THE PATHOLOGY OF NON-SUPPURATIVE NEPHRITIS IN CHILDREN.

By

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A STUDY OF THE PATHOLOGY OF NON-SUPPURATIVE NEPHRITIS IN INFANCY AND CHILDHOOD.

INTRODUCTION.

Within the last few years many excellent articles have been written dealing with individual aspects of juvenile nephritis, but so far as the present writer is aware, there has appeared recently no monograph of wider scope purporting to give a general review of the pathology of this protean disease in the child, comparable to the studies of nephritis in the adult published by Russell (1929), Addis and Oliver (1931), and Gray (1933). It appeared, therefore, that such an investigation with a survey of the recent literature on the subject might be of some interest. In children nephritis manifests itself in purer form than in adults, since in the former there is no wear and tear of past life to complicate the picture, nor do we have to think of the circulatory system in relation to the kidneys, Hill (1919), while the absence of previous attacks which often complicate the disease in the adult, simplifies the evaluation of the etiological factor in the child, and also the problem of correlating renal structural changes and functional damage, Paterson (1926).

In a previous short study of juvenile nephritis by the writer some interesting results emerged even from the limited series/

series of cases then investigated - among others the fact that in young children death can take place at a very early stage, with little evidence of disease on macroscopic, or even on microscopic examination, and that even when definite pathological changes are evident to the naked-eye, these often form no reliable indication of the type or stage of lesion actually present. Another feature of note was the total absence in many cases of any etiologic factor to which the attack of nephritis might be attributed, though, according to modern views some general or focal infection of etiological significance is rarely lacking. These points have all been more fully investigated in the present study and will be dealt with later.

Before proceeding further it appears advisable to give a definition of the nature of Bright's Disease. Addis and Oliver (1931) define it as "That sort of a lesion where protein from the blood plasma passes through the kidney into the urine, and also that sort of a lesion which damages but does not altogether disintegrate the architecture of the kidney." As these authors state, casts, being a mould of the interior of the tubules, demonstrate the maintenance of at least the essential elements in which they originate, and are not formed in conditions such as suppuration and new growth, for these destroy renal tissue, but in Bright's disease the lesion is of such a nature that it can become a part of the life of the kidney, entering into all the intricacies of its structural and functional reactions. A large amount of autopsy material is not readily/

readily available for the study of nephritis in children, since the disease in them is relatively non-fatal, particularly the mild haemorrhagic type confined almost exclusively to young subjects, and which has an extremely good immediate prognosis. Though many cases of Bright's disease may be admitted to the wards of a children's hospital in the course of a year, perhaps only two or three on an average may succumb. This is true at least of the Glasgow Royal Hospital for Sick Children, where, according to the hospital statistics, during the last 10-year period from 1923 to 1932 inclusive, 477 cases of nephritis were admitted but only 34 died, the case mortality rate thus being 7.12 per cent. Since, in addition, permission for a post-mortem examination is not granted in every fatal case, the percentage of autopsies on all cases of juvenile Bright's disease is necessarily very small.

MATERIAL OF THE PRESENT STUDY.

The material of the present investigation comprises altogether 94 cases of nephritis and these can be subdivided into two groups: (A) 57 cases of primary nephritis where the child was brought to hospital with nephritic symptoms dominating the clinical picture, and (B) 37 cases where nephritis developed during the course of some other illness; the existence of the former, even when recognised clinically in some instances, was always overshadowed by the accompanying disease. These 37 cases were discovered during the examination (macro-

and microscopic) of 163 kidneys removed at autopsy from patients with a variety of diseases, e.g., septicaemia, peritonitis, pneumonia, meningitis, rheumatic endocarditis and other septic and toxic conditions.

Group A can be further split into: (1) 47 fatal cases of primary nephritis, (2) 10 non-fatal cases where the nephritic patients were subjected to the operation of decapsulation of the kidneys, when portions of the organs were removed for histological examination. The kidneys in these 10 cases, along with one other single kidney removed at operation and the seat of a rare abnormality, comprise the only material in this study not obtained post-mortem. The 47 fatal primary cases represent the great majority, though not quite a consecutive series of all cases of nephritis coming to autopsy in the Pathology Department of the Glasgow Royal Hospital for Sick Children between the beginning of the year 1915 and the end of the year 1933, and occurring in a series of approximately 3,800 post-mortems. The gaps in continuity in the total series of recorded cases are occasioned by the fact that material for histological examination was not available in a few of the earlier cases of nephritis.

METHODS EMPLOYED.

Representative portions of both kidneys (where obtained by the writer in the post-mortem room) were fixed in 10 per cent formol-saline and in Zenker's or Helly's fluid and were embedded in/

in paraffin in the usual way, or cut frozen for the demonstration of fat after formalin fixation. Paraffin sections were stained by haematoxylin and eosin and by Gallego's or Van Gieson's stain as a routine, while special stains were employed in investigating features of particular interest, e.g., Haidenhain's iron haematoxylin for nuclear division in the process of cell regeneration, Gram's stain for hyaline droplet degeneration and for organisms, Unna and Pappenheim's stain for cellular exudates, while frozen sections were stained by Sudan III, or scarlet red. Sections stained and unstained were examined with the polarising microscope for the presence of doubly-refractile lipoid. In the older cases only paraffin-embedded blocks of formalin-fixed material were available.

CLASSIFICATION.

"Of making many books there is no end" and the same is also true with regard to classifications of nephritis. Their name is legion, and it appears to the writer that the employment of a variety of different terms for the same pathological entity merely results in "confusion worse confounded."

To give merely one example, the same disease picture is called by Munk "lipoid" nephrosis, by Volhard and Fahr "genuine" nephrosis, by Epstein "chronic nephrosis", by Addis and Oliver "cryptic degenerative Bright's disease," while Russell in her monograph has coined for it the name of "Nephritis mitis," and Gray/

Gray, shortening the term "Nephritis mit Nephrotischem Einschlag" of recent German writers, designates it by the somewhat paradoxical name of "Nephrotic Nephritis."

On the other hand one particular term such as "Parenchymatous Nephritis" or "Chronic Interstitial Nephritis" is used to describe more than one type of renal lesion. The present classification will, therefore, be made as simple as possible to avoid any confusion.

The 47 fatal cases of Primary Nephritis are subdivided as follows:-

Acute glomerulo-nephritis	....	37 cases
Subacute " "	....	2 cases
Chronic " "	....	7 cases
Acute interstitial nephritis	....	1 case.

The 37 cases of acute glomerulo-nephritis can be further split into:-

Acute haemorrhagic nephritis	....	4 cases
Acute exudative nephritis	....	28 cases
Mild glomerulitis with severe tubular degeneration	....	4 cases
Severe glomerulo-nephritis with extensive tubular necrosis	....	1 case.

Of the 7 cases of chronic nephritis mentioned in the above classification 2 occurred in patients with a single kidney and one in an infant with bilateral renal hypoplasia of extreme degree.

Of the 28 cases of acute exudative nephritis one was present/

TABLE I.

Age and Sex Distribution of 37 cases of Secondary Acute Nephritis.

Age.	M.	F.	
0-6/12	5	7 (2 acute interstitial nephritis; 5 acute glomerulo-nephritis.)	
6/12+ - 1 yr.	1 acute interstitial nephritis	2	
1 yr.+ - 2 yrs.	1	1	
2 yrs.+ - 3 yrs.	-	2	26.
3 yrs.+ - 4 yrs.	4	1	
4 yrs.+ - 5 yrs.	1		
5 yrs.+ - 6 yrs.	1		
6 yrs.+ - 7 yrs.		1	
7 yrs.+ - 8 yrs.		1	
8 yrs.+ - 9 yrs.	2	1	11.
9 yrs.+ - 10 yrs.	2	3	
10 yrs.+ - 11 yrs.		1	
Total:	17	20	

TABLE II.

Age and Sex Distribution of 57 Nephritis Cases. (Primary).

	ACUTE NEPHRITIS.		SUBACUTE AND CHRONIC NEPHRITIS.		
Age.	M.	F.	M.	F.	
0-6/12	2	4 (1 acute interstitial nephritis).	3 (1 subacute, 2 chronic)	1 chronic	
6/12+ - 1 yr.	1	1			
1 yr.+ - 2 yrs.	2	3	2 chronic.		
2 yrs.+ - 3 yrs.	2	2			40
3 yrs.+ - 4 yrs.	4	2			
4 yrs.+ - 5 yrs.	1	5			
5 yrs.+ - 6 yrs.	5	-			
6 yrs.+ - 7 yrs.	1	1		2 (1 subacute (1 chronic	
7 yrs.+ - 8 yrs.	-	2			
8 yrs.+ - 9 yrs.	2	2			
9 yrs.+ -10 yrs.	4	-			
10 yrs.+ -11 yrs.	1	1			17
11 yrs.+ -12 yrs.					
12 yrs.+ -13 yrs.					
13 yrs. +				1 chronic	
Total:	25	23	5	4	

present in an infant with kidneys of rather immature type, while the 4 cases of mild glomerulitis with severe tubular degeneration correspond to the "parenchymatous nephritis" or "tubular nephritis" of various authors.

On referring to the tables inserted here giving the age and sex distribution both for the 57 cases of primary nephritis (including the 10 ward cases) and for the 37 cases of secondary nephritis, it is seen that of these 57 patients with primary nephritis 30 were males and 27 females, while 40 were under the age of 6 years - thus dying in the first half of childhood. Of the 37 secondary cases, 17 were of the male and 20 of the female sex, and of these 26 died under the age of 6 years.

On combining these results, it is seen that of the total 94 cases, 47 occurred in male and 47 in female children, while 66 patients died under the age of 6 years. (70.20 per cent.), 27 being under 1 year at the time of death (28.72 per cent.), and other 9 under the age of 2 years, 38.30 per cent. thus dying under the age of 2 years.

NAKED-EYE APPEARANCE OF THE KIDNEYS IN ACUTE NEPHRITIS.

A short description of the naked-eye characters of all the kidneys in the above group of 37 cases will be given before proceeding to a detailed examination of the particular types comprised within it.

Acute Haemorrhagic Nephritis (4 cases).

Of these patients one was of the female and 3 were of the male sex, the ages being 22 days, 6 months, 3¾ years, and 11 years respectively. The striking feature in this small group was the marked congestion shown by all the organs which were closely similar in appearance, all being deep red in colour throughout both cortex and medulla, with a tendency to drip blood on section. In 2 cases slight yellowish mottling was present on the dark red background. The organs were all markedly swollen and tended to bulge out of the renal capsule which was thin, and stripped readily in every case, leaving a smooth congested surface.

Acute Exudative Nephritis (28 cases).

This group includes a premature infant where, however, the organs appeared normal macroscopically, except for marked foetal lobulation. Of these patients 14 were male and 14 female, the ages varying from 5 weeks to 11 years. The naked-eye appearance of the kidneys in this group presented much variety with/

with regard both to size and to colour. Enlargement of varying degree was noted in 15 cases, these kidneys being described as swollen with a tendency to bulge out of the capsule, while on section enlargement was sometimes general, sometimes limited to the superficial or interpyramidal cortex. In the other 13 cases it was either stated that the kidneys were not enlarged or no mention was made of the size. Regarding colour, the general impression was one of pallor in 13 instances or approximately half the cases, with or without irregular congestion, the latter when present producing a network of reddish mottling on a whitish or yellowish background. In the other half, the kidney substance was either of the normal reddish tint, or more or less congested, areas of tubular degeneration showing as pale striae on a reddish foundation. Petechial haemorrhages into the renal substance were noted 3 times in this group, including the immature kidney where the pyramids were congested and the seat of scanty minute haemorrhages. In another instance purpuric spots were present not only in the kidneys but in the skin and various other internal organs. In a number of cases the glomeruli were mentioned as visible on naked-eye examination, or with the aid of a hand lens, as grey or greyish-red points, and twice they were seen as small red dots. Histological examination in these 2 cases revealed intense glomerular congestion as the only noteworthy pathological change. The texture, like the size and colour, was subject to marked variation/

variation, the organs in some cases being described as firmer and tenser than usual, in others as soft and flabby, and sometimes oedematous. The capsule was not thickened in any instance and stripped with ease except in one case, where the underlying cortex was finely granular with a very slightly adherent capsule. No abnormality was detected in the renal pelves in any instance.

