GLOMERULAR DISEASE IN CHILDHOOD: A REVIEW OF 150 CONSECUTIVE CASES*

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The development of the technique of renal biopsy and the use of the electron microscope have brought about profound changes in concepts of kidney disease. Acute glomerulonephritis has been described pathologically as proliferative, exudative, focal, or interstitial, and other disease complexes are described as lipoid nephrosis (children), membranous glomerulonephritis (adults), and chronic glomerulonephritis.[1] For many years, however, the clinician has adhered to Ellis's classification of nephritis for the reason that it is simple and based on clinical presentation although it is apparent that this classification is not complete. The ready availability of renal tissue from biopsy has prompted us to present this paper, in which we propose to discuss our experience of the clinical aspects of glomerular disease in childhood and to present a classification of the various diseases encountered. This classification, though based on clinical presentation, correlates well with the severity of the renal histological changes as seen in our cases by light microscopy and with the ultimate prognosis.

150 consecutive cases, aged 0 - 14 years, seen at the Transvaal Memorial Hospital for Children, Johannesburg, between August 1959 and January 1963, are presented. We have classified these cases as follows:

	Total cases	*Male*	*Female*	*Deaths*
1. *Acute nephritic syndrome*[2]*				
(*a*) Poststreptococcal glomerulonephritis	96	56	40	—
(*b*) Haemolytic uraemic syndrome	23	8	15	7
(*c*) Subacute bacterial endocarditis	5	1	4	—
(*d*) Henoch-Schönlein purpura	5	2	3	—
(*e*) Glandular fever	3	0	3	—
2. *Nephrotic syndrome*	8	5	3	1
3. *Nephritic-nephrotic syndrome*				
(*a*) Mainly nephritic	8	3	5	2
(*b*) Mainly nephrotic	2	2	0	—
Total	150			10

*Other causes of the acute nephritic syndrome, such as disseminated lupus erythematosus and polyarteritis nodosa, were not seen in this series.

Renal biopsy was carried out by the method described by Kerr[3] with a modified Menghini needle (Fig. 1). Where

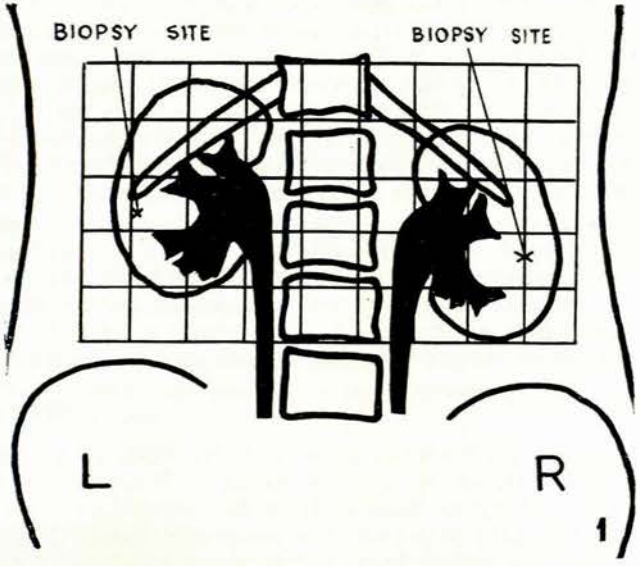

Fig. 1. Diagram to show site of renal biopsy with kidneys outlined by IVP against a grid placed over the patient's back.

renal function has precluded the use of an intravenous pyelogram, we have performed the biopsy blind in the angle formed by the 12th rib and the erector spinae mass[4] (Fig. 2). Precautions taken are attention to bleeding and

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clotting times, platelets, and prothrombin index. No major complications occurred in this series of 31 biopsies, in

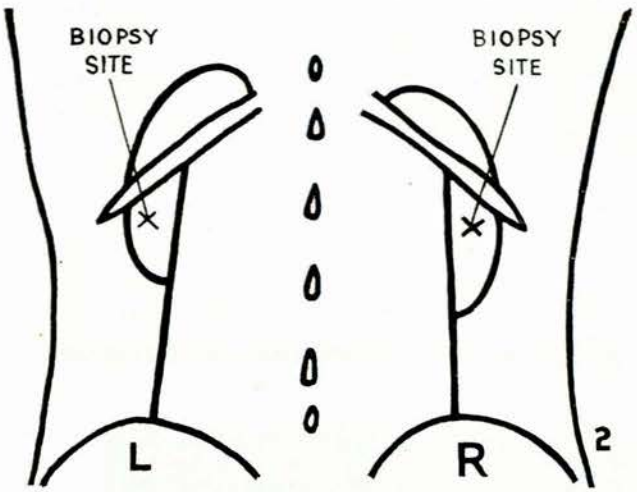

Fig. 2. Diagram to show position of insertion of needle for 'blind' biopsy between angle of 12th rib and erector spinae mass.

which the youngest patient was 4 months old. In several cases we have obtained over 40 glomeruli, and in 1 case over 50.

