
30.10.45	1,400	945,000	86,000

(2) I.W. (female) aged 4 years- was dismissed well on 20.10.44.

Date.	Casts.	Red cells	White cells.
20.10.44	10,000	7,200,000	2,860,000
30.11.44	4,600	1,892,000	890,000
1. 2.45	3,200	1,126,000	404,000
6. 6.45	-	972,000	434,000
6.10.45	5,600	1,960,000	236,000

(3) H.B. (female) 9½ years- was dismissed well on 29.4.44. four weeks after the onset of a mild initial attack.

Date	Casts	Red cells	White cells.
28. 4.44	14,800	11,960,000	4,438,000
1. 6.44	10,600	4,320,000	2,986,000
10. 8.44	11,400	2,648,000	1,645,000
10.12.44	1,200	1,720,000	852,000
3. 5.45	-	912,000	684,000
29.10.45	1,400	1,690,000	1,364,000

(4) A.K. (female) 3 years - dismissed on 25.5.43, fourteen weeks after the onset of the initial attack. On dismissal the urine contained a trace of albumin and a few red cells, but since 8.9.43, the urine has been clear.

Date.	Casts.	Red cells	White cells
24. 5.43.	18,000	11,890,000	1,305,000
30. 6.43	11,000	2,453,000	4,680,000
8. 9.43	-	1,920,000	540,000
4. 2.45	1,200	784,000	368,000
30.10.45	-	1,690,000	482,000

(5) H.W. (male) 10 years- dismissed on 30.8.43, seven weeks after a second attack of acute haemorrhagic nephritis (the first attack was in October 1938 and lasted 19 weeks). The urine contained a trace of albumin on dismissal, but there was no nitrogen retention or hypertension and the renal function was good.

Date	Casts	Red cells	White cells.
29. 8.43	92,000	28,700,000	3,280,000
30. 9.43	24,500	16,710,000	2,465,000
26.10.43	11,400	2,890,000	1,480,000
5. 8.44	-	968,000	562,000
10.10.44	1,240	1,031,000	834,000
7.11.44	4,650	1,968,000	426,000
12.12.44	11,850	7,020,000	5,125,000
20. 3.45	-	1,369,000	236,000
27. 6.45	-	1,710,000	526,000
23.12.45	16,450	6,256,000	5,853,000

At times the urine was clear but at other times there was a trace to a cloud of albumin but there has been no evidence of renal failure.

3. Terminal stage. A short summary of each of the 3 cases in this stage is given.

(1) F.G. (female) 8 years, was in hospital from 23.11.42 to 12.2.43 with a moderately severe attack of acute nephritis. There was hypertension, nitrogen retention and poor renal function but these signs cleared up and on dismissal urine was clear. She was seen at intervals and urine was said to be clear until-

		Casts	Red cells	White cells
6. 9.44	Urine - alb. trace -but tests satisfact: :ory.	11,400	3.620,000.	2,960,000
18.5.45.	Child was small and pale. Polyuria and thirst. Urine - alb. + N.P.N. = 55.5 mg.% Urea concentration = 1.25 gm.% Urea clearance =54% of normal	-	1,522,000.	1,876,000
3. 8.45	I.S.Q. Serum Ca. and P. normal.	14,600	1,864,000.	2,480,000

(2) E.G.(female) 7 years was in hospital from 31.12.38 to 3.4.39 with a second attack of acute nephritis. She had a relapse while in hospital but on dismissal all renal function tests were normal, except that the urine contained a trace of albumin which was not orthostatic. From dismissal until June 1941, she had attacks of mild haematuria.

Date		Casts	Red cells	White cells
24.12.43	Urine clear N.P.N.=41.7 mg.%	3,800	1,880,000	2,180,000
8. 7.44	Urine alb. +	15,600	2,180,000	1,640,000
8. 6.45	Urine alb. ++ N.P.N. =55 mg.% Function tests unsatisfactory.	58,000	3,654,000	4,860,000

(3) L.G. (male) was in hospital from 8.4.42 to 21.6.42 when he was dismissed home as a chickenpox contact. On dismissal there was still slight nitrogen retention and haematuria: but these had cleared by 26.6.42 although there was still slight albuminuria.

13.8.42 - urine alb. tracebut tests satisfactory.

		Casts	Red cells	White cells
17. 7.43	Small thin child urine alb. + N.P.N. =50 mg.%	-	1,080,000	45,000
3. 8.45	Urine alb.++ N.P.N. =55.5 mg.%	20,000	960,000	282,000
16.10.45	Urine alb. ++ Urea conc.=1.29g% Urea clear=34% of normal.	14,600	1,360,000	684,000

3. THE NEPHROTIC SYNDROME.

(1.) RESULTS OF ALL CASES.

Of the 60 cases in this group, 8 could not be traced and therefore 52 cases, which had been admitted since 1933 were followed. The results of the investigation are given in Table (32).

Stage at present	Duration of the disease (years)	Number of cases	Percentage of total
(1) Recovered		14	26.9
(2) Latent	under 2 over 2	2) 6) 8	15.4
(3) Active	under 2 over 2	2) 4 2)	7.9
(4) Terminal		3	5.5
(5) Dead		Total 23/52	44.3
Probable eventual mortality		34	65.3

Table 32. The condition of the 52 cases of the nephrotic syndrome on final examination

From the above results, it is seen that 44.3 per cent of the cases had died either during the acute stage or subsequently. Of the 55.7 per cent alive, 14 (26.9 per cent) recovered, 8 (15.4 per cent) were in the latent stage, 4 (7.9 per cent) in the active stage and 3 (5.5 per

cent) in the terminal stage. Three patients have been in the recovered stage, for less than 2 years and may relapse as in the case of one child (A.W.)

A.W. was admitted on 29.8.44 aged 14 months. The signs of nephrosis cleared up after severe gastro-enteritis and she was dismissed home well on 1.10.44 with a clear urine. Thereafter she reported monthly to hospital. The urine remained clear with normal Addis counts until 10.11.45 (13 months after dismissal), when she had a relapse with albuminuria and slight oedema, which disappeared in three weeks time. She has been well since and the urine remains clear with normal Addis counts.

A recovery rate, therefore, of 26.9 per cent (14 cases) is perhaps too high in the nephrotic syndrome. Two cases have been in each of the latent and active stages for less than two years and may heal.

The probable eventual mortality rate will be 34 cases (23(dead)+ 6 (latent) + 2 (active) + 3 (terminal)-), that is 65.3 per cent. This may be a low estimate as those who have been in the latent and active stages for less than two years may not recover. The prognosis in the nephrotic syndrome is, thus, more grave than in acute haemorrhagic nephritis.

The time from the onset of the initial attack to the

final examination is shown in Table 33.

Time in years	Recovered	Latent	Active	Terminal
less than 1	1	2	1	-
1 - 1½	2	-	1	-
1½ - 2	-	-	-	1
2 - 4	5	3	2	1
4 - 8	4	3	-	-
8 -13	2	-	-	-
Total.	14	8	4	3

Table 33. Time from onset of the initial attack to the final examination.

From Table 33 it is seen that 7 patients have been followed for less than two years and of these, 3 have recovered, 2 are in the latent and 2 in the active stage,

(2). Results in different stages.

In the recovered stage, 2 of the 14 cases were unable to attend for examination. A short summary of each history is given.

(a) T.McG. who was admitted on 16.2.32 and dismissed on 15.7.32 much improved, is now 20 years old. He has been well since dismissal, has been in the Navy for two

and a half years and is at present overseas. It is thirteen years since his dismissal, therefore it is assumed that he has recovered.

(b) H.F., who was admitted on 15.1.37 and dismissed on 1.4.37, is now 17 years old. He weighs 10st.9lb., and has been well since dismissed. He is training to be an architect but lives too far from Glasgow to report back. He has been placed in the recovered group, as it is eight and a half years since his dismissal.

On examination the children in the recovered and the latent stages were well. In the active stage, all gave a history of intermittent puffiness of the eyes or swelling of ankles. Two had oedema, but were fairly well. The other two were attending school. In the terminal stage, one of the three cases had no complaint, but the others were easily tired. One had headache and the other polyuria and thirst.

The state of the nutrition in both the recovered and latent stages was good but was poor in the active and terminal stages. The two cases in the active stages, who were over weight, had oedema at the time of examination. As there is marked wasting as well as oedema in the active stage, the state of nutrition is often difficult to determine.

The results are in Table 34.

Stage	Number	Percentage over weight.	Percentage average weight	Percentage under weight.
Recovered	14	50	42.8	7.2
Latent	8	37.5	50	12.5
Active	4	50	-	50
Terminal	3	-	-	100

Table 34. The state of nutrition in the nephrotic syndrome.

Infection and relapse. From Table 35 it is shown that only a few cases had acute infections after dismissal and that there was no association between infection and relapses which were more frequent in the later stages.

Stage	Number	Number of infections	Number of relapses	Infection + relapses
Recovered	1	1	-	-
Latent	5	1	4	-
Active	2	-	2	-
Terminal	3	1	2	-

Table 35. The number of acute infections and relapses since dismissal.

Hypertension. The blood pressure readings were normal in the recovered, latent and active stages, but were raised in 2 of the 3 cases in the terminal stage, that is, 150/90 and 190/120.

Nitrogen retention. In the recovered, latent and active stages, the non-protein nitrogen results were within limits but in each terminal stage, there was mild nitrogen retention. The results are shown in table(36).

Stage	No.	N.P.N. results (mg.%) Range	Average.
Recovered	12.	20 - 38.5	27.8
Latent	8	20.8- 32	27.
Active	4	20.8- 38.5	30.5
Terminal	3	41.6- 83	58.2

Table 36. The non-protein nitrogen (N.P.N.) results in each stage.

Oedema. There was no oedema on examination in the recovered, latent and terminal stages, but 2 cases in the active stage had oedema of ankles.

Serum proteins. In the recovered, latent and terminal stages, the total protein and the albumin fraction were within normal limits. In the active stage, both the

total protein and albumin levels were low, less than the critical levels (5 gm. per cent total protein and 2 gm. per cent albumin) which are usually associated with the presence of oedema. Probably these levels were in proportion to the amount of albuminuria. The upset of the albumin/globulin ratio showed that the renal lesion was still active.