4 Cases of Mild Glomerulitis, associated with marked Tubular Degeneration.

Of these patients 3 were of the female, and one was of the male sex, the ages being 26 months, $4\frac{1}{2}$ years, 23 months, and $2\frac{3}{4}$ years respectively. The kidneys were enlarged in 3 instances, considerably in 2, and moderately in the third, no mention of the size being made in the last case. All the organs were pale, though with marked mottling due to alternating areas of congestion and fatty change. In one instance the fatty material in the cortices had a peculiar glistening yellowish appearance suggestive of myelin, and the capsules in this case stripped with slight difficulty leaving a rather irregular surface. Some blurring or irregularity of the cortical markings was present in the other kidneys.

One case remains to be considered - that of a girl, 9 years of age, with widespread necrosis of the tubular epithelium in addition to a marked inflammatory lesion in the glomeruli. The kidneys here were small, pale and extremely soft/

soft and flabby, with loss of demarcation between cortex and medulla.

On reviewing the naked-eye appearance of the whole series of 37 cases of acute nephritis it is evident that, except for the few cases of haemorrhagic nephritis where the kidneys were closely similar in appearance and were obviously pathological, no typical picture was present in the entire group pathognomonic for acute nephritis, thus enabling diagnosis to be made on macroscopic examination alone. In several instances, indeed, the swollen, pale, and mottled cortex was suggestive of a subacute rather than of an acute lesion and in 2 cases the finely granular surface might have been considered indicative of a still more chronic lesion. In some kidneys the seat of an early lesion, there was only very slight departure from the normal. Thus, in a case observed recently, where the patient was admitted moribund with a history of one day's illness, the kidneys were normal in size and shape, the markings were not distorted, there was no noteworthy congestion, and the only abnormal feature in the organs was the fact that their consistence was rather firmer and more elastic than usual. The unreliability for diagnostic purposes of the naked-eye appearance of the kidneys both in juvenile and adult nephritis has been repeatedly emphasized in the literature. Carpenter (1905) describing the kidneys of a syphilitic infant states "There is no doubt that infantile/

infantile kidneys may be seriously diseased, and yet not show any pathological changes whatever to the naked-eye, and these would therefore at autopsy be deemed normal and recorded as such. It follows, therefore, that these organs cannot be pronounced sound on mere ocular inspection at post-mortem." Various other writers support this view in describing syphilitic renal lesions in infants. Abt (1924) finds that in mild glomerulo-nephritis in children, the kidneys on naked-eye examination may not differ from the normal. Dealing with adult patients Volhard and Fahr (1914) describe the kidneys in the first stage of glomerulo-nephritis as showing nothing characteristic while the picture is very variable. Shaw Dunn and McNee (1917) in cases of war nephritis found change from the normal slight. Kaufmann (1924) and Muir (1933) agree that there may be no observable macroscopic lesion in early cases, and Russell (1929) considers that the naked-eye appearance in Bright's disease is not only unsafe as a guide to pathological changes in the kidney, but may even be misleading, a similar macroscopic appearance representing lesions of entirely different nature histologically. Hadfield and Garrod (1932) sum up the matter in stating "All modern work shows that no reliance can be placed on the naked-eye appearance of the kidney, redness or pallor frequently being due to the presence or absence of heart failure, and large normal kidneys often showing unsuspected, widespread inflammatory change or even amyloid degeneration."

NOTE ON THE HISTOLOGY OF THE KIDNEY IN THE CHILD.

Before proceeding to describe the microscopic changes in kidneys the seat of nephritis, it would be well to describe shortly the histological features in the normal child's kidney. In the first place, the organ at birth presents some special features, and changes take place with increasing development till an appearance is reached in older children which approximates closely to that in adults. Since the histological picture varies somewhat at different ages, it was found advisable in the course of microscopic study of kidney sections to group these together according to the age of the patients. A better idea of the normal appearance was thus obtained, and slight degrees of pathological change were more readily recognised at various ages between birth and puberty, than by attempting to compare the kidneys of infants with those of older children. Perhaps the most striking feature in the kidneys of infants immediately after birth is the crowded appearance of the glomeruli, which appear unduly numerous because they lie close together as a result of the relatively unexpanded state of the convoluted tubules, which are of very narrow calibre with epithelium of rather cubical type, while the collecting tubules resemble more closely those in adults. Corresponding to the small size of the secreting tubules, the renal cortex in infants is narrow, sometimes strikingly so, in relation to the medullary/

medullary portion. Foetal lobulation is often marked on naked-eye examination of the kidney, thus indicating the development of its secretory portion in groups around a tubal stem, Frazer (1931). Another noteworthy feature observed microscopically in infantile kidneys is the marked prominence of the epithelial layer covering the glomerular tufts. The cells are cubical, with a relatively large, darkly-staining nucleus. The striking appearance of this epithelium has been pointed out by Russell (1929). The epithelium lining the capsule of Bowman though higher than in adults is less conspicuous than that covering the tuft. The glomerular capillaries are extremely thin-walled, being formed by a layer of endothelium resting on a delicate basement membrane. A frequent finding in infantile kidneys is the presence of a variable number of unripe glomeruli in the superficial cortex immediately under the capsule. There is no actual "neogenic zone" as in foetal kidneys, several of which, at different periods of development, have been examined for comparison, but isolated glomeruli are distinctly immature, appearing either as small rosette-like structures not yet vascularised, or as tubules lined with the characteristic cubical darkly-staining cells. These tubules are sometimes seen in the actual process of coiling to form the rosettes mentioned above. The presence of such structures in small numbers appears to be normal since ~~it was~~ they were frequently found in the kidneys of infants dying of some acute infection in/

in whom there was no suspicion of a syphilitic taint. It does not appear to constitute the retardation in development described by Stroebe (1891), Stoerk (1901), and Cassel (1904), among other German writers, who found a neogenic zone still present after birth and attributed delay in renal development to the action of the syphilitic virus. Such premature glomeruli were most common under 6 months and thereafter became progressively fewer, though an occasional individual example might still be found after the end of infancy. Volhard and Fahr indeed, found single glomeruli of embryonic type even in a boy 9 years old. Another abnormality noted in the kidneys of infants was the presence of single hyalinised glomeruli similar to those seen in adult ischaemic glomerular atrophy. Such glomeruli occurred also at times in small groups, arranged one above the other, as if they derived their blood supply from the same arteriole. The afferent branches to these glomeruli occasionally seen in section, appeared to have slightly thickened walls. Narrow strands of connective tissue corresponding to the distribution of such groups of hyaline glomeruli were present, in addition to small cellular exudates, consisting chiefly of round and plasma cells. One case in particular appeared to throw light on the nature of this degenerative process affecting, it must be emphasized, only a very occasional single glomerulus, or small group of glomeruli. The patient in question was a child, 14 months of age, suffering from anaemia, whose kidneys/

kidneys at autopsy showed no lesion beyond pallor. Histologically the organs appeared normal for this age, the convoluted tubules having expanded, and the glomeruli having lost their peculiar infantile character. In a few foci, however, the appearances resembled exactly those of a kidney immediately after birth, small, primitive glomeruli covered by a prominent epithelial layer, lying close together, along with glomerular anlage, some still in the uncoiled tubular stage. Some of these primitive Malpighian bodies were undergoing sclerosis with thickened capsule, adhesions between capsule and tuft, and peri-glomerular fibrosis. Nothing similar was seen in the surrounding fully-developed structures. It would therefore appear that such immature glomeruli are particularly prone to degenerative changes, the arterial twigs also from which they derive their blood supply being possibly hypoplastic. After the first few months of life the glomeruli and tubules gradually expand, the epithelium becoming flattened in the process. Primitive structures become more and more rare; and hyalinised glomeruli also disappear, apparently as the result of complete absorption. Transition to the adult type is gradual, the epithelium covering the tufts remaining relatively high, and the capillary walls delicate in structure for some considerable time after the kidney has lost its infantile characteristics.

HAEMORRHAGIC NEPHRITIS.

It was thought advisable to place the haemorrhagic cases, though few in number, in a group by themselves, since haemorrhagic nephritis, according to recent work, is a type which, though not exclusively confined to children, is very much more prevalent among them than among adults, and when it does occur after puberty, is generally found in comparatively young people. Thus Bennett (1919) in his study of war nephritis came across a number of patients with nephritis of haemorrhagic type, in whom, as in children, gross haematuria was the outstanding feature, the urine in the early stages being of the colour of arterial blood, while oedema was slight or absent, and casts were only occasionally present. The average age of the individuals with this form of nephritis was much less than that of patients with the ordinary exudative type. Hill (1919), one of the first to describe this haemorrhagic type of nephritis, found it the most common form of renal lesion in childhood, and especially likely to follow tonsillitis. According to his description, haemorrhagic nephritis is characterised by the presence of abundant blood in the urine, with only a moderate amount of albumin and a very few casts. The latter may be absent, indeed, in one or more specimens, and considerable numbers of pus cells and round kidney cells may be present. The child is not very ill, with little tendency to suppression of urine or to uræmia, and prognosis is good, the process tending towards recovery, though occasionally/

occasionally chronic nephritis may develop. It is rare for a fatal termination to take place in the acute stage. The urine may contain a few red blood corpuscles and casts for months, and then finally become, and remain, normal. There is only moderate diminution of the functional capacity of the kidney. On contrasting the haemorrhagic with the exudative type, the latter is characterised by oedema of moderate or severe degree with moderate albuminuria, and a fair number of blood cells, and many casts in the urine. There is always oliguria at some time, chiefly at the onset. The blood pressure is always moderately elevated, and functional tests show diminution of renal capacity but with a tendency to recovery. The severe types approach more closely the adult form of the disease, with much oedema, and in the scanty urine abundant albumin and blood, and many granular, cellular and blood casts. One of the most striking features in Hill's haemorrhagic cases was the fact that most of the children did not appear very ill, not nearly so ill as adults with acute nephritis. Of 49 cases only 8 could be said to be dangerously ill, and only one died. He emphasizes particularly the fact that haemorrhagic nephritis generally does not resemble the usual adult type of case. Wyllie and Moncrieff (1926) observed 22 cases of acute haemorrhagic nephritis in 3 years at Great Ormond Street. They noted the sudden appearance of haematuria, generally a few days after acute or sub-acute infection in the naso-pharyngeal region, blood being abundant and albumin scanty, and accompanied in about one/

one third of the cases by a few epithelial, granular or blood casts. They also emphasize the slight degree of constitutional disturbance and state that oedema, if present, is limited to puffiness round the eyes, though Osman (1925) describes an otherwise typical case of haemorrhagic nephritis with considerable dropsy of the face, arms, and legs, accompanied by slight ascites. This child, after dismissal, suffered from recurrent attacks of haematuria during the next 5 years. These attacks were accompanied by malaise, but oedema never recurred after the first illness. The relatively mild constitutional disturbance in the haemorrhagic type would appear to point to a focal nephritis involving a limited number of glomeruli, thus leaving intact sufficient renal units to maintain a fair degree of kidney function. Similarly the acute nephritis sometimes associated with various septic processes is at times clinically silent, being discovered only at autopsy, and Shaw Dunn and Thompson (1921) have shown that in such cases the lesion in the kidneys is frequently focal. In acute streptococcal endocarditis also, a focal lesion in the kidneys may not be suspected during life.

Histology of the 4 Cases of Haemorrhagic Nephritis.