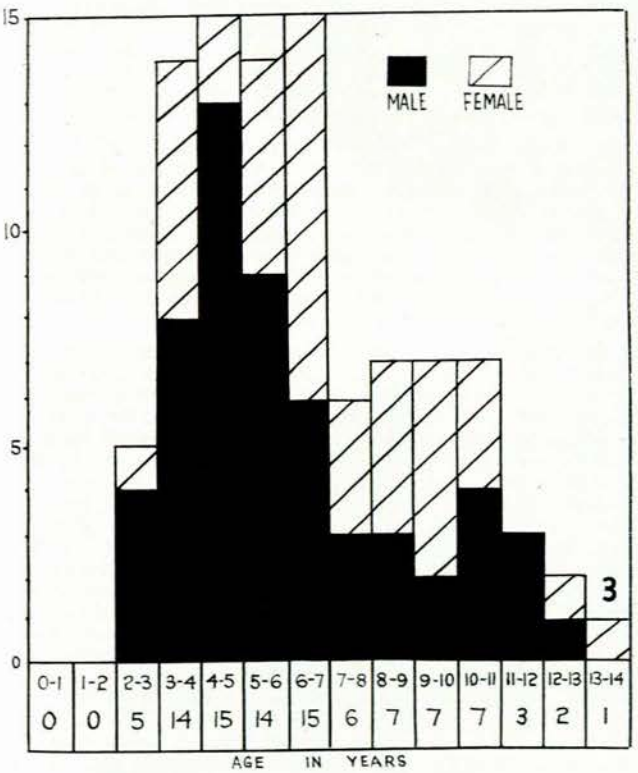

Fig. 3. Age and sex distribution of cases of acute post-streptococcal glomerulonephritis. The numbers of cases are shown on the vertical coordinate, and the totals written along the horizontal coordinate.

I. ACUTE NEPHRITIC SYNDROME

This term very adequately describes the syndrome of hypertension, azotaemia, oliguria, haematuria, and albuminuria. There are many causes of this syndrome, each of which has its own characteristic features.

(a) *Poststreptococcal Glomerulonephritis*

96 cases of this disease were encountered in our series, 56 male and 40 female. No cases occurred under the age of 2, which is the age group of the haemolytic uraemic syndrome, and the majority occurred between the ages of 3 and 7 (Fig. 3).

The presenting symptoms were as follows: haematuria 61%, oedema 53%, sore throat 50%, malaise, etc. 32%, vomiting 19%, abdominal pain 19%, headache 9%, impetigo 8%, epistaxis 3%, convulsions 1%.

The presenting signs were as follows: oedema 60%, hypertension 50%, tonsillitis 43%, pyrexia 43%, hepatomegaly 20%, pulmonary oedema 4%.

Urine investigations. The urine showed markedly increased numbers of red cells and slight increase of white cells, casts were hyaline, granular or cellular, and there was moderate proteinuria (Esbach ± 1 G. in 24 hrs.).

Blood investigations. The haemoglobin was usually normal and the white-cell count on the average was 11,000/cu. mm., with an occasional polymorphonuclear leukocytosis. Platelets were adequate and the erythrocyte sedimentation rate (ESR) was usually markedly elevated, the mean elevation being to 35 mm. in the hour. Antistreptolysin O (ASO) titre was elevated on admission in the majority of cases and reached maximal levels within 3 weeks of admission. The mean level on admission was 650 units per ml. and 20 cases had levels of between 1,000 and 2,000 units per ml. Eight cases only had levels between 50 and 200 units per ml. The C-reactive and mucoproteins were inconstantly elevated, and, in our opinion, were of no diagnostic value. Serum-protein electrophoresis showed a very typical pattern in that the serum albumin was decreased and the gamma globulin increased (to levels of between 1·5 and 2·5 G. per 100 ml.). Blood urea was between 30 and 121 mg./100 ml. in 61 cases. The serum cholesterol was below 300 mg./100 ml. in all cases, and in 6 cases only was between 250 and 300 mg./100 ml.

Renal biopsy was performed in 4 of these children. The changes found were confined mainly to the glomeruli, which had swollen tufts containing excess neutrophils and filling Bowman's space. There were adhesions between the visceral and parietal layers of Bowman's capsule, which contained proteinaceous fluid.