Stage.	No.	Total protein (gm.%)	Albumin (gm.%)	Globulin (gm.%)	Cholesterol (mg.%)
Recovered	12	R=6.01-8.6 A= 7.07	3.26-5.54 4.76.	1.91-4.24 2.47	53.8-98.2 69.9.
Latent	8	R=5.7-7.81 A= 6.84	2.48-4.66 3.86	2.25-3.57 2.96	60.4-96.8 79.47
Active	4	R=4.24-5.47 A= 4.95	1.12-1.74 1.64	2.50-4.08 3.28	188 -690 318.6
Terminal	3	R=5.62-6.90 A= 6.47	2.31-3.94 3.3	2.96-3.31 3.16	89-177.4 144.5

Table 37. Serum protein, total and fractional, and blood cholesterol results in each stage. (R= range. A=average).

Blood cholesterol. The results were normal in the recovered, latent and terminal stages, but high (average result more than 300 mg. per cent) in the active stage showing that the kidney lesion had not healed.

Urea concentration and clearance tests. In the recovered

latent and active stages, the results were well above the lowest limit of 60% of normal, although in the active stage the clearance of urea was poorer than in the other two stages. In the terminal stage, both tests were below the lowest normal level, indicating upset of renal function due to gross destruction of the kidney tissue. The results are given in Table 38.

Stage.	No.	Urea conc. gm. %	Urea Clearance in % of normal. before urea	after urea
Recovered	9	R=2.85-3.375 A= 3.18	90 - 180 130	66.5 - 135 104.5
Latent	6	R=2.4-3.05 A= 2.808	92.5 -140 108.4	118 - 179 142.
Active	3	R= 2.3 - 3.16 A= 2.7	70 -132 101	72 - 84 78
Terminal	3	R= 0.95-1.95 A= 1.34	18.5 -43 33.1	18- 36 24.3

Table 38. Urea concentration (conc.) and urea clearance tests in each stage. (R= range. A= average.)

The urine and the Addis counts. In the recovered stage, the urine was clear to the routine tests and the Addis counts were normal. It was not possible to do repeated counts on the urine of the 4 cases in this stage who were

dismissed during 1943- 1945 and who were followed at regular intervals from dismissal. These children were at first too young to co-operate in the collection of the urine, but later, specimens were obtained. In the latent stage, the urinary findings fell into 3 different groups (a) albumin + and Addis count raised - 6 cases.

(b) albumin + and Addis count normal- 1 case.

(c) urine clear and Addis count raised-1 case.

The amount of albumin in the cases in the latent stage varied from a trace to a cloud on different examinations. In each of the 4 cases in the active stage the urine contained abundant albumin and 2 of the 4 cases had mild haematuria at the time of examination. In the terminal stage, the urine contained a trace to a cloud of albumin. In both the active and the terminal stages the Addis counts were raised.

Stage	No.	Casts	Red cells	White - epithelial cells	Protein (mg.)
Recovered	12	R 0-3,400	0-357,000	0-602,000	4.3 - 50.4
		A 636	94,090	189,540	21.2
Latent	8	R 0-75,000	35,000-3,060,000	246,000-3,650,000	14 - 200
		A 11,456	1,420,500	1,068,750	73
Active	4	R 0-88,500	360,000-26,542,000	698,000-21,058,000	200- 1200
		A 35,875	10,096,750	6,598,000	900
Terminal	3	R 0-14,640	786,000-2,482,000	396,000-2,640,000	600 - 1200
		A 4,810	1,474,000	1,308,000	1,000

Table 39. The Addis counts R- range. A- average in each stage.

In Table 39 are the Addis counts in each stage. In the recovered stage, the counts are within the normal upper limits given by Snoke. The average red cell count is higher than that found in healthy children. This may be due to the fact that there are fewer zero counts (25 per cent) in the present cases, than in normal children. The average cast count is lower than normal, but the zero counts were high (75 per cent). This may account for the low average figure. The number of white cells and the

amount of protein are within normal average limits.

In the latent stage, the counts are above normal in 7 of the 8 cases. The child with the normal count, had a trace of albumin in the urine, but during her stay in hospital, did not have haematuria at any time. One other child (H.C.) had no haematuria in the initial attack but the Addis red cell count is now raised. In the 7 other cases, the casts, cells and protein gave values above the normal limits. There was only one zero count for casts . This was found in the case which had a normal red cell count.

In the active stage, the counts were higher than those in the latent stage. In 3 of the 4 cases, the red cell count was raised as well as the cast and white cell counts, but in the fourth case, although the cast and white cell figures were raised, the number of red cells was normal. This latter patient (S.M.) is the only one in this stage who was free of haematuria throughout the period in hospital. The degree of proteinuria was very marked, but slightly less than that obtained in this stage by Addis.

In the terminal stage, many of the counts were above the normal upper limits, but the only one with a raised average value was the red cell count. There were several zero cast counts which reduced the average figure to within normal limits, although much higher than the

average count in normal children or in those who have recovered from the nephrotic syndrome. The amount of protein in the urine was high, but in keeping with the levels given by Addis.

It will be seen, therefore, that Addis count is of value in deciding whether or not the kidney lesion has healed.

(3) Causes of death.

Twenty three of the patients in the nephrotic group were found to have died, and as in acute haemorrhagic nephritis, the causes of death were-

1. Infection
2. Uraemia
3. Unknown, that is, there were 2 cases in which the cause of death was uncertain.

1. Infection of different types was the cause of death in19 of the 23 patients:

(a) Bronchopneumonia. Of the 9 children who died of bronchopneumonia, 4 died in hospital one week to four months after admission, although in each instance 'sulpha' drugs had been used. After a long course in hospital 2 other children were transferred to a convalescent hospital, where they died three and four months later. The remaining 3 children died at home, one month to two and a half years after dismissal from hospital while still in the active stage. Of the last 5 cases, 3 had not been given 'sulpha' drugs and it is doubtful if the other cases

had been thus treated. The importance of such treatment in relation to the prognosis will be discussed later.

(b) Peritonitis was the cause of death in 8 children. Four of these developed pneumococcal peritonitis two days to three years after the onset of the initial attack. One of these four children had been re-admitted to hospital five times within three years prior to developing peritonitis. In the fifth child, who died suddenly soon after admission, the type of peritonitis was not known. The three remaining children were transferred to other hospitals before death.

(c) Meningitis. Two children died of meningitis. The first child (M.L.) had a meningeal haemorrhage with hemiplegia on 27.7.40, two months after admission. This progressed to septic meningitis (coliform) and she died on 17.8.40 in spite of sulphonamide treatment.

2. Uraemia. Two children after a prolonged course in the active stage, died of uraemia.

(a) One child (M.M.) was admitted on 4.1.36. Her condition remained unchanged until 16.3.36, when the non-protein nitrogen, which had been 40.7 mg.per cent rose to 87.7 mg. per cent although the oedema was still marked. By 1.6.36 she was very weak and had a convulsion lasting for five minutes. There was now hypertension and marked

nitrogen retention although the oedema and albuminuria remained unchanged. The serum calcium had fallen from 9 mg. per cent to 7.5 mg. per cent. On 5.6.45 there were further convulsions and she became comatose. She did not respond to treatment and died on 9.6.45 after a period of anuria.

(b) The second child (A.W.) was admitted on 4.8.33. After a long illness without improvement, a course of protein shock (T.A.B. injections) was tried without benefit. On 18.4 34 he was given 1 cc. salyrgan intravenously. Haematuria ensued and the oedema increased. By 30.7.34 the renal function tests were unsatisfactory. On 30.8.34 paracentesis abdominis was done and 136 ounces of fluid withdrawn. In this state he was taken home on 10.11.34. There he became very drowsy and two weeks later he died after having several convulsions.

3. Unknown. In 2 cases the cause of death was uncertain and permission to hold a postmortem examination was refused.

(a) The first child (R.M.) was admitted on 7.4.36. On 2.5.36 he was given 1cc. salyrgan intravenously with slight diuretic result. On 9.5.36 2 cc. salyrgan were given but shortly after the injection he collapsed and died.

(b) The second child (M.H.) was admitted on 21.2.41 with anasarca. She improved gradually and by 5.5.41

there was no oedema, but she suddenly became very listless, collapsed and died the following day. No cause of the collapse could be ascertained.

The cause of death in the 23 cases is charted in Table 40.

Cause of death	Number of cases	Percentage of total
infection	19	82.6
uraemia	2	8.7
unknown	2	8.7
Total	23.	

Table 40. Cause of death in the nephrotic syndrome (23 cases).

(4) FACTORS AFFECTING THE PROGNOSIS.

There are various factors which may affect the prognosis of the nephrotic group that is, age, sex, renal function, degree of oedema, urinary findings, hypertension, diet and treatment during the attack.

(1) Age. The relationship between the age at the onset and the prognosis is shown in Table 41.

Age in years	No of cases	Recovered	Latent	Active	Terminal	Dead
0 - 2	13 (25%)	7 (53.9%)	1 (7.6%)	1 (7.6%)	-	4 (30.9%)
2 - 4	8 (15.4%)	1 (12.5%)	-	1 (12.5%)	1 (12.5%)	5 (62.5%)
4 - 8	23 (44.2%)	5 (21.7%)	4 (17.4%)	2 (8.7%)	1 (4.4%)	11 (47.8%)
8 - 12	8 (15.4%)	1 (12.5%)	3 (37.5%)	-	1 (12.5%)	3 (37.5%)
Total 52		14	8	4	3	23

Table 41. Age at onset in relation to the prognosis of the initial attack.

From Table 41, it is seen that 13 (25 per cent) of the cases were under 2 years of age, and of these 53.9 per cent recovered and 30.9 per cent died. In the 2 - 4 years group were 8 cases (15.4 per cent) of which 12.5 per cent recovered and 62.5 per cent died. In the 4 - 8 years group were 23 cases (44.2 per cent); 21.7 per cent recovered and 47.8 per cent died. There were 8 cases in the oldest age group in which 12.5 per cent recovered, with 37.5 per cent dead. The 2 - 4 years group, therefore, has the highest mortality rate. This, however, is fairly similar in the other three groups. Those cases of less

than 2 years of age have the best recovery rate which is much lower in the other groups. In the older children, there is a greater tendency to pass into the latent stage.

It would appear, therefore, that the prognosis is fairly good in the youngest age group, but very poor in the older children.

(2) Sex. The relationship between sex and the prognosis is shown in Table 42.

Sex	No of cases	Recovered	Latent	Active	Terminal	Dead
Male	30 (57.7%)	8 (26.7%)	5 (16.7%)	3 (10%)	2 (6,6%)	12 (40%)
Female	22 (42.3%)	6 (27.4%)	3 (13.6%)	1 (4.5%)	1 (4.5%)	11 (50%)
Total.	52	14	8	4	3	23

Table 42. Sex of patient in relation to the prognosis of the initial attack.