The 4 cases in this group, though definitely haemorrhagic in type, since histologically haemorrhage was the salient feature, and on naked-eye examination the organs were conspicuous from their deep-red colour, differ from the descriptions generally given of this variety of nephritis by reason of the fact that the lesion/

lesion here was diffuse instead of focal. Wyllie and Moncrieff (1926) believe that while such a lesion is generally focal, prolonged infection may result in the supervention of a widespread glomerular or catarrhal nephritis. All 4 cases showed an essentially similar histological picture, with, in practically every microscopic field, haemorrhage into the capsule of Bowman of nearly every glomerulus. The amount of blood varied from a few red cells to a massive haemorrhage distending the capsular space in crescentic fashion, and compressing the glomerular tuft. In most capsules the red cells were apparently freshly shed and were discrete, though in some there was definite separation into serum and coagulum, and in a few, even early organisation of the small thrombus. These cases afford confirmation of the view expressed by Volhard and Fahr (1914), Shaw Dunn, Haworth and Jones (1924), Addis and Oliver (1931), and Hadfield and Garrod (1932), that in acute nephritis the glomeruli are the source of the blood frequently seen in the lumina of the tubules though no red cells may be present in the capsular spaces. Apart from these striking haemorrhages, the glomeruli as a whole were enlarged, generally to a moderate degree, with proliferation of the capillary endothelium and slight exudate of polymorphonuclear cells into the tufts. In one of the cases, a few glomeruli showed very early crescentic proliferation of the capsular epithelium. In all four kidneys, the striking feature in the tubules as in the glomeruli was widespread haemorrhage, many of the/

the proximal convoluted tubules being distended with blood, while relatively few entirely lacked red blood corpuscles. In addition to discrete red cells present throughout the whole tubular system, including the collecting tubules and the Ducts of Bellini, abundant blood casts were seen at all stages of formation, some consisting of fresh red cells coagulated by fibrinogen, which, according to Addis and Oliver, is derived from the glomerulus at the same time as the red corpuscles. In other casts the corpuscles had undergone lysis, the "shadows" only remaining, while in others again, there was complete cellular disintegration, the casts being composed of strongly eosinophil amorphous débris, in which were incorporated granules of greenish pigment. In these blood-casts at all stages a few leucocytes were naturally present. Scanty cellular casts derived from desquamated epithelium were also noted in several of these cases. The epithelium as a whole showed degenerative changes of a relatively mild degree, chiefly of the nature of cloudy swelling, though in one instance slight hyaline droplet degeneration was noted in individual tubules. The epithelium in the tubules distended with blood was decidedly flattened. The interstitial tissue showed no noteworthy departure from the normal in 2 cases. In the other 2 it was the seat of slight oedema, with, in one of them, early fibrosis and a very slight polymorphonuclear exudate round some glomeruli. Apart from intense engorgement of the vessels, no vascular change was noted in any case. Frozen sections were examined for fat in 2 instances. In both, fat was negligible in amount.

Histology of 28 Exudative Cases.

Histological changes varied in severity and several cases were of particular interest, as showing the slight degree of structural damage actually present in view of the well-marked clinical symptoms. In one case, for instance, the patient, a female infant 12 weeks old, was well until a week before admission, and was brought to hospital with slight oedema, which rapidly spread to involve the face and eyelids, lumbar region and back, while the output of urine was diminished and specimens contained albumin and casts. Death occurred 2 weeks after admission. At autopsy there was widespread oedema of the abdominal viscera and brain, with effusion into the serous sacs. Yet, apart from desquamation of the prominent visceral epithelium, the only noteworthy lesion in the glomeruli, which were not enlarged or unduly cellular, was marked congestion, the glomerular capillaries being distended with blood throughout. The tubular changes were relatively slight, the epithelium being rather flat, with granular débris in the lumina of the convoluted tubules along with red blood corpuscles in a few, and some hyaline casts in the collecting tubules.

In a second patient, an infant of 5 months, the naked-eye and histological appearances of the kidneys closely resembled those just described. In this child, however, no oedema was found on clinical examination, the chief symptom being irritability followed by drowsiness, finally passing into coma a few days before death. Thus, although in these 2 patients the kidneys/

kidneys were almost exactly alike both macro- and microscopically, the clinical symptoms were entirely different, oedema being the chief feature in the first case, while no trace of dropsy was seen in the other, whose symptoms were entirely cerebral. It was also the experience of Gainsborough (1932) that the kidneys in 2 cases might have similar histological appearances, though massive oedema, while present in the one, might be absent in the other.

In a third patient again, a child moribund on admission, with a history of illness of one day's duration, the autopsy findings resembled those in case one - water-logging of all the serous sacs and marked oedema of the abdominal viscera and brain. Microscopic examination here showed in contrast to congestion of the glomerular capillaries almost complete occlusion of most of these, the result of rapid proliferation of their endothelial lining, the rapidly-dividing cells lying in clumps and showing large irregular hyperchromatic nuclei. The glomeruli contained in addition, many polymorphs, and similar cells were also present in small numbers in the peri-glomerular tissue.

Other two infantile cases illustrate further the great discrepancy possible between the clinical history and the actual findings at autopsy. The patients in question were two infants of approximately the same age, 22 and 14 days respectively. One, a member of the haemorrhagic group, was admitted with snuffles and/

and difficulty in sucking, with nothing in the appearance or the history suggestive of a nephritic condition, beyond the fact, stated by the mother, that the child had been passing very little urine. The other infant was oedematous, and the history on admission was one of complete anuria of 3 days' duration. A few drops of urine obtained by catheter showed abundant albumin and the child had several convulsive seizures while in hospital. In the former, the kidneys at autopsy were striking in appearance, even on naked-eye examination, from enlargement and marked congestion, and microscopically were the seat of severe diffuse haemorrhagic nephritis. In the latter, a very narrow cortex was the only abnormal feature, macroscopically, and sections showed a kidney perfectly normal for the child's age except for the presence in the convoluted tubules of a fair amount of neutral fat. Brüning and Schwalbe (1913) found likewise, in many cases, discrepancy between the microscopic findings and the clinical symptoms, and were often astonished at the slight histological changes in kidneys with severe clinical manifestations, and vice versa.

Another case, that of a female child 9 years of age, merits a more detailed description. The patient, who was very large and stout for her age, was admitted with a slipped left femoral epiphysis when, in addition, dyspituitarism was diagnosed. Manipulation was twice performed under ether on 15/8/31 and 19/8/31 and a Thomas's splint was applied. The child was apparently/

apparently in good health, when she became sick and vomited, and died suddenly on 6/11/31 after several similar attacks of vomiting without pain. Slight intermittent albuminuria had been present during the child's stay in hospital, though this fact was elicited only on special enquiry, and had evidently not been pronounced enough to focus attention on the kidneys. Otherwise there was nothing in the history or in the appearance of the patient to suggest a renal lesion. On naked-eye appearance the kidneys were small, compared with the other abdominal viscera, and strikingly soft and flabby. Both organs were pale, including the pyramids, and demarcation between cortex and medulla was lost. The cortex showed whitish areas with some more opaque yellowish foci alternating with reddish streaks and spots. The capsules were not thickened, and stripped with ease, leaving a variegated yellowish surface mottled with red. The renal pelves were normal.

Histology. Sections of the thyroid, pituitary, and suprarenal glands were free from any evidence of disease on microscopic examination. The kidneys presented a striking picture of combined glomerular and tubular involvement. The glomeruli without exception were greatly enlarged, with endothelial proliferation and polymorphonuclear infiltration. In addition an extremely interesting feature was the presence, within the glomerular capillary lumina, of long cells resembling endothelium and apparently lying free. In one section, an afferent arteriole/

arteriole, seen entering its corresponding glomerulus, contained within its lumen cells of this same type. No picture similar to this, was seen in any other case in the whole of the present series, though the presence, within the glomerular capillaries, of endothelial-like cells has been described by Shaw Dunn and McNee (1917) in their paper on war nephritis and by von Kahlden (1891). The former authors describe the glomeruli in their cases as enlarged and cellular with little or no blood. Many capillary loops, however, were dilated and contained numerous nucleated cells with oval or flattened nuclei, like endothelia lying close together in a syncytial arrangement, mitoses sometimes being present. In such cases dyspnoea was a prominent symptom, and at autopsy the lungs were the seat of an acute bronchitis with swelling and oedema of the walls of the terminal bronchioles and infundibula. The authors believe that some mild irritant was present in the blood stream, and they presume that the excess of cells in the glomerular capillaries was derived from the walls of systemic and pulmonic blood vessels damaged by the circulatory irritant. Von Kahlden in nephritis following measles and also scarlet fever found similar cells, resembling endothelia the seat of fatty degeneration, in the glomerular capillary loops. He considers that such cells were not all derived from the loop endothelium but partly from larger vessels, having reached the glomeruli by the blood stream, as in one case they were seen entering the glomeruli from the vas afferens as in the case

under/

under discussion. To return to the latter, the lesion here appeared to be acute, with only a very occasional slight early adhesion between the glomerular tufts and capsules and slight early peri-glomerular fibrosis round isolated glomeruli, along with a scanty exudate of round, plasma and polymorphonuclear cells. The tubules showed marked degenerative changes, whole microscopic fields in various sections having undergone complete necrosis, with disappearance of the nuclei and collapse of all the cells into the lumina of the tubules, so that only the slightly thickened basement membranes remained as landmarks. The thick Henle loops as well as the proximal convoluted tubules had suffered severely. At places scanty foci of early fibroblastic proliferation were noted between the tubules, with, in these areas, small collections of lymphocytes and polymorphs. In the medullary portion there was some slight fibrous tissue increase though the collecting tubules were well preserved and showed nuclear staining, thus contrasting markedly with the areas of complete cortical necrosis. The stroma showed oedema, in addition to early fibrosis.

The post-mortem findings in this case showed nothing which could throw light on the extremely pathological state of the kidneys, or account for the source of the endothelial cells in the glomerular capillaries, though from the extreme degree of tubular necrosis some toxic agent would appear to have been at work, which might possibly have damaged the vascular endothelium/

endothelium as well as the kidneys. The lungs were the seat of congestion and oedema, easily accounted for by the condition of the heart which was dilated, with pale, soft myocardium, also a toxaemic manifestation. No pneumonic consolidation was present. The stomach and bowel were slightly congested, with some increase of the lymphoid tissue, and the spleen was slightly enlarged. The liver showed early fatty change. No abnormality was observed in the other organs.

Cases such as those just described show the need, so often emphasized in the literature, for close co-operation between pathologist and clinician, since the microscopic, like the naked-eye appearances, form no reliable guide as to the duration or severity of the disease, as shown by clinical symptoms. Thus in the case first described though the illness had lasted for about 3 weeks and the patient was waterlogged, the glomerular lesion had not advanced beyond capillary congestion, while in the third instance the child was to all appearance well until the day before death, though at autopsy a well-marked, diffuse glomerular lesion was present. Apart from the 6 cases described above, the other acute glomerular lesions can be roughly divided into 2 groups of milder and severer type respectively, the histological appearances resembling more or less closely those described as characteristic of acute glomerulo-nephritis in adults, though in both groups, and particularly in the first, death resulted in a number of instances when the histological changes were still comparatively slight./

slight. These consisted in moderate enlargement of the glomeruli, with proliferation of the capillary endothelium, not sufficient to cause blocking of all the capillaries, since many remained patent and even distended with blood. Complete or partial loss of the tuft epithelium, which in children quickly desquamates in any inflammatory glomerular lesion, was frequently noted in addition. The capsule of Bowman was generally free from abnormal contents or showed merely slight albuminous exudate, a few desquamated epithelial cells, or red blood corpuscles. Degenerative changes in the tubular epithelium consisted of mild or severe cloudy swelling with some cell desquamation, swollen or disintegrated epithelial elements being present in the lumina. A few convoluted tubules contained, in some cases, small numbers of red blood corpuscles though in no instance was gross haemorrhage noted, like that occurring in the haemorrhagic type of nephritis. Beyond a slight degree of oedema no abnormality was seen in the interstitial tissue and the blood vessels were normal. The majority of the cases with histological changes of least severity occurred in children under two years, such patients evidently being less resistant to nephritis and succumbing more quickly than older children, though the degree of intensity of the glomerular lesion was, however, by no means invariably correlated with the age of the patient, since, in the haemorrhagic group described above, the microscopic appearances were exactly similar in all 4 cases, though the ages varied/

varied from 22 days to 11 years. In the remainder of the acute exudative cases - those between the ages of 3 and 11 years - the degree of inflammatory reaction was, on the whole, more intense. The glomeruli were more markedly enlarged and generally digitate, with greatly increased cellularity. The majority were relatively bloodless, from endothelial proliferation and blocking of the capillary lumina, though one or two of the loops in each tuft might remain patent or even dilated. Thrombosis with hyaline necrosis of individual tufts was noted in only 2 cases. The covering visceral epithelial layer which had lost the infantile characters was largely desquamated, individual cells lying free in the capsule of Bowman along with scanty red cells, leucocytes or albuminous exudate, though the capsular space was more often empty. The stroma of the tuft showed little departure from normal, beyond slight thickening and oedema in a few instances, while with Gallego's stain there was no noteworthy fibrosis in the great majority of cases. In the child's kidney normally the stroma is extremely scanty and delicate. The flat capsular epithelium was generally normal, but in a few cases individual glomeruli showed very early crescentic thickening with fine adhesions between capsule and tuft. An extremely slight degree of peri-glomerular fibrosis with a few polymorphs was a rare finding, and when it did occur affected only single glomeruli. The secreting tubules in these severer cases showed degenerative changes of moderate degree proportionate/

proportionate to glomerular damage. Addis and Oliver (1931) consider that there is nothing surprising in the association of such tubular degeneration with the inflammatory process in the glomeruli. It would be impossible, in their opinion, to conceive of a lesion limited to one or other structure in view of the fact that the kidney circulation is flooded by bacterial toxins which affect every element of the renal unit. Hadfield and Garrod (1932) believe that 2 combined factors come into play in the production of tubular degeneration - first, the fact that the whole blood supply of each tubule first passes through the capillaries of the related glomerular tuft, and second, that toxin escapes from the glomerular capillaries, after having damaged the latter, into the tubules, and directly affects the tubular epithelium, rendered more susceptible as a result of the inflammatory ischaemia. Gray (1928) finds that in the later stages of acute glomerulo-nephritis tubular damage becomes progressively greater as the glomerular tufts become more permeable to toxins, since the latter, instead of remaining concentrated in the tuft capillaries, diffuse more and more readily into the tubules.