Infection investigations. Coxsackie-A virus was recovered from the stool of 2 patients, one of whom had encephalitis, pneumonitis and nephritis and showed only slight elevation of the ASO titre. Group-A beta-haemolytic streptococci were isolated from the throats of 10 children.

Complications. Five patients had convulsions after admission and 2 developed papilloedema and 3 pulmonary oedema. Two developed pleural effusions and 2 pneumonia.

Diuresis took place in three-quarters of the cases within 4 days of admission, and in all by the 9th day.

Treatment. Bed rest was the most important single factor in therapy initially, but prolonged bed rest after diuresis and disappearance of albuminuria was of no value. Fluids were restricted until diuresis occurred. A solution of 20% lactose was used and the amount given was the previous day's urinary output plus the insensible loss, which was calculated roughly as 7 - 10 ml./lb/day for ages 2 - 5 years, and 4 - 7 ml./lb/day for ages 5 - 14. After diuresis occurred, a low-protein, high-carbohydrate, low-salt diet was used, after which the patient was gradually put on a full diet. Penicillin was administered as a routine measure in the acute phase only. Hypertension was treated only when complications threatened, with intramuscular 'serpasil' and oral or intramuscular 'apresoline', since neither of these drugs depresses the renal blood flow. Magnesium sulphate was of value in the treatment of encephalopathy. Paraldehyde and phenobarbitone were used to control convulsions. Digitalis and morphine were used for left ventricular failure.

Progress. All these cases recovered completely, and after

follow-up, which varied between 3 months and 3½ years, there were no instances of urinary abnormality. Total 24-hour urinary protein was elevated for an average of 14 days after admission, with extremes of 1 and 90 days. Two cases were allowed up early, and relapsed. Addis counts and ESR were of no value in gauging the period of enforced bed rest, a better gauge being the disappearance of excess protein from the urine.

(b) *The Haemolytic Uraemic Syndrome*

In 1955, Gasser *et al.*[5] described a syndrome of uraemia, haemolysis and thrombocytopenia, which we have seen with increasing frequency since 1958; reports of cases seen in this hospital have already been made by Griffiths and Irving[6] (1960) and Javett and Senior[7] (1962). 23 cases were encountered in the 3½ years covered by this series, all in children under the age of 18 months (Fig. 4). Of these, 8 were male and 15 female, and all came from good homes, being more than well nourished. The majority of patients were aged 7-9 months. All except one gave a previous history of mild diarrhoea and vomiting preceding the onset of the illness by 1-5 days, occasionally up to 10 days; the exception was a child who had an upper respiratory-tract infection. The gastroenteritis was so mild that in 5 cases no treatment was given.

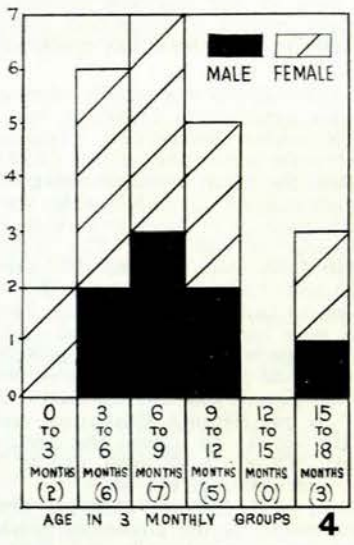

Fig. 4. Age and sex distribution of cases of the haemolytic uraemic syndrome. The numbers of cases are shown on the vertical coordinate and the totals written along the horizontal coordinate.

Clinical Features. The syndrome was characterized in every one of our cases by an abrupt onset of lemon-yellow pallor. Hypertension was a prominent feature, the systolic blood pressure (BP) being between 100 and 180 mm.Hg in 18 cases. Purpura was found in 10 cases on admission. Vomiting occurred in 8 cases. Convulsions were seen in 7 cases probably due to the uraemic state, the rectal temperature never being above 101°F. at presentation. Oliguria was a presenting symptom in 7 cases. Obvious haematuria occurred in 3 cases, and generalized oedema in 5. All the patients that died developed total anuria. Nine cases showed enlargement of the liver and 3 of the liver and spleen. Three infants developed cardiac failure.