Of the 52 patients, 30 are boys and 22 girls. Therefore as in acute haemorrhagic nephritis boys are more frequently affected. Of the 30 boys 26.7 per cent recovered and 40 per cent died, and of the 22 girls, 27.4 per cent recovered and 50 per cent died. Sex does not seem to play a part in the prognosis.

(3) Preceding infection. In only 4 (7.7 per cent) cases, was there any history of preceding infection. In 3 cases

there was a history of 'chill' from one to four weeks before the onset of the oedema. A fourth case had chickenpox one week previously. Therefore preceding infection does not appear to play a great part in the etiology or prognosis.

In 3 more cases, swelling of the face was noticed by the mother shortly after the first or second dose of diphtheria antitoxin had been given for immunisation. Two of these children died. One of them had had microscopic haematuria. It is doubtful if the injection of antitoxin can be considered to be the exciting factor in the onset of the nephrosis. Mild symptoms may have been present previously but unnoticed until after the antitoxin had been given.

Oedema. The degree of oedema at the onset in relation to the prognosis is given in Table 43.

Oedema.	No	Recovered	Latent	Active	Terminal	Dead
slight.	3 (5.8%)	3 (100%)	-	-	-	-
moderate	17 (32.7%)	5 (29.4%)	2 (11.8%)	2 (11.8%)	1 (5.8%)	7 (41.2%)
severe	32 (61.5%)	6 (18.7%)	6 (18.7%)	2 (6.3%)	2 (6.3%)	16 (50%)
Total	52	14	8	4	3	23

Table 43. Degree of oedema in relation to the prognosis of the initial attack.

Of the 52 patients, 3 had slight oedema, 17 moderate oedema and 32 severe oedema. Of the 3 cases with slight oedema all recovered. Of the 17 with moderate oedema, 29.4 per cent recovered and 41.2 per cent died. Only 18.7 per cent of the cases with severe oedema recovered and 50 per cent died. If the oedema, therefore, was more than slight, the prognosis was poor, especially in the cases with gross anasarca.

Hypertension. Only 8 of the 52 patients gave a reading of more than 110 systolic blood pressure. Of these, one is now in the latent and one in the active stage; 2 are in the terminal stage and 4 have died. Therefore hypertension which is unusual in the nephrotic syndrome is of poor prognostic significance.

Nitrogen retention. Only 5 children had nitrogen retention

throughout the course of the initial attack and of these 2 died and 3 are in the terminal stage. Nitrogen retention is uncommon in the nephrotic syndrome but when it does occur, it is suggestive of marked glomerular involvement which leads to the terminal stage.

The serum proteins. In most of the cases, the serum proteins were estimated at frequent intervals throughout the course of the disease.

T.P. gm.%	No of cases	Recovered	Latent	Active	Terminal	Dead
3 - 4	8	1 (12.5%)	3 (37.5%)	1 (12.5%)	1 (12.5%)	2 (25%)
4 - 5	22	6 (27.3%)	5 (22.8%)	1 (4.5%)	1 (4.5%)	9 (40.9%)
5 - 6	13	2 (15.4%)	-	1 (7.7%)	-	10 (76.9%)
6 - 7	6	3 (50%)	-	1 (16.6%)	1 (16.6%)	1 (16.6%)
not done	3	2 (66.6%)	-	-	-	- (33.3%)
Total. 52.		14	8	4	3	23

Table 44. Total protein levels at the onset of the initial attack.

It is seen that from Table 44, 8 of the 52 patients had a total serum protein level of 3 - 4 gm. per cent and of

12.5 per cent recovered and 25 per cent died. Of the 22 patients with a total protein of 4 - 5 gm. per cent, 27.3 per cent recovered and 40.9 per cent died. In the 5 - 6 gm. per cent group are 13 patients of whom only 15.4 per cent recovered and 76.9 per cent died. Of the 6 patients in the over 6 gm. per cent group, 50 per cent recovered and only 16.6 per cent died. From these results, it would appear that the 5 - 6 gm. per cent group has the worst prognosis, but more cases with the lower protein levels pass into the latent, active and terminal stage. The eventual mortality rate is, thus, fairly similar in each of these groups. Therefore, if the total protein at the onset is less than 6 gm. per cent, the prognosis is poor but the level of total protein below this is of no prognotic value, that is, the ultimate prognosis is no worse in the under 4 gm. per cent group than in the other two groups.

The blood cholesterol. The relationship of the level of the blood cholesterol at the onset to the prognosis is given in Table 45.

Chol.in mg. %	No.of cases	Recovered	Latent	Active	Terminal	Dead
under 200	6	4 (66.6%)	1 (16.7%)	-	-	1 (16.7%)
200-300	11	2 (18.2%)	3 (27.3%)	1 (9.1%)	-	5 (45.4%)
over 300	24	2 (8.3%)	4 (16.7%)	3 (12.5%)	3 (12.5%)	12 (50%)
not done	11	6	-	-	-	5
Total	52	14	8	4	3	23

Table 45. The blood cholesterol (chol.) results in the initial stage in relation to the prognosis.

Of the 52 patients, 6 gave cholesterol readings of less than 200 mg. per cent and of these 66.6 per cent recovered and 16.7 per cent died. Values of over 200 mg. per cent were found in 35 patients. Only 11.4 per cent of these recovered and 48.6 per cent died. In 11 cases the cholesterol readings were not recorded. Of the 35 patients in the over 200 mg. per cent group, two sub groups were made (1) 2oo - 300 mg. per cent with 11 cases of which 18.2 per cent recovered and 45.6 per cent died and (2) over 300 mg. per cent with 24 cases and of these,

only 8.3 per cent recovered and 50 per cent died. Therefore it would appear that the higher the cholesterol level, the lower is the recovery rate.

Urea concentration and clearance tests. In 27 of the 52 cases the urea concentration test was done but the urea clearance was determined in only 15 cases. Many of the children died before the tests could be carried out or were too young to co-operate and unsuitable for repeated catheterisation.

U.Conc. gm.%	No.of cases.	Recovered	Latent	Active	Terminal	Dead
Under 2	3 (11.2%)	-	1	1	-	1 (33.3%)
2 - 3	16 (44.4%)	3 (18.7%)	4	1	2	6 (37.4%)
3 -more	8 (22.2%)	2 (25%)	1	-	-	5 (62.5%)
not done	25	9	2	2	1	11
Total	52	14	8	4	3	23

Table 46. Urea concentration (U.Conc.) tests in relation to the prognosis.

Of the 27 patients whose urea concentration was tested, only 3 gave results below the lower normal limit of 2 gm. per cent and of these, one died and 2 are in the

latent and active stages. Results of more than 2 gm. per cent were obtained and in 24 cases, of whom 20.8 per cent recovered and 45.8 per cent died. Of these 24 cases, 16 gave readings of 2 - 3 gm. per cent and only 18.7 per cent recovered with a death rate of 37.4 per cent. Eight had concentrations of more than 3 gm. per cent and of these, 2 recovered with 62.5 per cent dead. Therefore although most of the children in the nephrotic syndrome have good renal function, that does not affect the prognosis of the disease.

U.C. % normal after urea	Number of cases		Recovered	Latent	Active	Terminal	Dead
under 40	1	-20%	-	-	-	1	-
40 -60	2		-	-	1	-	1
60 - 100	8	-80%	1	4	-	-	3
100- 120	4		1	1	-	1	1
Not done	37		12	3	3	1	18
Total	52		14	8	4	3	23

Table 47. Urea clearance tests (U.C.) in the relation to the prognosis of the initial attack.

Table 47. - Of the 15 cases tested, 3 gave clearances of less than 60 per cent of normal which is taken as the lower limit of normality. Of these 3, one died, one is

in the terminal stage and one in the active stage. Clearances of more than 60 per cent of normal were obtained in 12 patients, 16.6 per cent of whom recovered with 33.2 per cent dead. Therefore the urea clearance results do not appear to affect the ultimate prognosis.

The only significance of the urea concentration and clearance tests is that although normal tests do not mean that the outlook is good, tests with results below normal show that the child is approaching the terminal stage and death.

Haematuria. The 52 patients were divided into those who did not have haematuria (even microscopic) during the course of the disease and those who had haematuria.

Urine	Number of cases	Recovered	Latent	Active	Terminal	Dead
No blood	25	11 (44%)	2 (8%)	1 (4%)	2 8%)	9 (36%)
Blood	27	3 (11.1%)	6 (22.2%)	3 (11.1%)	1 (3.7%)	14 (51.9%)
Total.	52	14	8	4	3	23

Table 48. Haematuria in relation to the prognosis.

Of the 52 patients, 25 had no haematuria and of these 44 per cent recovered and 36 per cent died with 20 per cent still active. Of the 27 with haematuria only

11.1 per cent recovered, 51.9 per cent died and 37 per cent are still in the active, latent or terminal stage. Of the 23 children who died, 6 had been without haematuria and all died of infection. Of the 17 cases which had haematuria, 15 died of infection, 2 of uraemia and in 2 the cause of death was unknown. Therefore the cases without haematuria ('nephrosis') have a much better prognosis.

Duration of the initial attack. The relationship between the duration of the attack and the prognosis is given in Table 49.

Duration in weeks.	Number of cases	Recovered	Latent	Active	Terminal	Dead
2 - 6	5	3 (160%)	-	-	-	(2
6 -14	27 (13	14 7	1	-	-	10 (5
	(	(51.9% (155.8%				(37%) (
14 -22	(9	4 (44.4%	1	1	-	(3
22 - 30	7	-	3	1	1	(2
30 - 38	25 (9	-	1	1	-	13)7
40	(9	-	2	1	2	(52%)4
Total	52	14	8	4	3	23.

Table 49. Duration of the initial attack in relation to the prognosis.

Table 49. shows that the first attack lasted less than 22 weeks in 27 patients of whom 51.9 per cent recovered and 37 per cent died. Of the 25 patients with

attacks of more than 22 weeks duration, not one recovered and 52 per cent died. The recovery rate fell from 60 per cent to 44.4 per cent as the duration of the attack lengthened. After 22 weeks, there was no increase in the immediate death rate, but the ultimate mortality will probably be 100 per cent. Therefore if the attack lasts less than 22 weeks the outlook is good, but if the duration is longer the prognosis is poor.

Complications. It is known that the most frequent cause of death is infection, but it has also been reported that after an acute infection there may be a sudden disappearance of all symptoms and the child may recover or pass into the latent phase.