Degenerative tubular changes produced in the manner described above included cloudy swelling of moderate or severe degree, and vacuolar degeneration, the cytoplasm of such cells having a swollen, rarefied and vacuolated appearance. In other instances the epithelium was flat and granular, and in the most severe cases hyaline droplet degeneration was present, though never/

never very widespread, involving only individual groups of tubules. These degenerative changes affected primarily the proximal convoluted tubules and to a less extent the thick limbs of Henle's loop, and this distribution agrees with the experience of other workers - Volhard and Fahr (1914), Russell (1929). The former authors quote the experiments of Aschoff's pupil, Suzuki, who in animals, demonstrated the marked susceptibility to various toxins of the proximal convoluted tubules, ("Hauptstücke" of German writers) in comparison with the "Schaltstücke" or distal convoluted tubules.

Since most of these exudative cases occurred early in the series only paraffin blocks were available, and examination for fat was not carried out except in a single instance where it was extremely scanty, being found only in a few scattered groups of proximal convoluted tubules, and occurring in the form of fairly large coalescing isotropic fat droplets. No fat was seen in the glomeruli, interstitial tissue or collecting tubules. With regard to the contents of the tubules, varying numbers of red blood corpuscles were found in the majority of the exudative cases, but even when sufficiently abundant to distend groups of convoluted tubules, such blood-filled structures were seen only at wide intervals, and haemorrhage was never a diffuse and striking feature of the sections as in the haemorrhagic cases, and in many instances scanty red cells were found only after search. Leucocytes were also sometimes present in the tubules in small numbers along with the red cells or more rarely/

rarely alone. Casts of various types were found in most cases both in the convoluted tubules and in the lower segments of the renal units, chiefly in the collecting tubules and Ducts of Bellini. These structures were of hyaline, granular or cellular type, or were composed of blood cells in the cases where haemorrhage was most abundant. In one case the large Ducts of Bellini were packed with loosely adherent débris, similar to the "renal failure" casts of Addis and Oliver. In addition to casts, cell débris and swollen degenerated cells were found lying free within some tubules. In some instances where the lining cells were seriously damaged, epithelial regeneration could be seen taking place. In such tubules, in contrast to those with flattened, granular, or swollen cells, often with pyknotic nuclei, the epithelium was of high cubical type with large darkly-staining nuclei occasionally showing mitotic figures. Owing to repeated cell division the epithelium was not regularly distributed, but tended to be heaped up in irregular fashion at one side of the tubule. Sometimes the epithelium was of flatter type and in such cells the nucleus was seen to project from the cell body. A better example of tubular regeneration than any present in this series will be described later in connection with a tuberculous case. The interstitial tissue was free from any noteworthy change in about one third of these exudative cases, and in the remainder slight oedema was present alone, or associated in some instances with early proliferative changes, indicated by/

by foci of fibroblastic formation either round the glomeruli, or more diffusely distributed, along with small cellular exudates consisting chiefly of round and plasma cells, though neutrophil polymorphs also participated. These cell infiltrations were occasionally arranged in strands running from the superficial or deep cortex to the cortico-medullary junction. With regard to the vessels no noteworthy structural alteration was noted in any single instance, the only departure from normal being intense vascular engorgement in some cases, well seen in the intertubular capillary plexus, and in the straight vessels in the medulla.

Before leaving the histology of the acute glomerular group, a remaining case will be described in some detail, since it differs from the rest, by reason of a particularly marked degree of immaturity, the infant having been born prematurely at 7 months. The patient, male and a twin, was admitted 5 weeks after birth, with a history of failure to thrive, wheezing and cough. Three days before admission he began to refuse feeds. When brought to hospital, râles were present all over the chest, but there was no definite dulness. He had many attacks of cyanosis with panting respiration, while in the wards, and there was considerable oedema of the legs, chest wall, and back. The urine contained a trace of albumin. The kidneys have already been described as congested, with a few minute haemorrhages in the pyramids on naked-eye examination. Histologically the striking feature was the presence of a persisting "neogenic zone" with/

with very primitive glomerular anlage at different stages, the earliest being represented by branched tubular structures not yet coiled to form glomeruli, while other similar structures were partly coiled, and others again were coiled but not yet vascularised. The ripe glomeruli were of infantile type with a very prominent covering epithelial layer. The appearances thus bore a strong resemblance to a foetal kidney about the seventh month of development though the embryonic structures were not quite so abundant in this case. In the "neogenic zone" connective tissue of foetal type was still present, and many of the tubules, particularly the collecting tubules, retained a rather primitive type of epithelium. The mature glomeruli were the seat of a commencing nephritis, being intensely congested throughout, while in some, the capsule of Bowman contained a few red blood corpuscles or degenerated epithelial cells. The tubules were the seat of early catarrhal change and contained some hyaline material, but no blood cells were found on searching sections. There was well-marked oedema of the interstitial tissue, and the intertubular capillary network was intensely engorged with blood, particularly at the cortico-medullary junction, where, on naked-eye examination, congestion was particularly marked and petechial haemorrhages were present. The other lesions found post-mortem were gastro-enteritis and early bronchopneumonic consolidation. The presence of a "neogenic zone" in this case could be attributed to the fact that the child was born prematurely, before the kidneys had reached their full development.

GENERAL POST-MORTEM FINDINGS IN THE CASES OF ACUTE NEPHRITIS.

General post-mortem findings and clinical manifestations in the haemorrhagic and acute exudative cases of glomerulo-nephritis will be discussed together since these types are closely similar except for the marked haemorrhagic tendency in the former. The few cases of mild glomerulitis with marked tubular change will then be dealt with separately since this type of lesion is one of particular interest, and the subject of much controversy.

Haemorrhagic Group (4 cases). In each of the 4 cases of acute haemorrhagic nephritis some acute terminal infection contributed to bring about the fatal result. Twice the lesion involved the lungs, a terminal broncho-pneumonia being present in one instance, and in the other, an acute bronchitis with much purulent exudate in the main bronchi. The third child developed double acute otitis media with pneumococcal meningitis, and the fourth acute gastro-enteritis. Subcutaneous oedema was not a feature of these cases, being present in only one instance, and appearing chiefly in the tissues of the neck and forming a swelling under the chin. This rather unusual site for oedema is rarely mentioned in the literature, but occurred in several other cases in the present investigation. In none of these 4 children had effusion taken place into any

of/

of the serous sacs, though 2 showed marked oedema of the liver, and one a dropsical condition of the bowel and spleen in addition. The brain was examined in 2 instances and was normal in one while in the other pneumococcal meningitis was present along with oedema of the brain substance. Hypertrophy of the left ventricle was found in 2 of these patients, aged $3\frac{3}{4}$ and 11 years respectively.

Acute Exudative Nephritis (28 cases). In contrast to the haemorrhagic group, widespread oedema was a frequent finding in the exudative cases and involved the subcutaneous tissues, the serous sacs, the internal organs, or any one of these, to a varying extent. Subcutaneous oedema was mentioned in the post-mortem report on 15 of these patients and was confined, in about half, to the lower limbs or face, and in the remainder was widespread, with more or less general involvement of the subcutaneous tissues. Regarding the effusions into the serous sacs, an excessive amount of clear, straw-coloured transudate was present in the pleurae, the pericardium, the peritoneum, or any one of these, in 13 instances. In other 2 cases the effusion had become secondarily infected, and shreds and flakes of fibrin were seen in the fluid. The serous sacs contained frank pus in 3 further instances, i.e., the serous sacs were abnormal in 18 cases altogether. In the remaining 10 patients no abnormality was found in these cavities. With regard to the abdominal viscera, oedema was also of frequent occurrence/

occurrence, and involved the liver and small bowel in about half the patients, and the spleen with rather less frequency. On section of such dropsical livers and spleens, the cut surface appeared moist, with much exudation of fluid, and the coils of bowel were distended and heavy, with watery contents. A catarrhal condition of the mucosa was a frequent accompaniment.

On turning to the thoracic organs oedema of the lungs formed part of a generalised dropsy in 4 instances, while slight degrees of oedema of cardiac type associated with a failing heart were of common occurrence. In the latter type congestion of hypostatic distribution was present in addition to oedema, while in the former, the water-logged lungs were of a pale greyish-pink tint. When general anasarca was present, the mediastinal tissues and thymus were sometimes involved.

The brain was examined in 15 of these 28 patients with exudative nephritis, and oedema of the cerebral substance, with excessive fluid in the sub-arachnoid space, was found in 9, congestion of the superficial vessels in one, and in another, superficial haemorrhage with petechiae scattered throughout the substance of the organ. In the remaining 4 cases no lesion was noted on the surface or in the substance of the brain.

Turning now to inflammatory processes, respiratory complications were present in rather more than half the cases, terminal broncho-pneumonia being found in 9, and acute bronchitis with congested mucosa and abundant purulent exudate in the/

the main bronchi, in other 8 instances. These respiratory lesions occurred either alone or in association with some other pathological process. Thus along with acute bronchitis there was found in 3 cases purulent pleurisy (previously mentioned above in connection with the serous sacs), and in 2 of these, early pericarditis was present in addition, while the 3rd case was associated with severe gastro-enteritis. Pericarditis of insidious onset was found by Barber (1926) a fairly common complication of nephritis in childhood. Accompaniments of the 9 broncho-pneumonic lesions were acute otitis media in 3 instances, affecting both ears in 2, and the left middle ear only in the third, while a fourth case with lung consolidation showed purulent pleurisy and peritonitis, and a fifth gastro-enteritis. Pericarditis as the sole complication of nephritis was found in one child, pleurisy in a second, otitis media in a third, and severe gastro-enteritis in other 2 patients, the intestinal mucosa being the seat of marked congestion. Another child had a similar lesion with a left otitis media in addition. In the 5 remaining patients no acute inflammatory process was discovered, but in this group the lungs showed intense congestion and oedema associated with a failing heart in 2 cases, marked oedema of renal type in a third, massive pleural effusion with collapse of the lungs in a fourth, and in a fifth, superficial haemorrhages were present over the vertex of the brain with petechiae in its substance.

On reviewing these complications it is thus seen that no less/

less than 23 of the 28 cases of acute exudative nephritis (82.14 per cent.) showed at autopsy some associated inflammatory lesion, while including the haemorrhagic group 27 out of 32 were involved (84.37 per cent.).

The respiratory tract had suffered in the majority of cases, with broncho-pneumonia or bronchitis in no less than 19 of these 32 patients (almost 60 per cent.).

Similarly, Russell (1929), found in 11 cases of acute nephritis that the clinical cause of death was renal insufficiency in many cases, though this factor was generally associated with other acute terminal infections, broncho-pneumonia and lobar pneumonia, acute infections of the serous sacs and heart failure being commonly found at autopsy. Oedema was also frequent, with or without ascites. Another factor which may contribute to bring about a fatal result is acidosis, which may be of extreme degree. Marriott and Howland (1916), Whitney (1917), Cabezón (1932).

Bacteriology of the Inflammatory Lesions associated with Nephritis.