Investigations. Urine examination showed changes indistinguishable from those of acute glomerulonephritis. Peripheral blood examination was very typical in that a haemolytic anaemia was present. The haemoglobin levels varied from 5 to 10·8 G./100 ml., and the red cells showed fragmentation and schistocyte formation, with an increased reticulocytosis of about 10%. The white-cell count was slightly elevated. Eighteen cases had platelet counts under 150,000/cu.mm., 9 of these being between 20,000 and 50,000/cu.mm. Bone marrow, where examined, was hypercellular and showed erythroid hyperplasia. The blood urea was usually grossly elevated, and was never below 30 mg./ml. This contrasts markedly with the usual mild elevation found in older children with glomerulonephritis. Severe electrolyte disturbances occurred frequently, and normal electrolytes were found in only 4 cases. Hyperpotassaemia was frequently encountered and in 3 cases the level was over 7·5 mEq/l. on first examination. One child died in the diuretic phase with severe distal tubular loss of sodium and potassium. The serum bilirubin was slightly increased, the highest level being 2·4 mg./100 ml., and the average 1·1 mg./100 ml. Protein electrophoresis was not grossly disturbed and 10 cases showed only a lowered serum albumin.

Infection tests. Virus culture of material from stools, urine, throat and nose, blood, bone marrow and postmortem tissue has, to date, been negative, with the exception of one child in whom Coxsackie-A virus was isolated from the stool. This child, however, also had encephalitis and positive toxoplasma dye and complement-fixation tests. Investigations such as the Coombs, Schumm, Wassermann, Paul-Bunnell and LE-cell tests, and blood cultures, have all been negative. Bacterial study of stools and urine have been non-contributory.

Treatment has been empirical and it is our conclusion that steroid has no appreciable effect on the course of the disease and may actually complicate it. Blood has been given in all cases where the haemoglobin was low. Renal failure has been managed with restricted fluid by mouth (where no vomiting has occurred). A solution of 20% lactose was used, the amount given being the previous day's urinary loss plus about 10 ml./lb/day. Where this has failed, intravenous fluid therapy with 5, 10, 20 or 40% glucose in distilled water has been given, the strength depending upon the level of the serum potassium. The serum potassium has been controlled by the use of insulin and glucose, rectal ion-exchange resin, anabolic steroids, and intravenous calcium. Where this has failed, we have dialysed 2 children on the artifical kidney, one of them twice, and used exchange transfusion in one case. More recently, and not in this series, we have used peritoneal dialysis. Digitalis (in restricted dosage because of anuria or oliguria) has been most important in therapy. Blood pressure has been treated with intramuscular serpasil and oral or intramuscular apresoline, and convulsions with paraldehyde and phenobarbitone. Secondary infection was controlled by the use of antibiotics.

Prognosis in all cases was governed by the severity of the renal abnormality (with the effects of thrombocytopenia as an extra hazard), and anuria was a bad prognostic sign. Of the 16 cases that were not fatal, haematuria and albuminuria persisted for a maximum of 5 weeks, with the exception of one very severe case. The latter patient was dialysed twice, had severe oliguria or anuria for 23 days, and still has albuminuria, haematuria and hypertension about 9 months later. The other children were all apparently normal at examination between 6 months and 3½ years later.

Postmortem examination was performed in 5 of the 7 children who died. All but one showed evidence of thrombocytopenia, with multiple petechial haemorrhages in all organs, 2 having large intracerebral haemorrhages. One child, who had been on large doses of steroids, had a large duodenal ulcer. In 4 children the kidneys were enlarged and tense in their capsules, 2 of these showing patchy cortical necrosis on histology, and in one, who died in the diuretic phase, the kidneys were enlarged, pale and flabby.

Renal histology (biopsy or postmortem). Renal biopsy was performed in 5 cases. Three were fairly mild and showed fine adhesions between the visceral and parietal layers of Bowman's capsule, which contained large, relatively avascular glomeruli; the basement membrane of the capsule was slightly thickened and the tubules contained proteinaceous material. Of the other 2 cases, 1 died and a fuller description is available from postmortem histology. In the other, a very severe case, biopsy in the diuretic phase showed both small and large glomeruli, and adhesions between visceral and parietal layers of Bowman's capsule, with hyaline material in the capillaries. The tubules contained casts and the interstitial tissue showed several aggregates of lymphocytes. Postmortem renal histology showed changes mainly in the glomeruli. The 2 with patchy cortical necrosis showed extensive areas of necrosis and haemorrhage. The glomeruli themselves were avascular and swollen, occasionally shrunken, and many had eosinophilic material in the capillary lumen, the walls of which were hyalinized and the basement membrane slightly thickened. Adhesions were present between the visceral and parietal layers of Bowman's capsule. Casts were found in the tubules, one case showed extramedullary haemopoiesis, and in 2 there were fibrin or platelet thrombi in afferent vessels.