Compli-cations.	Number	Recovered	Latent	Active	Terminal	Dead
1. Infection						
Upper res-piratory	3	3	-	-	-	-
Broncho-pneumonia	15	2	1	3	-	8
Empyema	2	-	1	-	-	1
Peritonitis	8	-	-	-	-	8
Meningitis	2	-	-	-	-	2
Gastro--enteritis	6	2	2	-	1	1
Cellulitis	3	-	1	1	-	1
Scarlet Fever	1	-	1	-	-	-
Total	40	7	6	4	1	21
11. Uraemia	2					2

Table 50. Complications in the initial stage and the prognosis.

In 52 cases, there were 40 infectious complications, from which only 17.5 per cent recovered and 57.5 per cent had resulted in death. The cases with upper respiratory infections, for examplem tonsillitis, otitis media and 'chill' all recovered. Of the 15 cases of bronchopneumonia, 2 recovered and 8 died. All cases of meningitis and peritonitis were fatal. Of the 6 cases with gastro-enteritis 2 recovered and one died and of the 3 cases of cellulitis, one is in the latent stage, one in the active stage and one has died. In the majority of cases of infection, therefore, the prognosis is poor. In several of the children the symptoms did clear up either temporarily or permanently after an acute infection. Four children in the recovered stage cleared up after an acute infection, for example, bronchopneumonia (2 cases), gastro-enteritis (1 case) and otitis media (1 case).

(1.) S.M. (female) aged 10 months. Six weeks after admission she developed bronchopneumonia, which was followed by the disappearance of the oedema and albuminuria. A loss of 2 kilo.in body weight resulted. The child has remained well since, that is, for two years.

(2.) M.M. (male) aged 9 months, developed bronchopneumonia three days after adnission. He lost 2 kilo. in weight in ten days. The oedema and albuminuria

cleared up and the child has remained well.

(3) A.W. (female) aged 14 months, developed gastro-enteritis one week after admission with the loss of 3.5 kilo. in weight in five days. She responded to treatment and the oedema, which had disappeared, did not return when the diarrhoea ceased. The albumin gradually cleared from the urine.

(4) D.M. (male) aged 3 and a half years, was dismissed home in the active stage on 27.9.36 after seven weeks in hospital. He remained in this stage until October 1937 when he had severe bilateral otitis media which was followed by the disappearance of the oedema and albuminuria. He was seen in December 1944 and was well with satisfactory renal function tests.

In the latent stage, one girl (B.D.) after a long course in hospital had cellulitis of the thigh which responded to sulphathiazole. Thereafter she lost 13.4 kilo. in weight with the disappearance of the oedema which has not returned. There was still albumin in the urine six months later.

In two of the children in the active stage, acute infection appeared to cause an almost complete but temporary disappearance of oedema, for example,

(1) J.H.(male) aged 4 years, who had generalised oedema, developed cellulitis of abdomen after para-

-centesis. His weight fell by 11 kilo. in less than three weeks and the oedema remaining, was very slight. One week later he had a relapse.

(2) J.W. (male) aged 2 years had three attacks of respiratory infection during his stay in hospital. Each was followed by marked diuresis and loss of oedema. This was temporary, the symptoms recurring within a few days.

Septic foci. Of the 52 patients, 11 had septic foci removed during their stay in hospital. Of these, 4 recovered, 3 died and in 4 the renal lesion is still active. Therefore it is doubtful if removal of the septic foci has any effect on the prognosis.

Diet. The effect of different types of diet on the 27 patients still alive was very variable. Of these children, 18 had in rotation, milk, full diet, 'salt free' diet and high protein diet without any definite effect on the course of the disease. In two young children the symptoms cleared up on a diet of milk and sugar only. One recovered on ordinary full diet and two others were improving on this diet when they had acute infections, after which they cleared up quickly. One child improved greatly but not completely, on high protein diet. The remaining 3 children were put on 'salt free' diet which contained a moderate amount of protein. There was definite improvement with dis-

appearance of the oedema. Two have recovered, but the third child has slight but persistent albuminuria and remains in the latent stage.

Of the 23 patients who died, many were given different diets without benefit. Others died of infection before it could be ascertained that the diet was influencing the course of the illness. No specific diet therefore can be stated to have a constant beneficial effect. The majority of cases tend to progress or heal irrespective of the diet given.

Plasma transfusion. In 5 patients concentrated plasma was given intravenously. Two of these are in the latent stage, 2 in the active stage and one in the terminal stage. The results of the transfusions in the five cases will be given briefly.

(1). B.D. (female) 12 years. After a prolonged stay in hospital she was given 162 cc. double strength plasma (12.9 grams total protein). The total serum protein, which, before transfusion, was 5.49 gm. per cent with albumin 1.16 gm. per cent fell to 3.76 gm. per cent with albumin 1.89 per cent. There was no diuresis and the oedema increased. No further transfusion was given and the symptoms eventually cleared after an acute infection.

(2) H.C. (female) 12 years. During her long course in hospital she was given 400 cc.double strength plasma

(22.72 grams total protein) at one transfusion. The total serum protein rose from 3.27 gm. per cent to 4.13 gm. per cent. This slight rise was followed by only a very mild diuresis. There was no change in the albuminuria and the oedema became more marked.

(3) J.H. (male) 5 years. After nine months without benefit from any treatment, he was given 180 cc. double strength plasma (16.27 grams total protein). The total serum protein rose from 3.19 gm. per cent with albumin 0.85 gm. per cent to 4.22 gm. per cent with albumin 0.94 gm. per cent. This was followed by a diuresis with the loss of 2 kilo. in body weight and a marked reduction in the oedema. Albumunuria remained unchanged. Unfortunately he was transferred to another hospital a few days later. He was seen after three months. The oedema had gradually disappeared except for occasional puffiness under the eyes. The total serum protein had risen to 5.68 gm. per cent with albumin 1.6 gm. per cent and the general condition was greatly improved.

(4) J.W. (male) 2 years. On 11.9.45, after a long course, he was given 240 cc. double strength plasma (26.6 grams total protein) with no change in serum protein, oedema or degree of albuminuria. As the condition was stationary and the haemoglobin had fallen from 7.6 to 4.95 gm. per cent, it was decided to give

a second transfusion. On 23.11.45, 180 cc. quadruple strength plasma (28.26 grams total protein) were given fairly quickly followed by a drip of 330 cc. packed red cells (18.8 grams total protein and 14.86 gm. per cent haemoglobin). The total serum protein and albumin were unchanged by the transfusion, but the haemoglobin rose to 7.01 gm. per cent. There was no diuresis and the amount of albuminuria was unchanged, but four days later (27.11.45) there was a sudden rapid loss of 4 kilo. in body weight in fourteen days which reduced the oedema to some puffiness of the eyes and mild ascites. The increase in the urinary output could not be measured but he was much 'wetter' than usual. The albuminuria did not change, nor did the total protein level of the serum. He was dismissed home on 24.12.45 but was seen on 9.1.46 much improved with only some puffiness under the eyes and slight oedema of the ankles. The total serum protein had risen slightly to 4.96 gm. per cent, but the blood cholesterol was still raised. The urine which contained albumin showed red cells on microscopic examination.

(5). J.R. 8 years. During a prolonged course he was given 200 cc. double strength plasma (18.08 grams total protein) without any effect on the blood chemistry, oedema, or general condition.

Therefore of the 5 cases treated, plasma transfusion did not influence the course of the attack in 3 cases, but in the other 2 there was great diminution in the oedema with marked improvement in the general condition.

(5) CASE HISTORIES.

1. In the latent stage;

(a) B.D. (female) aged 12 years, was admitted on 26.12.44 with a history of oedema of the face for two weeks, and swelling of the abdomen for one week. On admission there was generalised oedema. The urine contained abundant albumin, a trace of blood, and many casts. The total serum protein was 4.09 gm. per cent, with albumin 1.48 gm. per cent, and a blood cholesterol of 288 mg. per cent. The oedema and albuminuria remained unchanged but the haematuria was intermittent. Paracentesis abdominis was done twice with the removal of eight and sixteen pints of fluid. On 21.3.45 she was given 162 cc. double strength plasma intravenously (11.59 grams total protein) but the oedema became more marked. On 9.4.45, she had cellulitis of the thigh and on 11.4.45 there was a marked diuresis which resulted in the loss of 13.8 kilo. body weight in twelve days, and the total protein rose to 4.44 gms. per cent, with albumin 2.2 gm. per cent. On dismissal (12.6.45)

there was no oedema and the blood chemistry had improved with rise of total protein to 5.3 gm. per cent. The renal function was good, but there was still albumin in the urine. She was well when seen on 9.12.45 and the tests were satisfactory. Albuminuria, however, persisted and the Addis count was raised (Casts 15,250, red cells 2,745,000 and white cells 3,650,000). At present this girl is in the latent stage but she may yet recover.

(b) H.C. (female) aged 11 years, was admitted on 1.6.43 with a history of swelling of the face, legs and abdomen, of two weeks duration. The oedema was marked, and the total serum proteins were low, (3.28 gm. per cent) but on repeated examination of the urine, no albumin was found. The oedema increased after a transfusion of plasma (23.72 gm. total protein) on 12.6.43, and became still more marked on high protein diet. This was omitted on 16.6.43 and milk only given. In July 1943 she lost 3 kilo. in weight after three doses of salyrgan and on 14.7.43 the urine contained albumin for the first time. On 21.7.43 she was given baker's yeast, one ounce daily. Thereafter there was a steady fall in weight. By 4.9.43 the oedema had gone, and the total serum protein had risen from 2.76 gm. per cent to 4.37 gm. per cent. On 1.11.43 she was dismissed home well, apart

from low serum proteins, on ordinary diet. She reported monthly and remained well, but on 12.6.44 there was marked albuminuria. This has persisted, and is not orthostatic in nature. There has been no oedema and the total protein is 7.64 gm. per cent, with albumin 3.7 gm. per cent. When seen last, on 10.12.45, aged 14 years, she was well. There was still albuminuria, and the Addis count was raised (casts 75,000,000, red cells, 3,060,000 and white cells, 1,280,000). The other renal function tests were satisfactory.

This case is unusual. The appearance and persistence of the albuminuria, after the oedema had disappeared and the total protein returned to normal, is difficult to explain.