It is a well-known fact that nephritic patients are particularly susceptible to infections, especially those of pneumococcal and streptococcal nature. Bacterial investigations unfortunately, could not be carried out in more than a few cases. In 4 instances pus from one or both middle ears was examined and showed pneumococci alone in 2 instances, pneumococci and streptococci together in a 3rd, and streptococci with short Gram-negative bacilli in a 4th. In the flakes of fibrin from the single case of peritonitis short-chained streptococci/

streptococci were present in enormous numbers, and in one case of pericarditis, scanty pneumococci were present in films of the exudate.

Cardiac Findings in the 28 Exudative Cases.

It is now recognised that even in the young child the subject of acute nephritis, cardiac hypertrophy associated with rise in blood pressure, may be found to a hitherto unsuspected extent, and this fact is borne out by the present investigation, where in 8 instances slight hypertrophy of the left ventricle was seen, and in a 9th left ventricular hypertrophy was combined with dilatation. The right heart as a whole was dilated in 4 instances with hypertrophy of the right ventricle in one of these. Both ventricles were dilated in another case and the right ventricle alone in a last patient, some abnormality thus being present in no less than 15 cases. Concerning the ages of the 9 children with left ventricular hypertrophy the youngest was only 3 years of age, one was between 3 and 4, five were between 4 and 5, one was 6 years, and one 11 years of age, and including the haemorrhagic group, where hypertrophy of the left ventricle was present in 2 children of $3\frac{3}{4}$ and 11 years of age respectively, 11 cases or practically one third of the whole series showed cardiac hypertrophy.

Petechial Haemorrhage.

A final feature which may be considered worthy of note was the presence at autopsy in 5 of these 28 children with acute exudative nephritis, of petechial haemorrhages into various organs. (This lesion was not found in any member of the haemorrhagic group). In one instance petechiae were found scattered over the body and limbs, and in the lungs, kidneys and intestines. A second case showed small haemorrhages under the cardiac endothelium, a third, scattered petechiae under both the endothelium, and the visceral pleurae, a fourth, subpleural haemorrhages only, and in the fifth these were present in the brain substance, associated with haemorrhages over the vertex. Capillary bleeding was present, therefore, in considerably less than 20 per cent. of patients with acute glomerulo-nephritis, and this low incidence combined with Rennie's (1933) statement that 45 cases of acute nephritis examined ophthalmoscopically revealed haemorrhages in only one instance, would appear to militate against the modern view that acute nephritis is the renal manifestation of a generalised capillaritis.

CLINICAL MANIFESTATIONS

Haemorrhagic Group.

Complaint on admission (4 haemorrhagic cases).

Transient swelling of the face appeared in one instance about a month before admission, but the child appeared well until/

until 3 weeks later when headaches, sickness, vomiting, and haematuria were rapidly followed by convulsions and death. In a 2nd case there was nothing in the history suggestive of renal disease except oliguria, the infant having been admitted with a complaint of snuffles and difficulty in sucking. A third child developed mumps, oedema of the face appearing shortly thereafter, while the fourth on admission gave a history merely of haematuria of 10 days' duration.

Exudative Cases (28).

On reviewing the clinical histories the first thing to attract the relatives' attention in 17 of these children was "swelling", generally of the face, but sometimes of the legs or body. This oedema was frequently accompanied by a history of some urinary abnormality, generally oliguria, associated with scanty, high-coloured, or red urine, though in a few instances it was stated that the child had been passing more than the normal amount of urine. Paterson (1926) found in the Birmingham Children's Hospital that advice was sought in the greater majority of cases for one of two manifestations - either the passing of red urine, or swelling and puffiness of the face. In the present series, the appearance of oedema was frequently accompanied, or followed at a short interval by, abdominal pain and vomiting, sometimes so severe as to suggest acute abdominal disease. Sometimes however the illness was ushered in by an attack of abdominal pain accompanied by sickness and vomiting, without/

without oedema. Russell (1929) in her acute or "acris" cases found abdominal pain and vomiting,or general malaise,a frequent complaint, often in association with a rise in temperature, while oedema was frequently observed in the face, eyelids or legs of her patients. In the present writer's series symptoms referable to the respiratory tract were occasionally the first manifestation of disease. Thus, cough and wheezing were mentioned as precursors of oedema in a few instances. In one of these children with a respiratory lesion a previous attack of nephritis had been associated with broncho-pneumonia 6 months previously. With the recurrence of pneumonia shortly before death, the urine again became red.

Urinary Findings (4 haemorrhagic cases).

In 3 of these patients sufficient blood was present to give the urine a red colour on naked-eye examination, and albumin was also present, though only a trace was detected in one instance. In haemorrhagic nephritis albumin is frequently very scanty, being quite insignificant in amount compared with the quantity of blood present. In these 3 patients, microscopic examination of the urinary sediment showed red and white blood corpuscles and casts, generally epithelial or hyaline. In the 4th patient, 22 days old, oliguria was the only urinary abnormality mentioned.

28 Exudative Cases.

In 6 instances where the patients were admitted moribund and died in a short time, no information is available with regard to/

to the urine. Of the other 22 cases, in 9 some mention was made of the quantity excreted. Thus, in one instance, it was stated that the amount of urine was variable, in another frequency of micturition was present at the onset of the disease followed later by oliguria. Increased excretion or frequency of micturition was noted in 4 cases, and scanty, or very scanty, urine in 3. With regard to the presence of abnormal constituents, albumin in varying amount, from a faint trace to a heavy precipitate, was found in all but one of the 22 cases examined. In this last instance no ward examination was performed, the only information available being a relative's statement that the urine had been very scanty and high coloured since the onset of the illness. In several patients where the urine was examined daily for a considerable period albuminuria was an almost constant finding. Blood was present on naked-eye examination in 9 cases, and on microscopic examination of the sediment red cells were found in other 2. Casts were present in 15 cases alone or associated with epithelial cells, while the latter were occasionally seen alone. The casts were of varied type, hyaline, granular, fatty, epithelial, and blood casts all being mentioned, one or several varieties being present in individual specimens of urine.

Bacteriological Examination of the Urine.

The urine was examined bacteriologically in 4 cases, one belonging to the haemorrhagic group, and 3 to the exudative group. In the former case 2 specimens were cultured, the growth/

growth consisting of coliform bacilli (B. Proteus type) and staphyloccus albus in both. In the 3 members of the exudative group, a sarcina was present in films and culture in one instance, and coliform bacilli in the other two. These organisms were regarded as contaminations in every instance.

On consulting the literature on the bacteriology of the urine in nephritis, Gray (1928) finds it rare to obtain from the kidneys organisms other than probable contaminations. "Since," he states, "acute or chronic sepsis is in itself a proved cause of bacteriuria, a positive result may do little more than establish the fact that focal sepsis exists in the case." A similar opinion was expressed by Councilman (1897), who, though he isolated pneumococci, streptococci, etc. from the kidneys in 18 cases, considered these organisms part of a general sepsis, and Scheidemandel (1913) isolated streptococcus from the urine in a number of cases of acute nephritis, but in these patients either a focus of infection or a general septicaemia was present. Paterson and Wyllie (1926) obtained a negative result on culture of the urine in 6 cases of haemorrhagic and in 7 of parenchymatous nephritis. Shaw Dunn and McNee (1917) in their study of war nephritis examined the urine bacteriologically in 35 cases. They found streptococci fairly frequently, of a type growing luxuriantly on ordinary media and never pathogenic to animals, but as similar cocci were got in control specimens from non-nephritic patients, the authors attach no importance to them and emphasize the difficulty/

difficulty of obtaining complete asepsis, even in specimens of urine taken with the greatest care.

Dick and Dick (1915) in their series of 7 cases of acute, and 13 of chronic nephritis, isolated staphylococci and diphtheroid bacilli from both types, but considered these as normal inhabitants of the urethra. They obtained in addition streptococci 4 times from the acute, and 7 times from the chronic cases, associated in both groups with various other Gram-positive and Gram-negative, aerobic and anaerobic organisms. These authors found in a number of the above patients foci of infection with a bacterial flora similar to that in the urine, and they believe that the organisms in such foci gain entrance to the blood-stream and are excreted through the kidney, possibly causing a nephritis in the process of excretion, though the kidneys would appear to be able to excrete at least some organisms, e.g., B. Typhosus and B. Tuberculosis, without showing any clinical evidence of damage in the process. According to the general opinion, it would seem that so far, little information of value with regard to the causative organism in nephritis has been obtained from examination of the urine.

Cerebral Complications.

Symptoms suggesting a cerebral complication were present in 8 exudative cases or 10, including the haemorrhagic group, and took the form of increased irritability, drowsiness, convulsions, or coma, with nuchal rigidity in one case where pneumococcal meningitis occurred at the end. In acute nephritis in children, cerebral symptoms are related to a neuro-oedema instead/

instead of a neuro-toxaemia, MacAdam (1933), and of these 10 cases with cerebral symptoms 7 at autopsy showed marked oedema of the brain, one had superficial haemorrhages over the vertex with petechiae in the brain substance, in another the surface of the vertex was markedly congested, while pneumococcal meningitis associated with oedema of the brain substance was found in the last. The brain in other 2 instances was oedematous, though no cerebral symptoms had been noted during life. Aldrich (1931) prefers the name "cerebral complication" to "uraemia," for symptoms arising during the course of nephritis in children, and attributes them to the fact that the brain, like the other tissues, takes up water and becomes oedematous, the water being held in chemical combination with the brain cells. The resulting oedema causes increased intracranial pressure, and compensatory rise in blood pressure. This conception would appear to be justified by the results obtained on intravenous injection of magnesium sulphate, which, according to this author, shrinks the tissues of the brain with prompt relief of urgent clinical symptoms. He does not believe that magnesium sulphate acts by withdrawing fluid through the bowel, since it does not cause loose stools until after the disappearance of cerebral symptoms. Blackfan and Hamilton (1925) find a parallel between cerebral manifestations, raised blood pressure, and oedema of the brain in the acute nephritis of children. They quote the work of Cushing, who, experimenting with dogs, found that during compression of the brain, the arterial pressure rose commensurately with/

with intracranial pressure. In their cases, cerebral symptoms regularly followed increase in blood pressure, and they believe that such symptoms can easily be explained on the basis of cerebral oedema, with increase in intracranial pressure, and that arterial hypertension is at least in part the result of cerebral oedema. The term "uraemia" they consider misleading, since symptoms do not depend on the retention of nitrogenous products, and they prefer the name "cerebral symptoms in glomerulonephritis."

On investigating in the present series the relation between cerebral oedema, rise in blood-pressure (in the 9 cases where this was recorded) and symptoms referable to the central nervous system, oedema of the brain (associated in one instance with pneumococcal meningitis) was found at autopsy in 3 of these 9 patients. In the meningeal case nuchal rigidity was the only clinical symptom suggestive of an intracranial lesion. Coma was associated clinically with the second, while in the third, with a systolic pressure reaching 116 mm. of mercury there was nothing during life to suggest a cerebral complication. In other 2 patients where the systolic blood pressure was 120 and 118 respectively, the brain was not examined, but clinically, the first was unconscious with convulsions, and the second was delirious. In the remaining 3 cases with raised blood-pressure there was no suggestion clinically of any cerebral lesion, and the brain was not examined post-mortem. In 5 of 9 cases, however, with raised blood pressure, either cerebral symptoms or oedema of the brain or a combination/

TABLE III.

Table showing relation between the blood pressure and the cardiac condition.

Case	Age	Sex	BLOOD PRESSURE		BLOOD PRESSURE Normal for Age (Judson & Nicholson)		Interval between reading of B.P.& death of patient.	Condition of heart.	Approximate duration of clinical symptoms.
			Systolic	Diastolic	Systolic	Diastolic			
1.	4 yrs 11 mths.	F.	1(115 2(118	86 70	91.6	64.9	1 day.	Hypertrophy & dilatation of left ventricle	1 week.
2.	4½ yrs.	M.	1(98 2(116	72 80	91.6	64.9	2 days.	Slight hypertrophy of left ventricle	6 weeks.
3.	4½ yrs.	F.	144	88	91.6	64.9	1 day.	No cardiac abnormality.	1 week.
4.	4 yrs.	F.	108	?	91.6	64.9	1 day.	Hypertrophy & dilatation of left ventricle	1 week.
5.	3 yrs.	F.	140	98	91.8	65.6	2 days.	Slight hypertrophy of left ventricle.	9 days.
6.	1 yr.	M.	1(115 2(125	70 80	91.8 (nearest figure not recorded under 3 years).	65.6	3½ weeks (both)	Not mentioned.	6 weeks.
7.	4 yrs.	M.	80	?	91.6	64.9	1 week.	Slight hypertrophy of right ventricle.	16 days.
8.	11 yrs.	M.	120	78	97.1	65.5	Day of death.	Distinct hypertrophy of left ventricle.	4 weeks.
9.	3¾ yrs.	M.	116	68	91.6	64.9	3 days.	Hypertrophy of left ventricle	3 weeks.

combination of both was observed. The numbers, however, are too small to be of any significance.