(c) *Subacute Bacterial Endocarditis*

Children suffering from subacute bacterial endocarditis may present with macroscopic rather than microscopic haematuria. Five cases, 1 male and 4 female, occurred in this series, all with macroscopic haematuria. They included 3 patients with congenital heart disease, 2 of whom had undergone previous surgical correction, and 2 with rheumatic fever. The ages varied between 6¾ and 13 years.

All cases presented with a sudden onset of symptoms, and in none was there a previous history of a sore throat. Complaints were of haematuria, oliguria, oedema, malaise, and vomiting. The BP was elevated in 1 case only. Two children showed evidence of heart failure, with pulmonary oedema in 1. The temperature was elevated in 1 case only. Two children showed splenomegaly, 1 generalized oedema, 1 clubbing and 1 a pleural effusion, and 2 only gave a positive blood culture. Haemoglobin, white blood-cell count and platelets were normal. The ESR was normal in 2 cases with heart failure, and elevated in the other 3. Three cases showed moderately elevated ASO titres. The urinary changes were indistinguishable from those of acute glomerulonephritis. Blood urea was moderately elevated in 3 cases and the serum-protein electrophoresis was normal in all cases.

Serial renal biopsy was performed in 1 patient, who had persistent haematuria for 6 months. The initial biopsy showed glomeruli with thickening of the capillary walls, occasional areas of proliferation of the parietal layer of Bowman's capsule, and adhesions between the visceral and parietal layers of the capsule; some glomeruli showed early crescent formation. A repeat biopsy 6 months later showed increased cellularity of Bowman's capsule and some slight adhesions between the visceral and parietal layers of the capsule.

No case improved until massive penicillin therapy was instituted. Albuminuria and proteinuria continued for 2 - 6 months after the acute attack. All cases are now clinically recovered and 2 have undergone surgical correction.

(d) *Henoch-Schönlein Purpura*

Five cases occurred in this series, 2 male and 3 female. The ages varied from 3 to 12 years.

Two presented with joint involvement, 1 with abdominal pain (and actually had his appendix removed), 2 with haematuria, 3 with purpura, and 1 with vomiting. All the patients developed the rash of Henoch-Schönlein purpura in hospital, 2 an elevated blood pressure, 3 pharyngitis, and 1 generalized oedema.

The haemoglobin was normal, the white blood-cells varied from 5,800 to 13,000/cu. mm., and the platelets were normal. The ESR was elevated in 4 cases, the ASO titre was 250 units/ml. in 1 case and 400 in another, and the blood urea was moderately elevated in 3 cases. The urine was typical of acute glomerulonephritis. Serum-protein electrophoresis was quite normal.

Diuresis occurred rapidly and all cases are quite normal on examination between 6 months and 3½ years later.

(e) *Glandular Fever*

The acute nephritic syndrome occurred in 3 cases of glandular fever in this series. They were girls 4½ - 6 years old.

Two had a previous history of a sore throat and 1 of scarlet fever. Other symptoms were haematuria, oedema, weight gain, headache, glands in the neck, and vomiting. Hepatosplenomegaly and lymphadenopathy were found in 2 cases, slight oedema in 2 cases, pharyngitis in two cases, and hypertension in 1 case only.

The haemoglobin was normal, the white blood-cells varied from 9,300 to 23,000/cu.mm., and atypical lymphocytes were present. Platelets were normal. The ESR was grossly elevated, the ASO titre elevated in 1 case, and the Paul-Bunnell test positive in all 3 cases to a high titre. The urinary findings did not differ in any respect from glomerulonephritis. The blood urea was moderately elevated, the serum-protein electrophoresis normal, and the serum cholesterol not elevated. Virus culture of stools was carried out in all cases, but no virus was recovered. Renal biopsy was performed in 1 case and showed minimal changes, with adhesions between the visceral and parietal layers of Bowman's capsule.

Diuresis occurred rapidly within 1 - 3 days and all cases recovered completely.

2. NEPHROTIC SYNDROME

The nephrotic syndrome in childhood typically presents with an insidious onset of oedema, hypoproteinaemia, albuminuria, and hypercholesterolaemia. Other important features are that there is no previous history of a sore throat, nor is azotaemia, hypertension or haematuria present. Eight cases occurred in our series, 5 male and 3 female, which corresponds with the sex proportion in previous series.[8] The average age at onset was 4 years, with extremes of 2 and 6 years.

All cases began insidiously and the major complaints were malaise, weight gain and oedema. All patients were grossly oedematous and irritable when examined. In no case was the BP elevated. Two cases showed evidence of infection in the upper respiratory tract; one had a pleural effusion.