2. ACTIVE STAGE.

(a) S.McN. (female) was admitted on 18.11.43, aged 7 years, with a history of occasional puffiness of the eyelids, for two months, and swelling of feet for three days. The oedema was moderate in amount. There was marked albuminuria and the serum protein was low (4.53 gm per cent). She was given milk only, and the oedema disappeared rapidly, with a rise in the serum proteins to 5.1 gm. per cent. She developed scarlet fever on 30.12.43 and was transferred to a fever hospital, but re-admitted on 22.2.44, with slight oedema and gross

albuminuria. The total protein had risen to 6.5 gm. per cent, with albumin 2.7 gm. per cent, but the cholesterol remained high. She was given high protein diet without benefit. The degree of oedema varied from day to day, and in this active stage she was dismissed on 10.4.44. Since then she has had intermittent oedema with gross albuminuria and a raised Addis count, with the exception of the red cells. (Casts 12,5000, red cells 360,000 and white cells 2,705,000.) The serum proteins are still low (5.6 gm. per cent) and the cholesterol high (338 mg. per cent) but the renal function tests remain satisfactory.

(b) K.McN. (male) was admitted on 25.4.42 aged 3 years, with a history of swelling of the face for three months and a swollen abdomen of several days duration. There was marked oedema and albuminuria on admission. The serum proteins were low(4.49 gm. per cent). He was given milk and then 'salt free' diet without much effect on the condition. The oedema fluctuated and during a good phase, he was dismissed on 12.9.42 on 'salt free' diet. Since dismissal he has been seen several times. There has been intermittent oedema and marked albuminuria and Addis count is raised. The serum proteins remain low (4.54 gm. per cent) with a high cholesterol but renal function tests are normal.

3. Terminal stage.

(a) F.C. (male)was admitted on 9.6.42 aged 2 years 11

months with a history of intermittent swelling of the face of three months duration and swelling of the face and hands for two days. There was also thirst and irritability. On admission there was a moderate amount of oedema and marked albuminuria, but no haematuria. The total protein was low (4.84 gm. per cent) with upset of the albumin/globulin ratio and high cholesterol. He was given 'salt free' diet with some improvement in the general condition and a rise in the serum protein (5.2 gm. per cent). The condition remained unchanged until 19.11.42 when there was cellulitis of the abdomen which caused a slight loss in weight. He was sent home in the active stage on 25.11.42 on 'salt free' diet. Since dismissal, the oedema has cleared but he is never well. He is thirsty and passes a large amount of urine, which contains albumin and the Addis count is raised,(Casts 14,640, red cells, 2,482,000 and white cells 1,432,000). The total protein and the blood cholesterol are now normal, but the non-protein nitrogen has risen to 83.3 mg. per cent and the urea concentration and clearance tests are poor. He is now in the terminal stage.

IV. CHRONIC INTERSTITIAL NEPHRITIS.

(1) RESULTS IN ALL CASES.

Since 1934, 23 children with chronic interstitial nephritis have been admitted to the wards. Of this

number 15 have died either in hospital or subsequently; 5 have not been traced to the present time and 3 are still alive. (Table 51.)

Number of cases	Present condition	Percentage of total.
3	Alive	13%
15	Dead	65.2%
5	Not traced	21.8%

Table 51. Chronic interstitial nephritis (23 cases) - present condition.

(2) THOSE STILL ALIVE.

There are three children still alive. Two of them are 'renal dwarfs' who were admitted to hospital during the past year and are still attending as out-patients. The third girl (J.S.) is probably in the terminal stage of acute haemorrhagic nephritis, that is, chronic interstitial nephritis.

On examination, both dwarfs gave a history of failure to grow, thirst and polyuria, and the girl had attacks of headache and vomiting. The state of nutrition was poor. All were under weight and height. There was no oedema. One of the dwarfs had rickets with marked genu valgum.

Hypertension. The blood pressure readings were normal

in two of the children but the third child (J.S) had mild hypertension (B.P. 135/80).

Nitrogen retention. The three cases had mild nitrogen retention. The non-protein nitrogen results ranged from 41.6 to 71.4 mg. per cent with an average of 51.9 mg. per cent.

Serum proteins. The total protein figures and albumin fraction levels were rather low. The total protein results varied between 5.45 and 6.1 gm. per cent with an average of 5.88 gm. per cent. The range of serum albumin levels was 1.26 to 4.46 gm. per cent with an average result of 3.4 gm. per cent.

Blood cholesterol. The blood cholesterol was normal in each case. The results ranged from 60 to 120 mg. per cent with an average value of 91.3 mg. per cent.

Urea concentration. The values for the urea concentration tests lay between 1.07 gm. and 2 gm. per cent with an average of 1.39 gm. per cent.

Urea clearance. The standard urea clearance, before giving urea, ranged from 42 to 59 per cent of normal with an average value of 48.6 per cent, and after giving urea, varied from 24 to 56 per cent of normal with an average of 34.6 per cent.

The renal function, therefore, based on the urea concentration and clearance tests, was poor.

Serum calcium, phosphorus and phosphatase. In the two

renal dwarfs, the serum calcium level was normal (average 10.7 mg. per cent), except on one occasion in the case of J.G., when it fell to 6.8 mg. per cent, with the clinical appearance of tetany. The serum phosphorus averaged 2.9 mg. per cent. The plasma phosphatase was raised in J.G. (who had rickets) to 25.9 units but was normal in the other child.

The urinary findings. In each of the three cases, the urine contained albumin varying from a trace to a heavy cloud, and on microscopic examination occasional casts of hyaline and granular types were seen.

The Addis count was done in these three cases and also in two of the cases which have since died. The counts of the last two children will be included with those of the three children still alive. The results in these 5 children (2 of whom had hypertension and 3 had none ('renal dwarfs')) are given in Table 52. It was thought that the Addis counts might differ in the cases with hypertension and those without hypertension.

Urine		Renal Dwarfs.	Chronic nephritis with hypertension
Casts	R	0 - 40,000	0 - 88,000
	A	19,528	35,460
Red cells	R	612,000-4,500,000	1,774,000- 10,296,000
	A	2,236,200	4,268,400
White cells	R	686,000 -3,860,000	674,000 - 8,480,000
	A	1,505,600	4,887,800
Protein (mg.)	R	300 - 600	1200 - 1700
	A	500	1400

Table 52. Addis counts in 3'renal dwarfs'and 2 cases of chronic nephritis with hypertension. (R- range. A- average).

From Table 52. it is seen that in all cases the Addis count is raised, the average count showing a rise in all three formed elements, as well as in the degree of proteinuria. The counts were higher in the hypertensive group. In two 'renal dwarfs' the red cell counts were just above the normal upper limits, but in the third child (who has died) the counts were high, for example, Casts 10,740, red cells 4,356,000 and white cells, 3,860,000. This raised the average count in these cases

to well above the normal upper limit of 600,000. In each of the five urines the casts were of hyaline and granular types, only occasional 'broad' casts described by Addis were seen. Therefore although the casts, cells and the amount of proteinuria were higher in the cases with hypertension, the findings were similar and could not be used to differentiate the cases without hypertension from those with hypertension.

(3) DEATHS.

Of the 15 children who died, 6 had no hypertension and 9 had hypertension. Apart from this factor the course of the disease and death in uraemia was similar in all cases. As already stated, for convenience, those without hypertension have been termed 'renal dwarfs' and the others 'chronic nephritis with hypertension.'

(a) 'Renal dwarfs'. Two of these cases were babies, 6 weeks and 11 months old. Both had a history of vomiting from birth. In the other 4 cases the symptoms had usually been present for several years. Two gave a history of thirst and polyuria, whereas listlessness and loss of appetite were a feature of the other two cases. On examination, the 2 babies were small and emaciated. The 4 older children were markedly dwarfed, 3 having rickets and the fourth had 'wide epiphyses with late ossification ? rickets' on the skiagram. There

was no hypertension, cardiac enlargement or change in the optic discs. All had nitrogen retention, the non-protein nitrogen levels ranging from 90.9 to 180 mg. per cent with an average of 131.5 mg. per cent. All had urea clearances below normal. Two of the older children were treated with large doses of alkali and adexolin. One child died later in Ireland. The course of the other child (F.L.) will be given later. Unfortunately, post -mortem examination was not obtained in any of the 4 older children as they all died at home. It was however, performed on the 2 babies. In the 6 weeks old baby, the kidneys were very small, shrunken, irregular and nodular, suggestive of an intra-uterine inflammatory condition. The other baby, 11 months, had small fibrotic kidneys with foetal lobulation due to congenital hypoplasia.

(b) 'chronic nephritis with hypertension.' The majority of these 9 children had symptoms of several years duration. Four cases had had thirst and polyuria from one to four years. Vomiting, over a period of four days to two years,was a feature in 7 cases. On examination, only 2 cases were under weight and height. One of these had rickets. This child, however, having hypertension and cardiac enlargement in conjunction with rickets, can not be termed a typical 'renal dwarf'. Each of the nine cases had cardiac enlargement associated

with the hypertension. Ophthalmoscopic examination revealed 3 cases of optic neuritis and 5 of albuminuric retinitis. In one case the optic discs were normal. In each case, there was albuminuria and nitrogen retention. All died of uraemia, with drowsiness, acidotic breathing, convulsions and coma with rising non-protein nitrogen and blood pressure readings.

Of these 9 cases, 7 died in hospital and post-mortem examinations were made on 4 of them. In 3 the kidneys were found to be shrunken and fibrosed with adherent capsules. There was destruction of the cortex suggestive of an inflammatory lesion. In one of these cases, there was definite thickening of the renal arterioles. The fourth post-mortem examination showed atrophy of the right kidney due to congenital stenosis of the orifice of the right renal artery. This was associated with hypertrophy of the left kidney which showed recent inflammatory change. In no case was there any evidence of hydronephrosis or a congenital lesion, such as urethral valve.

Four cases gave a history suggestive of an inflammatory kidney lesion and in 3 of them there was no post-mortem examination. One had had scarlet fever with 'kidney trouble' one year previously and gave a history of passing 'dark' urine intermittently for two

years. The third child (A.M.) had a history of 'dark' urine and during one period in hospital, pyuria was discovered. This was suggestive of acute haemorrhagic nephritis or pyelonephritis. Therefore of the 9 cases, 4 had definite post-morten evidence of an inflammatory kidney lesion and 3 more had a history suggestive of such a lesion. The etiology of the other 2 cases is not known.

(4) THOSE CASES NOT FULLY TRACED.

The history of these 5 children is given.

(a) R.L. (male) aged 10 and a half years, was dismissed on 31.1.39 with renal rickets. While in hospital, he had poor renal function with impending uraemia and low blood calcium.