CLINICAL INVESTIGATIONS IN ACUTE NEPHRITIS.

Blood Pressure and the Cardiac Condition.

The blood pressure was examined in 9 of the 32 combined haemorrhagic and exudative cases, including 2 of the former and 7 of the latter, and the figures obtained are tabulated along with the normal figures for the various ages as recorded by Judson and Nicholson (1914), who investigated the blood pressure in a large series of normal children between the ages of 3 and 14 years. On referring to the table and comparing the results in the nephritic patients with those of normal children, a considerable elevation of the blood pressure is seen in all but one case, where the systolic pressure only is recorded and is low. The highest figures, 144 and 140 systolic in the series were found in children of 4½ and 3 years respectively.

Cardiac hypertrophy (diagnosed post-mortem) was associated in 7 of the 9 cases with raised blood pressure, as will be seen from the table. In one case (that of the child with a blood pressure of 144 mm. Hg.) the heart was normal, and in another patient with high blood-pressure the cardiac condition was not mentioned. In the case (with a B.P. of 144) where hypertrophy was absent, the illness as indicated by clinical symptoms had lasted only 1 week, though in other 2 cases of 7, and another of 9 days' duration, the left ventricle was distinctly/

distinctly hypertrophied.

According to Judson and Nicholson's figures for normal children the systolic blood pressure varies from 91 mm. in the 4th year to 105.5 in the 14th, with a slow but gradual rise from 3 to 10 years, a more abrupt increase between 10 and 14, and rapid elevation in the 14th year during adolescence. The total rise between 4 and 14 years represents only 14 mm. of mercury, while the diastolic pressure shows an almost uniform level between these ages. Wessler (1914) believes that in children there is considerable normal variation in the blood-pressure and in the opinion of Capon (1926) the emotional disturbances frequent in children, often render blood pressure estimations unreliable. Berkeley and Lee (1917) investigated the blood pressure in 93 cases of nephritis in children between 2 and 12 years. They found occasionally marked rise in the blood pressure in both acute and chronic nephritis, and report the case of a child of 10 years with a systolic pressure reaching 250 mm. of Hg. Aldrich (1931) also reports 2 cases in children with a systolic pressure of 230, and considers that such cases are probably of the nature of malignant nephrosclerosis, the result of general arterial disease. Lennox Gordon (1911) also emphasizes the fact that in the acute nephritis of young children the blood pressure is often raised to a marked degree, and arterial hypertension, since in children, it occurs only in nephritis is of great diagnostic value. In Hill's (1919) series he found the blood pressure more frequently normal than/

than raised, and believes that in nephritic children circulatory changes both with regard to cardiac hypertrophy and raised blood pressure are not so striking or so important as in adults. Nobécourt (1930) on the other hand considers the cardio-vascular syndrome more frequent in the child than in the adult, since in the former the greater elasticity of the cardiac fibres explains the ready distension and return to normal.

Blood Chemistry.

The Non-Protein Nitrogen of the blood was investigated in 6 of the exudative, and one of the haemorrhagic cases. In the latter, a child of 11 years, it reached the very high figure of 190 mg. per cent. and in the other 6 the figure varied between 36 and 62.2 mg. per cent., the normal being 25 to 50 mg. per cent, Harrison (1930) and 20.3 to 31.5 (average 25.9 mg. per cent.) Salvesen (1926). Though these figures are estimated for adults they are approximately similar in children. Tileston and Comfort (1914) believe that the estimation of the total N.P.N. is of the greatest value in prognosis, particularly in chronic nephritis. Patients with figures over 100, in their investigation, with one exception, did not live more than 35 days, and in the child in the present series with 190 mg. per cent. of N.P.N. estimation was performed only a few hours before death. Crawford (1924), on the other hand, found that quantitatively the blood urea (which represents/

represents the great bulk of the total N.P.N.) was no guide to prognosis, nor was the amount present commensurate with the severity of the symptoms in children first coming under observation in uraemia. In one case admitted with a history of headaches, and vomiting, though the blood urea reached the high figure of 208 mg. per cent. the patient was well in 6 weeks. In another of her patients with convulsions and coma, the blood urea was only 66 mg. per cent., and a 3rd similar case had a normal blood urea of 40 mg. per cent. Other blood investigations carried out in members of the present series, include estimation of the blood cholesterol in 2 patients, in one of whom it was normal (180 mg. per cent.) and in the other slightly raised (235 mg. per cent.). Calvin and Goldberg (1931) consider 200 mg. per cent. the upper level of normal in children. Further the blood chloride was estimated in 4 cases and was present in amounts of 340, 330 (in 2 patients) and 280 mg. per cent. respectively. (normal approximately 280 mg. per cent.). A further reference will be made to blood chemistry and renal efficiency tests in dealing with the 10 operated cases, as these children were all in the wards for a long period, and thus afforded an opportunity for thorough investigation.

Ophthalmoscopic Examination.

Another clinical investigation carried out was the examination of the fundi in 3 patients with acute exudative nephritis/

nephritis, when no abnormality was detected in 2, and only slight pallor of the discs in the third. Berkeley and Lee (1917) state that changes in the fundi due to nephritis are very rare in children, and Hill (1919) believes that in children with very high blood pressure changes in the fundi may be present, though they are not common. Rose Bradford (1908) however, found retinal changes of extreme severity in young subjects with nephritis, and considered the prognosis in such patients very grave. In contrast to the findings in adults, where the incidence both of renal disease and albuminuric retinitis is far greater in males than in females (in the proportion of 2 to 1), of a series of 51 cases of chronic interstitial nephritis under 13, quoted by the above author, 30 per cent. only were boys, and 70 per cent. girls. It would appear from a survey of the literature on this point that retinal lesions in childhood are most common in the comparatively rare cases of malignant nephro-sclerosis secondary to generalised vascular disease which resembles the adult type of lesion except in the one particular - that its young victims are more frequently of the female than of the male sex.

Low Powers of Resistance to Disease in the Child.

On reviewing the clinical and pathological findings in the 32 combined haemorrhagic and exudative nephritic patients, one of the most striking facts that emerges is the extremely acute course of the disease in the majority of cases - a very short/

short period intervening between the onset of clinical manifestations and the death of the patient. In the haemorrhagic group (4 cases) the history of illness in each case was only of about 3 to 4 weeks' duration in 3 instances. In the fourth, the patient, an infant of 22 days, had nothing in the history to suggest nephritis, so it is impossible to say how soon after birth the kidneys became diseased. In the exudative group (28 cases) the fulminating nature of the lesion is much more striking. Thus, the whole history of the illness did not exceed 36 hours in 3 of the patients, and was even under 24 hours in one of these. The histories of these children may be considered of interest so are described individually.

Case 1. Male, 6 years. The child, a well-built and well-nourished boy, appeared well on the morning of the day before admission and was playing about as usual. Later in the day he became ill and nephritis was diagnosed, then pleurisy, then an acute abdominal condition. On admission about 10 a.m. the following day he was unconscious and died in a few minutes.

Case 2. Male, 4 years. The child appeared well until about 36 hours before admission when he fell forward while playing. Shortly afterwards epigastric pain and vomiting set in, followed next day by vomiting, diarrhoea, and convulsions. He became unconscious and was moribund on admission to hospital.

Case 3. Female, 4½ years. The patient was apparently in good health/

health, when convulsions began and she was admitted to hospital in an unconscious condition and died in coma the following day.

Another child succumbed after an illness of only 2 days' duration, having been in apparently perfect health previously, while 8 other children had been ill one week, and 4 two weeks ante-mortem. In other 2 the illness had lasted 1 month, in 6 from 1 to 2 months, and in one instance nephritis, evidently associated with pneumonia, had begun about 6 months before death, though the nephritic symptoms had disappeared to recur with a second attack of pneumonia. In other 3 cases data are insufficient for the estimation of the probable duration of the disease. These fulminating cases illustrate very well the extremely rapid course of the disease in young children, in whom the powers of resistance are less developed than in adults. Some other diseases in children run a similarly rapid course, notably pneumonia and gastro-enteritis, where occasionally a fatal termination is reached in less than 24 hours from the onset of the disease symptoms. Pneumonia in children is a disease which illustrates well the increase in resistance pari passu with the age of the child. Thus Erös, Gyüre and Kramár (1931) found that relatively non-virulent Group IV strains of pneumococci are sufficient to cause pneumonia in infants who have no immunity, whereas one of the fixed types is required in older children, who have become slightly immunised by mild pneumococcal infections. The truth of this statement/

statement regarding pneumococcal infections is borne out by Blacklock and Guthrie (1933) who found that of 140 children with pneumonia, 112 were under 3 years of age, and from these only 5.4 per cent. of pneumococci isolated belonged to the fixed types, whereas in the remaining 28 children between 3 and 10 years the figure for fixed types rose to 25 per cent. An early investigator, Simmonds (1896) isolated B. pyocyaneus in 5 instances both from the middle ear and from the kidney in marasmic infants, and he refers to the work of Kossel who, investigating 32 cases of otitis media in infants, isolated B. pyocyaneus 8 times from the middle ear and occasionally also from the blood. Simmonds agrees with the latter's statement that B. pyocyaneus, which is generally harmless in adults, can be highly pathogenic in children and particularly in infants.

Karsner (1908) mentions among other factors sufficient to cause nephritis in young children such trifling causes as uric acid infarctions, and deposits of calcium and haemosiderin in the tissues. Blackman and Rake (1932) found acute nephritis of considerable intensity in 10 per cent. of 95 infants with pneumococcal infections, though Volhard and Fahr comment on the paucity of nephritic complications in pleuro-pulmonary diseases in adults, while Lyttle and Rosenberg (1929) agree that nephritic complications in pneumonia are rare in adults, though not uncommon in children.

Russell (1929) in speaking of acute glomerulo-nephritis ("nephritis acris" in her nomenclature) states that in the early/

early stages of nephritis the patients in whom the disease is fatal are mostly children, and she attributes this to the fact that adult tissues are more resistant to toxins.

FOUR CASES OF MILD GLOMERULITIS WITH TUBULAR CHANGES AS THE PREDOMINATING LESION.

Case 1. Female, 26 months. This child was admitted with a history of generalised swelling of 6 months' duration, with no previous cold, sore throat, or other illness prior to the onset of oedema, the only previous illness having been pneumonia at 15 months. The mother stated that along with the swelling there had been increased frequency of micturition, and the urine had been of a "dirty brown" colour. The child finally developed a red bulging area in the right flank and was sent to hospital as a case of peri-nephritic abscess. On admission oedema was generalised. The pharynx was red and the tonsils large, while many teeth were grossly carious. The urine contained abundant albumin and many clumped white blood cells, and rare casts (type not specified). The blood pressure a week before death was 80 systolic, and 45 diastolic. The blood N.P.N. was 44.4 mg. per cent. and the fundi oculi were normal. A week later, on the day of the child's death, the N.P.N. was 66.6 mg. per cent. Four specimens of urine were examined while the patient remained in hospital. Albumin was abundant though variable in amount, but no blood was found in any sample. Casts/

Casts were found on one occasion and leucocytes were sometimes present. At autopsy the kidneys showed marked mottling, particularly the cortices, due to intermingling of areas of fatty change and congestion. There was only slight irregularity of the markings. At places, the fatty material in the cortices had a peculiar yellowish, glistening appearance suggestive of myelin. The capsules stripped with slight difficulty leaving a rather irregular surface. The heart was dilated, particularly the right side. No lesion was found in the lungs beyond hypostatic congestion and oedema, and only a small amount of free fluid was present in the pericardium, pleural sacs, and peritoneum. The only lesion of note in the abdominal organs was slight oedema of the liver. The head was not examined. On microscopic examination of the kidneys, the glomeruli appeared essentially normal, with no noteworthy enlargement or increased cellularity, though in the majority albuminous exudate was present in the capsule of Bowman. Throughout the secreting tubules the epithelium was flat, atrophic, and granular, with loss of some nuclei and with much granular débris in the lumina of the tubules along with a few hyaline casts. The interstitial tissue showed well marked oedema with scanty, rather small foci of cellular infiltration, chiefly of round and plasma cell type. No abnormality was detected in the blood vessels.