Urine examination in all cases showed gross proteinuria of the order of 5 - 10 G. in 24 hours, hyaline casts on occasion, and no increase in red or white cells. Blood examination showed a normal haemoglobin, elevation of white cells with a polymorphonuclear leukocytosis, and normal platelets. The ESR was elevated in 6 cases. The ASO titre was 12½ units or less per ml. in 7 of the 8 cases, and in the 8th case 580 units per ml. Blood urea was not elevated. In all cases the serum cholesterol was elevated to levels of 354 - 720 mg./100 ml. All cases showed the typical nephrotic serum-protein electrophoretic pattern.

Renal biopsies were performed in 6 of the 8 cases, one serially. Minimal changes were found on light microscopy, with thickening of basement membrane, fine adhesions between the visceral and parietal layers of Bowman's capsule, proteinaceous material in the tubules, foci of calcification on occasion in the interstitial tissues, and normal blood vessels. Adequate electron miscroscopy was available in one case only and fusion of podocytes was demonstrated.

All patients were put on steroid, high-protein diet, and prophylactic antibiotics; and diuresis appeared in 5 on high dosage of prednisone within 10 days of starting the therapy. Two patients who had relapsed showed second diureses with this drug. Three patients failed to respond, 2 of whom were given triancinolone followed by ACTH and 'celestone'. One died in coma with an elevated BP, both features being possibly steroid-induced. Where diuresis was produced, proteinuria disappeared totally in 5 - 10 days. All of these cases are being maintained on small doses of prednisone.

3. THE NEPHRITIC-NEPHROTIC SYNDROME

We use this term to denote certain patients who quite obviously from the onset have illnesses different from those described above as glomerulonephritis or the nephrotic syndrome. In all these cases, features of both syndromes were present from the beginning and we have divided them into two groups, (1) mainly nephritic and (2) mainly nephrotic.

Mainly Nephritic

There were 8 patients in this series, 3 male and 5 female. Their ages varied from 1½ to 12¾ years. Three presented with oliguria; 3 with non-specific symptoms such as headache, feeling off-colour, etc.; 2 with abdominal pain; and 1 with haematuria. Two were discovered incidentally. In 6 there was moderately elevated BP, and oedema in all cases was more marked than would normally be expected of a case of acute poststreptococcal glomerulonephritis. In 2 there was papill-oedema and in 1 convulsions, and 1 was drowsy.

Urine examination showed a moderate increase in red cells in most cases; a mild to marked increase of white cells; hyaline, granular and cellular casts; and a marked proteinuria with protein losses of 5 - 13 G. in 24 hours. Haemoglobin levels were normal. In 6 cases the white blood-cell counts were normal, but in two they were moderately elevated. Platelets were normal. The ESR was elevated in 6 cases. The ASO titre was mildly elevated in 2 cases only. The blood urea was grossly elevated. The serum cholesterol was elevated in 5 cases. The serum-protein electrophoresis was normal in 1 case only, and the pattern was typically nephrotic in the other 7 cases.

Renal histology is available in 7 cases, in 1 of which it was obtained at postmortem. Six showed sclerosed glomeruli and 2 enlarged glomerular tufts; 1 case was followed from the stage of enlarged tufts to that of sclerosis. Other findings were of adhesions between the layers of Bowman's capsule; occasional crescent formation; occasional atrophic glomeruli; and increased cellularity of the glomeruli. The interstitial tissue showed non-specific infiltration in 4 cases. The tubules were not remarkable, nor were the blood vessels. The one autopsy showed small shrunken kidneys.

All the children were put on the therapeutic regime outlined above under 'acute poststreptococcal glomerulonephritis'. In 2 cases only a reasonable diuresis followed after 10 days. Two patients died. The remaining children still show haematuria and albuminuria 6 months to 3½ years later.

Mainly Nephrotic

Two cases of this syndrome, both males, were encountered in this series, aged 2½ and 3 years at onset. One case presented abruptly with haematuria, oliguria and hypertension. The other began insidiously. Both were grossly oedematous when first seen.

In both cases urine examination showed increased amounts of red and white cells, hyaline and granular casts, and marked proteinuria. In both cases blood examination showed a normal haemoglobin, the white cells not elevated, platelets adequate, and the ESR elevated. The ASO titre was not elevated in either case. In both cases the cholesterol was markedly elevated, the serum-protein electrophoretic patterns were nephrotic in nature, and the blood urea was normal. Other tests such as Wassermann, Paul-Bunnell, and for LE cells, were negative.