(b) P.B. (male) aged 6 years was in hospital in 1938 and 1939. He was one of 3 renal dwarfs in a family of 9 children. The other 2 had died. When he was last seen there was nitrogen retention, poor renal function and rickets. He had however grown 6 cms. in fourteen months. He had been having adexolin minims 15 three times a day and calcium lactate and sodium bicarbonate gr. 30 of each three times daily.

(c) J.B. (male) aged 7 years and 4 months, who was dismissed on 25.5.43, was a renal dwarf with rickets, poor renal function, nitrogen retention and low serum

calcium. He was given adexolin and alkali and was still alive in June 1944.

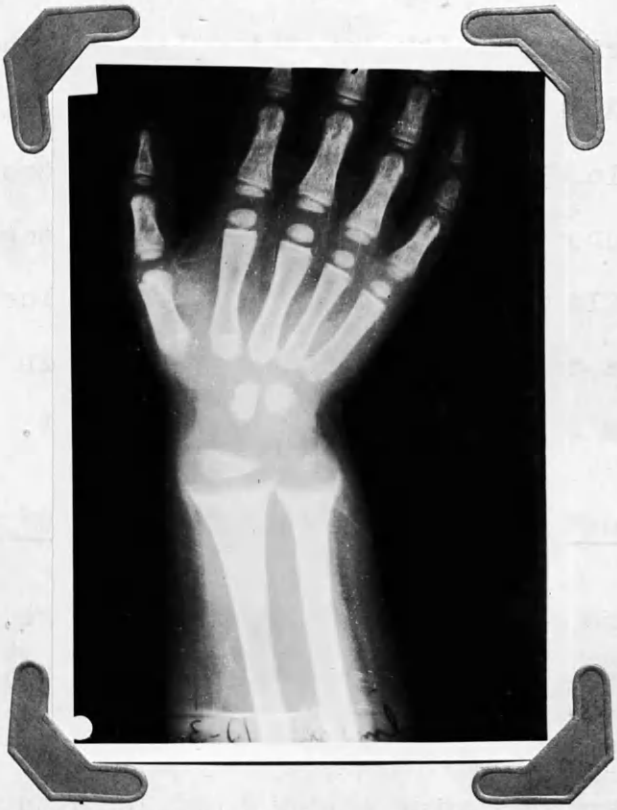
(d) J.C. (male) aged 9 years, who was dismissed on 24.1.36, was a renal dwarf with poor renal function and was in a state of latent uraemia on dismissal.

(e) L.T. (male) aged 10 years, was in hospital from 16.5.34 to 25.8.34. He was dwarfed with mild albuminuria and nitrogen retention and poor urea clearance. He improved slightly before dismissal but was still pale and underweight and mild nitrogen retention.

The prognosis of these 5 children together with the 3 children alive, who have been traced, is poor. Therefore the ultimate mortality rate in this type of nephritis will probably be 100 per cent.

(5) FACTORS INFLUENCING THE PROGNOSIS OF CHRONIC NEPHRITIS.

As the ultimate mortality is so high, it is unnecessary to discuss in detail the factors influencing the prognosis, but the giving of large doses of alkali, calcium and vitamins A and D may help to prolong life by combatting the latent acidosis (Graham and Oakley 1938). In the present series of cases, the two renal dwarfs, who are alive, were given alkali and vitamins A and D with a resulting rise in the blood carbon dioxide content and improvement in the general condition and in the renal



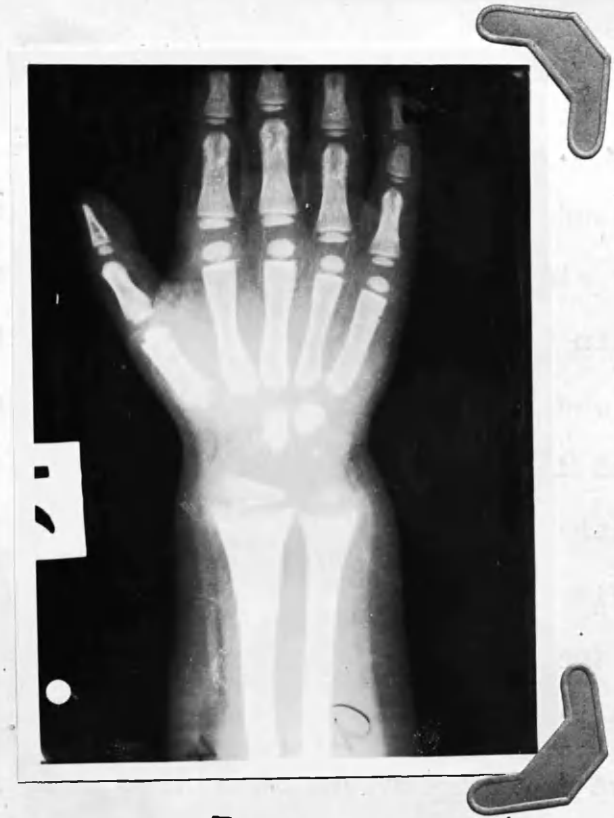
Skiagram 2. 'Rickets' taken 12.4.45.

function. There was some prelininary healing in the bones of the child with rickets, but this has now become stationary, probably because the alkali and adexolin were not given constantly at home. Four other cases ('renal dwarfs') who have died, were treated in this way. One grew 6 cm. in fourteen months but without healing of the rickets. In another, the acidosis was relieved but there was no growth. The other two cases could not be traced. The result of the treatment therefore was not known. One of the hypertensive cases received similar treatment, with some improvement in the general condition, but she died in uraemia one month later.

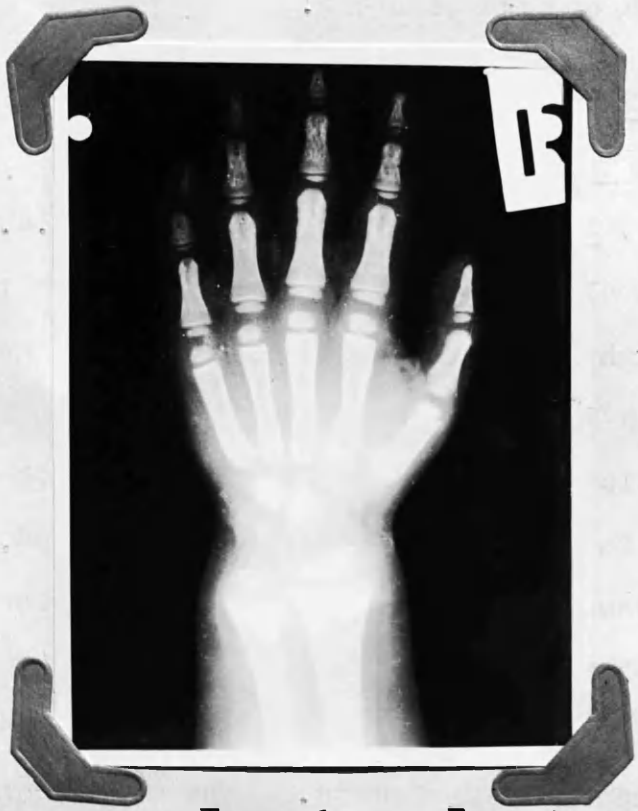
(6) CASE HISTORIES.

1. Those who are alive.

(a) J.G. (male) was admitted on 3.4.45 aged 5½ years. He was always small for his age. For two years he had had right-sided genu valgum which had not improved with sun-ray treatment. He was first seen by us just before admission and complained of thirst with a tendency to vomit in the mornings. He was dwarfed, but fairly well nourished. The skin had a lemon yellow pallor. There was marked enlargement of the wrist and ankle epiphyses and bilateral genu valgum. The skiagram (2) confirmed the presence of rickets. The urine contained a cloud



Skiagram 3. Taken 4.7.45 showing the degree of healing.



Skiagram 4. Taken 5.2.46. There is no further healing.

of albumin and the Addis count was raised (Casts 12,500, red cells 4,500,000 and white cells 1,200,000). There was no hypertension but there was nitrogen retention (non-protein nitrogen = 71.4 mg. per cent). Both the urea concentration and clearance tests were below normal. The blood carbon dioxide content was 50.4 vols. per cent. An intravenous pyelogram was done, but no shadow was seen on the film. The serum calcium was 8.6 mg. per cent; phosphorus was 2.9 mg.per cent and the phosphatase 26.8 units (Jenner and Kay). He was given sodium bicarbonate and calcium lactate, 30 gr. of each six times a day, adexolin minims 10 three times daily (Vitamin A 21,000 units and vitamin D 3,600 units), and Ferrous Sulphate 3 gr. three times daily.

The general condition remained unchanged, but there was a rise in serum calcium to normal, although the phosphorus remained low. There was persistent mild nitrogen retention. Skiagrams (3 and 4) of the wrist showed marked and rapid healing until the end of July 1945, when the rate of healing slowed. Adexolin was increased to 30 minims twice a day (Vitamin A 42,000 units and Vitamin D 7,200 units). The child was dismissed home on 24.8.45 on alkali and adexolin.

Since dismissal, there has been no further healing of the bones. On 23.11.45 he was drowsy and vomited

and on re-admission the serum calcium had fallen to 6.8 mg. per cent. The phosphorus remained low, and the alkali reserve was 37.6 vols. per cent. The urine contained albumin and the Addis count was raised (Casts 10,740 red cells 4,356,000 and white cells 3,860,000). He responded to alkali and adexolin and was dismissed on 8.12.45. He remained well until 2.2.46, when headache, vomiting and spasm of the feet occurred. It was found that he had been without alkali and adexolin for two weeks. He was seen on 5.2.46, when the signs of active tetany had disappeared, but the serum calcium was 7.5 per cent and the non-protein nitrogen 45 mg. per cent. He was given alkali and adexolin. On 7.2.46, carpopedal spasm appeared. This, however, disappeared after calcium gluconate (10 cc. of a 10 per cent solution) had been given. Blood examination ten days later showed a non-protein nitrogen level of 41.6 mg. per cent, serum calcium 10.2 mg. per cent, phosphorus 2.9 mg. per cent and phosphatase 14 units. The condition of the bones remains unchanged and he has not grown.