Case 2. Male, 2 years, 9 months. This patient had, on admission, a history of puffiness round the eyes of one week's duration, with swelling of the legs, and vomiting for several days. There/

There had been no previous illness, the only noteworthy fact in the history having been a small abscess on the chin some 4 or 5 weeks prior to admission. On examination the child was markedly oedematous, with swelling of the legs and abdomen, and puffiness round the eyes. The throat was inflamed, with enlarged tonsils. The urine contained abundant albumin, no blood, and microscopically abundant granular and hyaline casts, a coliform growth resulting on culture. The blood pressure was 90 systolic and 70 diastolic. Oedema kept on increasing until death 4 days after admission. The kidneys at autopsy were much increased in size, owing chiefly to cortical enlargement, and the markings in the cortical-medullary zone were definitely blurred. The kidneys were decidedly mottled, yellowish areas alternating with patches of congestion, the whole appearance that of a "large white kidney," suggesting a subacute nephritis. The capsules stripped with ease, leaving a slightly mottled surface. The heart and pericardium showed no abnormality. The lungs were congested and oedematous, with slight broncho-pneumonic consolidation in both lower lobes. Purulent pneumococcal peritonitis was the immediate cause of death. The only other findings of note were oedema of the liver and bowel. On microscopic examination, the glomeruli were only slightly enlarged, though a few appeared digitate. No polymorphs were seen in the tufts. Some of the capillary loops appeared congested, and in others there was very slight

evidence/

evidence of endothelial proliferation. The only abnormal contents in the capsule of Bowman consisted of an occasional red blood corpuscle, a desquamated epithelial cell, or a very small amount of coagulated albumin. The tubules showed a very flat, atrophic type of epithelium, while a fair number of cells had lost their nucleus. Thus sections of some convoluted tubules might have only 1 or 2 nuclei. Much granular débris was present in the lumina. A rare tubule contained a few red blood-cells while after prolonged search one single convoluted tubule was seen filled with red corpuscles. The interstitial tissue was slightly oedematous with an occasional single round cell or a small group of such cells between the tubules. The blood vessels were moderately congested.

Case 3. Female, 4½ years. This patient showed swelling round the eyes for 3 months, with generalised oedema for 1 month before admission. There had been no previous illness and nothing of etiological significance was revealed either in the history or on clinical examination. The illness under discussion began with puffiness round the eyes and rather scanty urine. After the child had been in bed for 5 weeks the swelling round the eyes disappeared, the urine increased in amount, and she seemed fairly well for 2 weeks, when peri-orbital oedema reappeared and shortly after, the legs and abdomen swelled, and oliguria recurred. On admission she was very pale with generalised dropsy, and the right leg showed an area of purplish discolouration/

discolouration, with dark blisters on the surface, while on the outer side of the right thigh a slightly fluctuant swelling was observed which yielded pus on puncture, films of this material showing abundant pneumococci. The single specimen of urine obtained in the ward (as the child died on the day of admission) contained a trace of albumin. At autopsy the kidneys were markedly enlarged, from increase mainly of the cortical substance. They were extremely pale in colour with well-marked tubular catarrh. The capsules stripped readily. The heart was normal and only a small amount of free fluid was found in the pericardial, and in both pleural sacs. The lungs showed only some muco-pus in the main bronchi. In the peritoneum was present a large amount of fluid containing flakes of fibrin, smears of which showed Gram-positive diplococci (? pneumococci). The swelling of the right leg was due to cellulitis with no evidence of bone disease. Histologically the glomeruli were not swollen, but rather collapsed, with dilated capsular spaces. The striking feature regarding the glomeruli was the presence of a large amount of albumin in the capsule of Bowman, seen as a broad crescentic layer between capsule and tuft. No adhesions were present. The tubules showed a granular flat type of epithelium with much escape of granular débris into the lumina. A few fresh red blood corpuscles were seen on searching sections, as well as a few hyaline casts with adherent granular material. The interstitial/

interstitial tissue was rarefied from oedema but showed no cell infiltration or fibrosis, and the vessels were normal.

Case 4. Female, 1 year 11 months. This last member of the group was admitted to Hospital with a complaint of swelling of the feet, legs, abdomen, and puffiness of the face for three weeks. The urine had been scanty, thick, and "dirty", for the same period. The only previous illness was chicken pox at 18 months, and a slight "cold" a week before the onset of oedema. On admission there was great oedema, pitting on pressure, of the feet, legs, thighs, abdominal wall, back, and face. The throat was red, but the condition of the tonsils is not mentioned in the case report. The thick smoky urine was solid with albumin on boiling, and blood was present on microscopic examination, along with epithelial cells and a few casts (type not specified). The second specimen of urine showed abundant albumin, and blood was evident to the naked-eye. The figures for blood N.P.N. were 56.4, and 55 mg. per cent. on two separate examinations. The oedema remained stationary during the child's stay in hospital, (5 days). A red swollen area appeared on one thigh several days ante-mortem and streptococcal peritonitis ushered in the fatal termination. At post-mortem both kidneys were somewhat enlarged with capsules which stripped easily leaving a pale, rather variegated surface, and on section the cortices were also enlarged, pale, and slightly mottled, with very slight irregularity of the markings. The pyramids were congested though/

though no naked-eye evidence of any septic condition was present either in the kidneys or renal pelves. Purulent peritonitis was the only other post-mortem finding of note, streptococci being extremely abundant in the pus. On microscopic examination the glomeruli showed general enlargement but not much digitation. Some were slightly more cellular than normal, chiefly as the result of increase in endothelial cells, though a few polymorphs were present in the tufts in addition. The endothelial proliferation tended to occlude the capillary lumina, though some loops were still filled with blood. The secreting tubules showed flattening of the epithelium, while many convoluted tubules were packed with red blood cells or their "shadows." In the collecting tubules fresh red corpuscles were present, along with blood casts formed either of fresh or disintegrated red blood corpuscles. The interstitial tissue was the seat of oedema, with small groups of cell infiltration, lymphocytes predominating. There was no noteworthy fibrous tissue proliferation and the vessels were normal. In the cells of some convoluted tubules, a small amount of fat was noted, of which a small proportion was doubly refractile, and in the collecting tubules were seen casts, all giving the reaction for neutral fat. These 4 cases, therefore, were all characterised by marked oedema, the most striking feature of the illness in each. Albumin was abundant in the urine of 2 and in the 3rd a trace was present in the one specimen examined during the child's sojourn in hospital, but as there was a history of scanty urine at the time of onset of the illness/

illness, in this case in all probability the presence of a larger amount of albumin would have been detected had more thorough examination been possible. In the 4th patient, both albumin and blood were abundant. In 2 of these patients the blood pressure was estimated and was 80 systolic and 44 diastolic in one aged 26 months a week before death (duration of disease 6 months), and in the other, aged 2 years 9 months, a few days ante-mortem the systolic pressure was 90 and the diastolic 70, low, therefore, in both cases. Of these children 3 died from a terminal peritonitis and one of these also developed a septic condition of the subcutaneous tissues of the right leg and thigh, and in the 4th, although no infection of the serous sacs was found at autopsy, an inflammatory swelling developed in the right flank, all the patients thus showing a marked tendency to bacterial infection. With regard to etiology, in one instance no factor with a possible bearing on the onset of the renal lesion was mentioned, while inflammation of the throat was found in other 2 of the children, one of whom had, in addition, very large tonsils, and many carious teeth, while the other had an abscess on the chin shortly before the attack of nephritis. In the 4th child the throat was red, but the appearance of the tonsils was not mentioned in the case report. At autopsy the kidneys showed marked cortical enlargement in 3, with mottling and blurring of the cortical markings in all 4. On histological examination the striking feature in all was the relatively slight glomerular involvement in comparison with the marked degenerative changes/

changes in the tubules, while inflammatory reaction in the interstitial tissue was absent, except for the presence of small scattered collections of round cells, though in one case the disease had lasted 6, and in another 3 months. On naked-eye examination there was a suggestion of myelin fat in the renal cortex in one instance, and in another the post-mortem report states that yellowish fatty areas were intermingled with patches of congestion, but as frozen sections were not available in these cases, the presence of single or doubly refractile fat could not be confirmed, and there was no note of the cholesterol content of the blood, during life.

The 4th case appears to be more closely related to frank glomerulo-nephritis than the 3 preceding. In the former, the glomeruli were rather larger than normal with slight cellular increase in the tufts due to endothelial proliferation, and in addition to degenerative changes, abundant blood was present in the tubules in the form both of discrete red blood corpuscles, and blood casts, definite glomerular involvement thus being indicated, according to many recent workers. Blood was not detected in the urine in the three first cases, and on histological examination scanty red cells were seen in sections of the kidneys in only one of these patients, after prolonged search. But for the presence of tubular haemorrhage in the transitional case it might have been classed as a degenerative lesion since glomerular changes were not pronounced, and as haematuria is often intermittent, the inflammatory nature might readily have been/

been overlooked. The 4 cases just described may, therefore, be classed as mainly parenchymatous or tubular, though with a mild inflammatory glomerular lesion as a basis, since slight changes in the glomeruli were present in all, though quite insignificant in the first three, 2 of which showed merely albuminous exudate in the capsular spaces, thus indicating the fact that the glomeruli had become "leaky filters", Gainsborough (1932). In the 4th, in addition to the presence of red cells in isolated tubules the glomeruli showed slight enlargement with early endothelial proliferation.

In all 4 cases the severity of the clinical symptoms was quite out of keeping with the relatively mild changes revealed on histological examination of the kidneys.

Cases of a similar type have been described by numerous investigators, thus Davison and Salinger (1927) describe cases of "parenchymatous nephritis," where the tubules are more markedly implicated than the glomeruli and interstitial tissue, though the latter structures too are abnormal, and Wolbach and Blackfan (1930) report a series of 21 cases of "acute tubular nephritis" examined by them during a period of 5 years. Of these children 10 died and 8 came to post-mortem when various degrees of tubular degeneration from cloudy swelling to cell necrosis were found, while the glomeruli were generally intact though a few showed slight signs of damage, as for example, cellular increase in the capillaries or hyaline thickening of the/

the cement substance in the capillary walls. Clausen (1925) divides nephritis in children into 2 main classes, haemorrhagic or glomerular, and parenchymatous or tubular, and his description of the latter type corresponds more or less closely with those cases of the writer's series described above, and Marriott (1924) describes a similar lesion.

Having dealt with acute glomerulo-nephritis and mild glomerulitis with marked parenchymatous change, the subject cannot be left without a brief reference to another form of renal disease, a prolific source of controversy in the literature on nephritis at the present time, - namely nephrosis. No case fulfilling all the requirements for this diagnosis occurs in the present series. Rennie (1933) who has recently investigated clinically a large number of cases in the Royal Hospital for Sick Children, also states that no case of lipoid nephrosis occurred in the wards during the preceding 2½ years. By this type of lesion corresponding to the "genuine" nephrosis of Volhard and Fahr is implied a sub-acute or chronic kidney lesion, the changes consisting in tubular degeneration and lipoid infiltration accompanied by a definite clinical syndrome, comprising insidious onset, obstinate or recurring massive oedema, marked albuminuria, no haematuria or cardio-vascular changes, and no rise in the blood N.P.N. According to modern workers Epstein (1917) being one of the pioneers, this particular lesion represents a type of parenchymatous nephritis where the primary disease is one of metabolism to which renal changes are secondary.