In one child, renal histology showed fibrosed glomeruli, with a few foci of interstitial calcification; in the other it showed adhesions between the layers of Bowman's capsule, with proteinaceous fluid in the capsule. Electron microscopy showed podocyte fusion.

Both children were put on antibiotics and steroids. One has relapsed 4 times and the other 3 times though they respond well to re-administration of steroids. Neither is free of protein or blood in the urine at follow-up, which has been between 2 and 6½ years.

DISCUSSION

For many years, controversy has raged about classification of glomerulonephritis, the principal difficulty being the establishment of the common meeting-ground between acute glomerulonephritis (Ellis type-1 nephritis) and the syndrome of idiopathic nephrosis (Ellis type-2 nephritis), if such meeting-ground exists. De Wardener[2] suggests that there is a syndrome of acute glomerulonephritis that may present as a 'rapidly progressive renal failure, a persistent proteinuria, recurrent haematuria (usually with persistent proteinuria), a nephrotic syndrome, or chronic renal failure'. Wilson[9] suggests that there is a spectrum of events that occur in both diseases, and that both type-1 and type-2 nephritis may develop renal failure and hypertension as terminal events in long-continued cases of both syndromes.

We believe that much of the confusion that exists in classification has resulted from elastic interpretation of what comprises acute glomerulonephritis and what idiopathic nephrosis.

The syndrome of acute poststreptococcal glomerulonephritis has a clear pattern in that there is a preceding history of group-A beta-haemolytic streptococcal infection, and that in approximately 2 weeks from this infection the disease begins with the sudden onset of generalized oedema that is moderate in amount, hypertension (not in every case), azotaemia, haematuria (the most characteristic finding), oliguria, albuminuria, and cylinduria. The ESR is elevated, the ASO titre markedly elevated, and the serum-protein electrophoretic pattern typical in that serum albumin is depressed and gamma globulin elevated. If the child is put to bed, diuresis occurs in under 10 days and complete recovery ensues, provided death does not occur in the acute phase as a result of renal failure, pulmonary oedema, or encephalopathy. The renal histology is remarkable for the minor nature of the changes encountered.

The syndrome of idiopathic nephrosis in childhood also has a clear pattern. The disease begins insidiously, with no preceding history of a streptococcal infection, and when first seen the child has marked generalized oedema, no elevation of BP, marked proteinuria, no haematuria, no elevation of blood urea, high serum cholesterol, and a typical serum-protein electrophoretic pattern with diminished albumin, elevated alpha-2 globulin, and diminished gamma globulin. Provided that diuresis occurs on steroid therapy the prognosis is good. Again the renal histology shows minimal changes on light microscopy.

According to these definitions then, a child with idiopathic nephrosis could not have haematuria, hypertension or azotaemia, and a child with glomerular nephritis could not have hypercholesterolaemia or a nephrotic serum-protein electrophoretic pattern. Among our cases, those children who actually presented with features of nephritis and nephrosis together pursued totally different clinical courses from either of these syndromes, and it was quite apparent from the outset that we were dealing with a different disease complex. For this reason, we have classified these cases separately and named them the nephritic-nephrotic syndrome, because they have features of both acute glomerulonephritis and idiopathic nephrosis.

The cases that were mainly nephritic presented without a previous history of streptococcal infection, and oedema was more than one expected of a case of Ellis type-1 nephritis. BP was grossly elevated, haematuria was moderate, proteinuria was marked, blood urea was high, serum cholesterol was high, the ASO titre was not raised, and the serum-protein electrophoretic pattern in the majority of cases was typically that of nephrosis. Diuresis, if it occurred at all, was long-delayed and all cases that recovered had persistent albuminuria and haematuria. Renal biopsy was marked by the severity of changes found, and many glomeruli were sclerosed. Two children died in renal failure.

The two cases that presented as mainly nephrotic again had no antecedent history of a sore throat, and the presentation was very similar to the presentation in the cases that were mainly nephritic, except that oedema, albuminuria, hypercholesterolaemia and hypoproteinuria were more marked. In addition, haematuria was present as well as hypertension in one case. The ASO titre was not elevated. Renal biopsy in one case again was marked by the severity of the changes found. In both cases the clinical course was punctuated by several relapses.