(b) J.Ga. (male) aged 3 years 9 months, was admitted on 1.10.45 with thirst, polyuria and failure to grow. He was dwarfed with knock-knees but there was no enlargement of the wrist or ankle epiphyses. His skin was sallow. The urine contained a haze of albumin and the Addis count

was raised (Casts 34,600, red cells 612,000 and white cells 918,000). There was no hypertension, but the non-protein nitrogen was raised to 62.5 mg. per cent, and the renal function was markedly impaired. The blood carbon dioxide content was reduced - 37.8 vols per cent. The serum calcium was 9.7 mg. per cent with phosphorus 3.1 mg. per cent and phosphatase 12 units. He was given sodium bicarbonate 30 gr. five times a day. The blood carbon dioxide level rose to 55.2 vols. per cent and there was improvement in the general condition. He was dismissed home on 20.11.45 with instructions to continue alkali and adexolin. Since then he has remained fairly well and has grown 2 cm. in four months. There is still mild nitrogen retention, poor renal function, albuminuria and the Addis count is raised (Casts 40,440, red cells 728,000 and white cells 865,000).

2. Thosewho died

(a) F.L. (female) aged 11 years, was admitted on 16.5.44 with a history of nocturnal eneuresis and frequency of micturition since infancy. She was a small thin girl- 11 cm. under the average height. There was no clinical evidence of rickets but the skiagram of wrist showed 'late ossification with wide epiphyseal lines- ? rickets' . The blood pressure was normal and there was no cardiac enlargement. The optic discs were

normal on examination. The non-protein nitrogen was 90.9 mg. per cent and the renal function was very poor. The serum calcium was 9.2 mg. per cent with a low phosphorus of 2.6 mg. per cent. The blood carbon dioxide content was 15.9 vols. per cent. The intravenous pyelogram was not satisfactory because the dye did not concentrate sufficiently to outline the kidney pelves. On 25.5.44, adexolin and alkali were given. The blood carbon dioxide level rose to 64.5 vols. per cent and there was slight general improvement. She was dismissed on 1.7.44 and was not seen again until 19.10.44 when marked albuminuria was found and the Addis red cell count was slightly raised. (Casts nil, red cells 965,000 and white cells 686,000). The non-protein nitrogen had risen to 169.4 mg. per cent. She did not report back On being sent for, her mother stated that on 1.12 44, the child complained of abdominal pain. There had been some bleeding from the gums and epistaxis. The next day, she had become drowsy and after two generalised convulsions, had become comatose and died on 5.12.44.

(b) A.M. (female) was admitted on 1.5.39 aged 4 years, with a history of frequency of micturition, nocturnal eneuresis and puffiness of eyes in the mornings of six months duration. The urine had, at times, been dark in colour. She was a healthy looking child but there was marked albuminuria with casts on microscopic examination.

Thealbuminuria persisted, but the condition otherwise settled and she was dismissed on 31.7.39. She was re-admitted on 23.10.39 with albuminuria, white cells 10/H.P.F. and a coliform growth. The blood pressure remained normal but the non-protein nitrogen was 49 mg. per cent and the renal function was poor. The urine cleared of pus in one week on treatment. An intravenous pyelogram showed the kidneys to be small but the pelves were not outlined by the dye which was not sufficiently concentrated. She was dismissed on 22.10.39 with persistent albuminuria. On 5.4.40 she was re-admitted with polyuria and occasional drowsiness. The condition remained unchanged but the urine, containing albumin, was sterile on culture. A second intravenous pyelogram was not satisfactory. and she was dismissed on 22.5.40. She was seen in December 1940, in 1941 and 1942. On each occasion the condition remained unchanged. She was examined on 13.2.44 when she was found to be small and sallow-skinned, with knock-knees. She had thirst and polyuria. There was albuminuria, nitrogen retention and hypertension (B.P. 135/80). On 10.10.44 the condition was unchanged but the urea concentration was only 0.69 gm. per cent in two hours. Skiagrams of wrist and knee showed 'rickets'. The child was re-admitted on 7.11.44. She was under

weight and height and the degree of genu valgum was more marked. The urine was of low specific gravity and contained albumin but no white cells. The Addis count was made on many occasions and was always raised. The average count was - Casts 29,300, red cells 4,364,000 and white cells 4,328,000. There was hypertension, cardiac enlargement and 'silver wiring' of the arteries on ophthalmoscopic examination. The non-protein nitrogen had risen to 120.3 mg. per cent and the renal function tests remained very poor. The serum calcium was normal but the phosphorus had risen to 8.3 mg. per cent. An intravenous pyelogram was done for the third time without success. On 10.11.44 she was given large doses of alkali and vitamins A and D with slight general improvement but on 7.12.44 she complained of headache. The non-protein nitrogen was 212 mg. per cent and the serum calcium had fallen to 7 mg. per cent with phosphorus 9.1 mg. per cent and phosphatase 18 units. The blood pressure was 155/100 and she had severe epistaxis. In spite of treatment she became very drowsy with severe headache and frequent vomiting. On 14.12.44 the child had a generalised convulsion followed by death. Unfortunately, permission for post-mortem examination was not obtained.

C. DISCUSSION

It has been shown the prognosis differs in the three types of nephritis.

In acute haemorrhagic nephritis 72.9 per cent recovered with a probable ultimate mortality rate of 24.3 per cent. These findings are in fairly good agreement with those of other workers. Five cases have been traced from the beginning through the latent to the terminal stage. Two of them have died. The course of these five cases, linking the acute with the chronic stages, corresponds to the fingings of Addis (1925) and has been confirmed by other workers.

In the nephrotic syndrome only 26.9 per cent recovered and the ultimate mortality will probably be 65.3 per cent. Three cases in this group have been traced from the initial stage with generalised oedema and gross albuminuria to the terminal stage with nitrogen retention and poor renal function. This confirms the findings of Addis (1925) and Ellis (1942) but differs from those of Volhard (1914) who stated that nephrosis did not progress to uraemia. Campbell (1930) followed 23 cases of 'subacute nephritis' in which decapsulation of the kidneys had been done. His results appeared to be better than those in the present series, where decapsulation was not done, but in Campbell's paper it was found that 5 of the 10 'recovered' cases still

had albuminuria and would therefore be in the latent stage. The recovery rate would correspondingly fall from 43.5 per cent given by Campbell to 21.8 per cent. Thus decapsulation, as Campbell stated, does not appear to alter the prognosis in the nephrotic syndrome.

In the chronic interstitial group the ultimate moraality will probably be 100 per cent - 65.2 per cent of the cases have died, 21.8 per cent could not be traced but are probably dead, and of the 13 per cent alive, all have very poor renal function and are likely to die soon. In the present series there is no indication of the etiology of 'renal dwarfism', but in the urine of the small number of cases examined, the Addis count for red cells was raised in each case. This is suggestive of kidney destruction rather than hypoplasia. In the group comprising 'chronic nephritis with hypertension', the etiology of 8 of the 10 cases is known or indicated. For example, 4 cases were found at postmortem examination to have definite inflammatory renal lesions; 3 gave a history of previous infection suggesting an inflammatory lesion and one of them who is alive and in the terminal stage, has a condition suggestive of renal inflammation. The etiological factor, however, does not have any effect on the prognosis.

Therefore in the three types of nephritis there were found to be 16 cases which have probably passed from the

initial attack into the terminal stage, which is synonymous with chronic interstitial nephritis, e.g.

(1) In acute haemorrhagic nephritis there were 3 cases in the terminal stage and 2 who had been traced through this stage to death.

(2) In the nephrotic syndrome, there were 3 cases in the terminal stage.

(3) In chronic interstitial nephritis there was one case in the terminal stage and 7, who had died, had findings suggestive of an inflammatory renal lesion.

Although the acute haemorrhagic type of nephritis has the best prognosis, it is apparent that it still carries considerable risk.

Of the factors influencing the prognosis, the age and sex of the patient were of no importance. In both the acute and the nephrotic types, the longer the initial symptoms lasted, the worse became the prognosis. The severity of the initial attack in acute nephritis also had a direct effect on the prognosis. This agrees with the findings of several other workers.

It is difficult to assess the value of the part played by recurrent or persistent infection in the chronicity of acute nephritis and to decide if removal of septic foci would prevent exacerbations. It is thought by many that nephritis in childhood, like rheumatism, is an allergic manifestation

of a haemolytic streptococcal infection, that is, toxins, produced by organisms in a septic focus elsewhere in the body, enter the kidney by the blood stream and cause glomerular damage, or that in a streptococcal infection with allergy, histamine-like substances are produced from the reaction of the body tissues to infection and cause hypersensitivity (Collins 1944). There is little evidence, however, to justify this latter opinion. In the present series, the type of preceding infection was of no significance either in acute haemorrhagic nephritis or the nephrotic syndrome, and even in the acute haemorrhagic cases, there was no definite relationship between the onset of relapses or exacerbations and acute infection. It was found also that removal of septic foci either during the stay in hospital or after dismissal did not have any great effect on the prognosis. Cass (1939) suggested that removal of septic foci may not protect the patient from subclinical nephritis. There may have been subclinical attacks of nephritis with acute infections in the present series, but this seems unlikely since 14 of the 22 cases who did develop acute infections are in the recovered stage. Also there were 8 cases showing exacerbation without any noted associated infection. Infectious complications occasionally caused death in the initial stage of acute nephritis but otherwise did not affect the prognosis.

In the nephrotic syndrome, however, infectious compli-

cations were the main cause of death, except in the few cases which were followed by temporary or complete disappearance of the oedematous state. It is seen, therefore, that although some cases respond to acute infection by disappearance of the symptoms, the majority die and there is certainly no justification for exposing these children to the risk of infection. Since the introduction of the sulphonamide drugs, the response to acute infections in both the acute nephritic and the nephrotic patients has shown a decided improvement.

In the present series, 2 brothers (G.S. and S.S.) were admitted within 5 days of each other with acute haemorrhagic nephritis following a 'cold' one week previously. Both had mild attacks and recovered. It would seem practical as suggested by Tudor (1943) to examine the urine of siblings in acute nephritis especially if there is a history of associated infection.

The degree of the oedema present at the onset plays a part in the prognosis. In acute nephritis, the cases with slight or moderate oedema had the highest recovery rates, but if the oedema continued the prognosis was less favourable. In the nephrotic syndrome, it was found that the greater the oedema, the worse the prognosis. Also in the nephrotic syndrome, those cases with persistently low serum protein and high blood cholesterol levels, had a lower recovery rate. In

the majority of these cases the degree of oedema and the cholesterol readings varied inversely with the total protein and albumin levels in the serum, as is shown in the following examples.

(1)	Total protein	(gm.%)	4.08	→	3.92	→	4.94
	albumin	(gm.%)	2.16		1.01		1.28
	oedema		+		+++		+
(2)	Total protein	(gm.%)	5.6	→	3.55	→	4.46 → 5.6
	cholesterol	(mg.%)	230		730		480 200.