Whatever the aetiology of this third picture of glomerular disease, we feel that it is sufficiently distinct to be separated from the entities of glomerulonephritis and idiopathic nephrosis. The importance of this separation lies in two facts, viz. that poststreptococcal glomerulo-

TABLE I. FEATURES OF THE DISEASES

	Acute nephritic syndrome					*Nephrotic syndrome*	*Nephritic-nephrotic syndrome*	
	Glomerulo-nephritis	*Haemolytic uraemic*	*S.B.E.*	*Henoch-Schönlein*	*Glandular fever*		*Mainly nephritic*	*Mainly nephrotic*
Number	96	23	5	5	3	8	8	2
Sex	M56, F 40	M 8, F 15	M 1, F 4	M 2, F 3	M 0, F 3	M 5, F 3	M 3, F 5	M 2, F 0
Age	2-14 years Majority 3-7	0-1½ years Average 7 mths	6¾ years	3-12 years	4½-6 years	2-6 years	1½-12¾ years	2½-3½ years
History	Sore throat	Diarrhoea and vomiting	—	—	—	—	—	—
Oedema	+	±	—	—	±	++++	+++	++++
BP	+	++	±	±	±	—	++	±
Urine: RBC	++++	++++	++++	++++	++++	—	++	++
Protein	++	++	++	++	++	++++	++++	++++
ASO titre	++++	—	±	±	±	—	—	—
ESR	++	—	+	+	+	++	+	+
Blood urea	++	++++	+	+	+	—	+	—
Blood cholesterol	—	—	—	—	—	++++	++++	++++
Protein electrophoresis	Nephritic pattern	—	—	—	—	Nephrotic pattern	Nephrotic pattern	Nephrotic pattern
Paul-Bunnell test	—	—	—	—	+	—	—	—
Glomeruli	Swollen, hypercellular	Swollen, Avascular platelet or fibrin thrombi	Swollen, hypercellular	—	Minimal changes	Minimal changes	Sclerosed	Sclerosed
Tubules	Casts	Casts	—	—	—	Casts	—	—
Vessels	—	Platelet or fibrin thrombi	—	—	—	—	—	—
Complications	Encephalopathy Heart failure	Renal and heart failure Encephalopathy	—	—	—	—	Encephalopathy Renal and heart failure	Relapse
No. of deaths	0	7	0	0	0	1	2	0
Survivors recovered	All	All but one	All	All	All	All	None	None

nephritis is shown thus to have an excellent prognosis for complete recovery provided the patient survives the acute attack, and that idiopathic nephrosis in childhood also has a good prognosis for complete recovery provided that diuresis occurs on steroid therapy.

There are several other features of note in this series of 150 consecutive cases, not least the extraordinary high proportion of cases of the haemolytic uraemic syndrome. All patients with this syndrome came from excellent homes, were well nourished, were under 18 months of age and, if they survived the acute disease, appeared to recover completely with the exception of one case. The severity of the disease was governed by the intensity of the renal lesion, and anuria or oliguria was a bad prognostic sign. Steroid was judged to have no effect on the course of the disease, which may well be infective in nature, though to date we have been unable to substantiate this hypothesis.

During the period of this study, no cases of subacute bacterial endocarditis were encountered with microscopic haematuria, all cases found presenting as the acute nephritic syndrome. Recovery in these cases did not begin until massive penicillin therapy was instituted. Our cases of Henoch-Schönlein purpura with nephritis all recovered completely, a feature in children that has been previously noted.[10] Glandular fever with the acute nephritic syndrome also seemed to have a good prognosis.

Prominent features of the disease encountered are summarized in Table I.

SUMMARY

150 consecutive cases of glomerular lesions in childhood have been classified and discussed. Renal biopsy was performed in 26 cases, some serially, 31 biopsies in all being available. Reasons are given for subdividing the cases into acute nephritic, nephrotic, and nephritic-nephrotic syndromes, each of which is a clinically distinct disease.

132 cases were of the acute nephritic syndrome, prominent causes of which were poststreptococcal glomerulonephritis (73%), and the haemolytic uraemic syndrome (17%). All except the severest cases of the haemolytic uraemic syndrome showed minimal histological changes on renal biopsy. All cases of poststreptococcal glomerulonephritis recovered completely.

Eight cases of idiopathic nephrosis were encountered, prognosis being excellent in those that responded to the administration of steroid. The renal histological changes on light microscopy were minimal.

Ten cases were encountered of a syndrome characteristic neither of nephritis nor nephrosis but with features of both, 8 mainly nephritic and 2 mainly nephrotic. This has been called the nephritic-nephrotic syndrome. All 10 patients showed a poor response to therapy, 2 died, and at follow-up those that survived have persistent haematuria and albuminuria. Renal histology was marked by the severity of the changes found.

Features of all of these diseases are discussed, as well as the methods of treatment employed.

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