If the total serum proteins are very low, however, gross oedema and hypercholesterolaemia do not necessarily occur. It was found that the average critical level for the occurrence of oedema was 5.5 gms. per cent total protein and 2.5 gm. per cent albumin. These figures are in agreement with those of most other workers.

A rise in the total protein level with a fall in the cholesterol to normal is a sign of recovery, but a fall in the total protein with a rising cholesterol is of poor prognostic significance.

The non-protein nitrogen and blood pressure levels were of no significance in the initial stages, but if at any stage in the three types of nephritis there was a rise in these levels then the outlook was grave.

The effect of diet in the acute haemorrhagic and nephrotic types is of doubtful benefit. As suggested by Graham & Oakley

(1938) the addition of large doses of alkali to the diet in chronic nephritis was found to prolong life by counteracting the acidosis. Large doses of calcium and vitamins A and D caused some healing of associated rickets, although there was no effect on the ultimate prognosis. In the present series, the 2 renal dwarfs who are still alive, improved on this treatment. One of them grew 2 cm. in four months and in the other child who had rickets, there was some healing in the bones. These 2 cases were unusual in that the serum calcium was normal and the phosphorus low, making it difficult to understand why the calcium, alkali and vitamin D failed to heal the rickets. Cases of renal rickets, however, having normal serum calcium levels have been reported by other workers. One of the renal dwarfs who died, grew 6 cm. in fourteen months on this treatment but without healing of the rickets. In another case the acidosis was relieved and life probably prolonged. One of the hypertensive cases was also treated with alkali thus temporarily relieving the acidosis.

Transfusions of concentrated plasma may be of benefit in the nephrotic syndrome by causing at least temporary relief from the oedema. In the present series, the 2 cases which received benefit had had haematuria, a finding which differed from that of Aldrich and Boyle (1939). Other workers, e.g. Lyttle et al (1939), Leutscher (1943) and Brown et al (1942)

had poor results with plasma transfusions in the nephrotic syndrome. It may be that the protein transfused is lost to the tissues to replace material from which serum proteins are made, a theory suggested by McQuarrie (1939). Although the results of plasma transfusions are not yet satisfactory, it is suggested that if the condition does not respond to the usual methods of treatment, plasma should be given, in fairly high concentrations. The transfusion should be given early in the course of the attack rather than as a last resort, since it has been shown that if the disease lasts for more than five months, the prognosis is less favourable. The plasma transfusion may result in at least a temporary improvement in the general condition, although the ultimate prognosis may not be affected.

The Addis count of the urinary sediment is of value in estimating the extent of the renal lesion in the different types of nephritis. In acute haemorrhagic nephritis it was found that an average of 62 days was required for the red cell count to fall to the 10 million level and 110 days (16 weeks) to fall below the accepted upper limit of 600,000 in the twelve hour collection of urine. In 1942, Rubin et al, following 40 patients with acute haemorrhagic nephritis during the acute stage, found that 76 days were required for the Addis red cell count to reach the 10 million level and 120 days

(17 weeks) to reach normal. These authors, however, accepted the upper limit of normal given by Soto, that is, 1,000,000. Therefore, in the cases in the present series, the Addis counts returned to normal in a shorter time. Of the 39 patients followed, 36 were dismissed from hospital by 11 weeks and 29 by 8 weeks, from the onset of the disease. As the Addis count does not usually return to normal until 16 weeks from the onset of the initial attack, these children were dismissed from hospital weeks before the renal lesion had healed completely. The cases of acute haemorrhagic nephritis in the present series, were regarded as healed or recovered only when the Addis count and all the other tests were normal.

In the latent stage, there were 41 patients with raised Addis counts. Of these,25 had satisfactory routine urinary tests and would have been termed 'recovered' but for the Addis count. The Addis count therefore detects the presence of renal damage even when the blood pressure, the non-protein nitrogen and total protein results are normal and the renal function found to be unimpaired by the urea concentration and clearance tests. The difference in the results obtained by various workers is probably due to the sensitivity and accuracy of the tests used. Many workers did not make use of the Addis count in estimating the prognosis in acute nephritis. Boyle et al (1930) who claimed that acute nephritis had a very good prognosis and were unable to trace any case into a chronic stage, only did one Addis count in each child.

Repeated counts might have shown some cases to be in the latent stage.

In the present series of acute haemorrhagic nephritis, not one case was found to be in the active stage, although two children passed through this stage before death.

In the terminal stage there was albuminuria and the Addis counts, although raised, were not of diagnostic importance since many of the other tests gave unsatisfactory results. For example, there was nitrogen retention and low urea concentration and clearance tests.

The Addis count in acute nephritis is therefore of great importance in telling when a case has recovered and in diagnosing the latent stage. It is also a confirmatory test in the terminal stage. It has been stated by Snoke (1937) and Gachet (1941), that recovery cannot be considered to be complete until the Addis counts have been normal for at least one year. It was also thought that no child should be placed in the definitely latent stage until he or she has been in this stage for more than two years. It is suggested, therefore, that the patient be kept in bed or at least in hospital until the Addis count returns to normal, as the extra rest may influence the ultimate prognosis. Each child should report monthly for three months and then three monthly for at least one year, so that the course of the disease can be followed closely.

In the nephrotic syndrome, it was found that those cases with haematuria, had a worse prognosis than the cases without haematuria. The cause of death in all the cases without haematuria was infection, not one case reaching the terminal stage. It has been found, however, that of the cases without haematuria, two have now nitrogen retention and poor renal function, and thus, being in the terminal stage, will probably die of uraemia. In the recovered stage of the nephrotic syndrome, the Addis counts as well as the other tests were normal. Only 3 of these cases had had haematuria.

In the latent stage, all cases had a trace to a cloud of albumin in the urine. The Addis count was raised for all elements in 7 of these 8 cases. The degree of albuminuria in some of the latent cases was slight and, with the evidence of clinical well-being and satisfactory renal function, given by the urea concentration and clearance tests, and the non-protein nitrogen and serum protein levels, might have been disregarded but for the fact that the raised Addis counts showed the kidney lesion still to be active.

In the active stage of the nephrotic syndrome, the degree of albuminuria was very abundant and was therefore unlikely to be disregarded. The Addis count therefore is merely a confirmatory test. The history of intermittent oedema, the low total serum proteins with an upset of the albumin/globulin

ratio, the high blood cholesterol and the marked albuminuria shows that the renal lesion is still active, although the urea clearance and concentration tests are within normal limits.

In the terminal stage, it was obvious from the nitrogen retention and the renal insufficiency, that the renal lesion was severe. The urine in each of the three cases contained albumin and the Addis counts were raised for all formed elements indicating some glomerular involvement. Two of the three cases had not had haematuria in the initial stages but the Addis counts were similar to those found in the case with haematuria.

The Addis count in the nephrotic group is useful in proving a case to have recovered, and in showing that slight albuminuria is of pathological significance, the kidney lesion still being active, but in the later stages, it is only a confirmatory test.

In the 5 cases of chronic interstitial nephritis there was albuminuria and the Addis counts were raised for all formed elements in the 'renal dwarfs' as well as in the 'hypertensive' cases, although the counts were higher in the latter group. The raised red cell count in the 'renal dwarfs' is suggestive of kidney destruction rather than hypoplasia as the causal factor. The symptoms, albuminuria,

nitrogen retention and poor renal function in this stage, make the Addis count only a confirmatory test, but it is suggested that if more cases of renal dwarfism were tested, it might be possible to distinguish those resulting from congenital hypoplasia from those caused by inflammatory or destructive lesions.

Therefore in nephritis, the Addis count is of value in the early stages in order to confirm recovery or to detect the latent stage, in which the still active renal lesion may not be discovered by the routine tests of renal function. In the active and terminal stages it is also a confirmatory test but is not of any definite specific value in prognosis.

D. SUMMARY.

1. The prognosis was found to differ in the three types of nephritis. The probable ultimate mortality rate was 24.3 per cent in acute haemorrhagic nephritis, 65.3 per cent in the nephrotic syndrome and 100 per cent in the chronic interstitial group.
2. The age and sex of the patient did not affect the prognosis.
3. The longer and the greater the severity of the initial attack, the worse was the prognosis in both the acute nephritic and the nephrotic groups.
4. In acute nephritis, neither the preceding infection nor infectious complications affect the prognosis, nor is there any definite relationship between renal exacerbations and acute infections.

   In the nephrotic syndrome, infectious complications are the main cause of death, but in a few cases they may be followed by temporary or permanent relief or symptoms.
5. In acute nephritis, cases with slight or moderate oedema at onset had the best prognosis, but in the nephrotic syndrome, the greater the oedema the worse the prognosis. Also a persistently low serum protein or high blood cholesterol indicated a poor prognosis.
6. The non-protein nitrogen of the blood and the blood pressure readings were of no significance in the initial

stage of acute nephritis but if either rose in the later stages of any of the three types of nephritis the prognosis was less favourable.

7. Transfusion of concentrated plasma did not give satisfactory results, but did cause disappearance of the oedema in 2 of the 5 cases of nephrotic syndrome treated. There was, however, no resultant improvement in the urinary findings.

8. By giving alkali, it is possible to prolong life in chronic nephritis by combatting the latent acidosis. Those cases with rickets may respond to large doses of vitamins A and D and calcium.

9. (a) In acute nephritis, it was found that an average of 110 days (16 weeks) was required for the Addis count to return to normal after the onset of the initial attack. It is suggested that children should be kept in bed or in hospital until the Addis count is normal.

The Addis counts were normal in the recovered stage, but raised in the latent and terminal stages. The latent stage, in which the more usual tests were satisfactory, would have been overlooked but for the Addis count.

(b) In the nephrotic syndrome, the occurrence of haematuria was of poor prognosis. The Addis counts were normal in the recovered stage but were raised in 7 of the 8 cases in the latent stage. Six of these cases had had haematuria. In the active and terminal stages, the counts with one

exception were raised for all elements although 2 of the 3 cases in the terminal stage had never had haematuria.

(c) In chronic nephritis, the 5 cases tested (3'dwarfs' + 2 'chronic nephritics with hypertension') had raised Addis counts for all elements. Therefore the probable cause of the dwarfism in these 3 cases was renal destruction, not hypoplasia.

(10)In both acute nephritis and the nephrotic syndrome, the Addis count is of greater value than any other test in deciding if recovery is complete or if the latent stage exists. It will give evidence of renal damage when other tests show normal function.

It is also a valuable confirmatory test in the late stages when evidence of renal failure can be be detected by other means.

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