Loss/

Loss of plasma albumin in the urine causes diminution in the osmotic pressure of the blood, thus permitting fluid to escape through the vessel walls, and accumulate in the subcutaneous tissues and serous sacs. Associated with these changes is a great increase in the cholesterol content of the blood, with secondary deposits of lipoid in the kidneys. This type of lesion is prevalent in relatively young subjects, and is of obscure or unknown origin. Kauffmann and Mason (1925) believe nephrosis to be an early manifestation of a general systemic cellular degenerative process, but the etiological factor underlying this is unknown. Rennie (1933) suggests the possibility of interference with protein synthesis. Epstein's theory as to the sequence of events in the production of this syndrome would appear to receive confirmation from Barker and Kirk's (1930) experiments on dogs, where oedema of varying degree was produced in these animals by plasmapheresis. Renal changes similar to those in nephrotic patients were the result of low proteinaemia. Still further proof that the disease is not essentially of renal origin can be deduced from the fact that the majority of investigators have found no renal lesion in dogs oedematous as a result of plasmapheresis (statement by Rennie (1933)). The existence of such a purely degenerative type of lesion as "genuine nephrosis" is becoming more and more a matter of doubt, in the light of recent research, modern opinion inclining to the view that so-called nephrosis represents an extremely mild and protracted glomerulonephritis, the glomerular changes, initially of minimal intensity, remaining/

remaining stationary, thus allowing the disease to run an extremely chronic course with a minimal tendency to proliferative changes, unless an intercurrent infection to which such patients are peculiarly liable, cuts short the disease. Thus in Ehrlich's (1930) case where the patient died at the age of 19 with a history of attacks of oedema existing over a period of about 17 years, the kidneys were still large, and he regards the case as one of genuine lipoid nephrosis, though even here glomerular changes were sufficient to render it very debatable whether it should not be interpreted rather as a case of mild glomerulitis with a "nephrotic Einschlag," since it has been repeatedly demonstrated that the nephrotic type of glomerulo-nephritis can copy genuine nephrosis in every particular. Thus Rennie in the Glasgow Royal Hospital for Sick Children, recently observed 4 cases clinically in whom a syndrome indistinguishable from that of lipoid nephrosis followed acute nephritis with well-marked haematuria at the onset in each instance. Gainsborough (1932) believes that "genuine nephrosis" and all forms of glomerulo-nephritis are essentially of the same nature, and that difference between the various groups is mainly one of degree, determined by the varied rate of progress of the disease. In acute glomerulo-nephritis, the nephrotic syndrome hardly shows. All cases of toxic nephritis in his opinion, show progressive loss of renal function, and tend to terminate in uraemia, but in most nephrotic cases this change is so slow, that these patients generally die from an intercurrent infection or recover before loss of renal function, as generally measured, is/

is recognised. Among other recent investigators in this country Russell (1929) coined the name "nephritis mitis" for the syndrome called by Fahr "genuine nephrosis," and by Munk "lipoid nephrosis", thus recognising the presence of a mild inflammatory glomerular lesion. Gray (1933) in the course of extensive investigations has not encountered a nephrotic case in which the kidneys showed no evidence of nephritis at autopsy, and considers that true lipoid nephrosis must be very rare, and that definite proof of its separate existence is lacking. In another renal lesion previously considered of degenerative tubular type, namely eclampsia, recent investigators have shown glomerular changes. Thus Baird and Shaw Dunn (1933) find the common lesion glomerular, with tubular changes of secondary importance. Baehr (1928) considers nephrosis is diagnosed too often, though he states that in children it is seen not infrequently, and Hadfield and Garrod (1932) think that it does undoubtedly occur in children and in young adults. It should be emphasized, however, that even in young subjects, as in the adult cases of Baehr (1928) and Bell (1929), clinical findings should be confirmed at autopsy, as the diagnosis of genuine nephrosis cannot be made with certainty during life. In this connection Eckstein's (1926) paper is important as showing the fallacy of forming a diagnosis on clinical grounds alone. This author reports 3 cases of intermittent lipoiduria in children, with other features suggestive of a pure nephrosis. Two of these cases came to autopsy, in one of whom was found a glomerulo-nephritis and in the other severe/

severe amyloid degeneration of the kidneys following a mixed luetic and tuberculous infection. No lipoid was found in the kidneys in either of these cases. Wolbach and Blackfan (1930) like Eckstein, report the finding of fatty acid crystals, and granules of doubly refractile fat in the urine during life, though no doubly refractile fat was seen in the kidneys post-mortem, and in the case published by Labbé, Boulin, Azérad, and Besançon (1930), that of a male tuberculous patient of 26 years with marked oedema, lipoiduria, (doubly refractile crystals) and hyper-cholesterolaemia, histological examination of the kidneys did not reveal the slightest trace of lipoid infiltration anywhere. In view of the doubt and even scepticism expressed with regard to the existence of true lipoid nephrosis, one would be inclined to agree with a statement in one of T. H. Huxley's well-known essays, that the more a statement of fact conflicts with previous experience, the more complete must be the evidence which is to justify us in believing it. No case, therefore, should be accepted as belonging to a purely degenerative type, unless it conforms in every particular to the classical description, and an inflammatory glomerular component can be entirely excluded.

ETIOLOGICAL FACTOR IN THE WHOLE GROUP OF ACUTE NEPHRITIS CASES (37).

The cases in this group including 4 of haemorrhagic, 28 of exudative nephritis, 4 of mild glomerulitis, and one of glomerulo-tubular type are discussed together. In 14 cases careful search of the case-records failed to show a history of any infectious disease or other antecedent illness, or even the mention of a focus of infection to which the nephritis might be traced. In the remaining 23, some abnormality in connection with the tonsils, the respiratory tract, the skin, etc., was observed clinically, and though in many cases the lesion was trifling, - such, for example, as enlargement of the tonsils, with no history of recent sore throat, still, in view of the etiological importance attributed in the literature to diseased tonsils, no lesion in these structures, however insignificant at first sight, can be disregarded as a possible factor in the production of nephritis. Thus Hill (1919) considers that far more cases of nephritis are secondary to tonsillitis than to scarlet fever. Billings (1912) believes that the excessive amount of lymphoid tissue in the faucial tonsils and nasopharynx in the child doubles the menace of systemic infection, while the partial removal frequently leads to a

condition/

condition as bad as the original or worse, since the operation scar may seal up infected tonsillar crypts. He states further that infected tonsils need not be large in bulk, as in some patients small and apparently innocent tonsils contain abscesses yielding a pure culture of streptococcus. To the abundance of lymphoid tissue in the child this author also attributes the frequency of acute rhinitis, diphtheria, and tonsillitis in early life. Ophüls (1917) found that 8 of 12 chronic nephritics had had severe, often repeated attacks of tonsillitis, though the tonsils in these patients were not enlarged, but generally more or less shrunken, and retracted behind the pillars of the fauces. The smooth surface showed white cicatrices partially sealing the openings into the narrow crypts, but on squeezing, grumous material could be expressed from these, often followed by much pus from dilated pockets behind, the pus often containing great numbers of streptococci alone or mixed with other organisms. These old "pus bags" in the opinion of Ophüls probably keep the inflammatory process in the kidney in a state of intermittent activity. The patient may be unaware of the fact that the tonsils are diseased.

The present writer can verify from experience the fact that the tonsils need not be enlarged or apparently unhealthy to harbour a virulent infecting organism. In a case of rheumatoid arthritis in a young adult seen by her, the/

the tonsils were suggested as a focus of infection, but on examination they were small and appeared healthy, and the patient had been singularly free from sore throats; yet, on culture from each, a heavy, almost pure growth was obtained of a haemolytic streptococcus, an unusually broad zone of haemolysis surrounding each stroke of inoculation on a blood-agar plate after incubation overnight. In Allison's (1925) experience, of 12 children with acute nephritis 10 had had no illnesses in the previous 2 years, but in 8 the tonsils and adenoids were enlarged, with crypts yielding muco-pus on pressure. Other 2 of these 12 children had, in addition, a catarrhal otitis. Rosenow (1915) thinks that foci of infection play a most important rôle in the causation of system disease, and regards a focus such as a pus pocket in a tonsil, which cannot heal and, is constantly teeming with bacteria, in the light of a culture tube with a permeable wall.

On examining in detail the histories of the 23 children with a possible focus of infection, these fall into 4 groups. In 12 there was some abnormality in the throat or respiratory tract; in 6 some septic condition of the skin or mucous membranes; in 2 nephritis followed closely an infectious disease, mumps in one case and chicken pox in the other; while in 3 instances in young infants, aged 25 days and 7 and 8 months respectively, there was a history of maternal illness during pregnancy, the mother in one case having suffered from headaches, sickness and vomiting,/

vomiting during the last 3 months, in a second from severe vomiting, and in the third from swollen legs and pain in the back. Much importance is attached to the hereditary transmission of nephritis, thus when the mother suffered from chronic nephritis or eclampsia one frequently finds in the urine of new-born infants considerable quantities of albumin and also casts, and though 2 of the infants apparently were healthy at birth, they may at least have inherited a predisposition to develop nephritis from some minimal infection. The third infant was admitted, with a history of wasting since birth, and at post-mortem the kidneys were only about the size of haricot beans, at the age of 25 days.

Of the 12 children with an inflammatory throat or respiratory lesion only one gave a history of tonsillitis, with apparent recovery before the onset of nephritis, such as is considered by Hill (1919) characteristic of nephritis in children, in whom the disease does not generally develop while the angina is actually present, but after the patient is apparently convalescent. The child in question, a girl aged 6 years and 9 months, developed a sore throat and was in bed for 10 days. It was not until she was apparently back to normal that swelling of her face ushered in a severe attack of nephritis, terminating fatally in about a week. Two infants in this respiratory group suffered from snuffles, These showed no evidence of syphilis at autopsy. Another had a depression of the bridge of the nose, with obstruction, but/

but no discharge, and still another, rhinitis. In this case small abrasions of the skin were noted in addition, and a number of the teeth were carious. In 3 other instances there was a history of cough, which had lasted for 2 years in one patient, dating back to an attack of whooping cough. Langdon Brown (1929) quotes Horder's opinion that extended, as well as focal sepsis may be important in the etiology of nephritis, and that a widespread infection of the bronchial tubes can cause trouble similar to that developing from a small collection of pent-up pus. Of these 3 cases, 2 were markedly rachitic. The third was a premature infant of 5 weeks. In 4 other cases the tonsils were enlarged, though there was no history of tonsillitis, and in 2 of these a "cold"or sore throat immediately preceding the onset of nephritis was specifically denied. In the group of 4 just mentioned, enlarged tonsils were accompanied by carious teeth, in one child; another showed areas of indurated skin on the inner aspect of both thighs; and a 3rd, a boy of 7 years, gave a history of discharge of clear fluid from the ears since infancy. Hill (1919) thinks that in children with nephritis of unknown etiology, the trouble frequently begins with a mild tonsillitis missed, as nearly all such children in his group had large unhealthy tonsils. Wyllie and Moncrieff (1926) mention carious teeth as a possible etiological factor, along with tonsillitis, cervical adenitis, and various other inflammatory lesions in connection/

connection with the respiratory tract. Boyd (1929), in mentioning foci of infection, states that surprisingly large abscesses often with haemolytic streptococci are found even in primary teeth in not too obvious a state of neglect. She advises the treatment of teeth before tonsils. Driak (1930) describes a case where the urinary findings pointed to nephritis. Tonsillectomy was performed, and impetigo and ozoena were treated, but the temperature remained sub-febrile, and real improvement set in only after the extraction of several teeth with granulomata at the roots. In several other cases in this author's experience, extraction of teeth resulted in improvement, even although various other complicating factors were present. In one case, where a streptococcus was isolated from the granuloma at the root of a tooth, the same strain was obtained from the urine shortly after extraction of the tooth. He concludes, however, that the whole etiological onus should not be thrown on the teeth without searching for other foci of infection. Hill (1919) states that nearly all his cases had carious teeth, though in only 2 was it reasonably certain that the nephritis was due to this condition. In both these children the teeth extracted had large pus pockets at the roots. Bumpus and Meisser (1921), in describing the etiology of 6 cases of pyelonephritis, found infected teeth in 5, culture from all but one tooth yielding a growth of streptococcus viridans, Primary cultures in glucose broth of these/

these streptococcal strains inoculated intravenously into 27 rabbits, produced lesions localised to the kidney in 24 of these (89 per cent.). Thus there appears to be some justification for regarding diseased teeth with suspicion in renal lesions.

To return to the cases of the present series under discussion, 14 showed no etiological factor, 12 had some respiratory or tonsillar abnormality, and in 3 there had been a maternal history suggestive of possible renal damage during pregnancy. Six other cases had some septic skin lesion, and in 2 the disease began shortly after mumps in one case, and chicken-pox in another. Of the 6 children with a cutaneous, as in those with a respiratory focus of infection, the lesions were comparatively trivial; thus one child had septic sores on both shins, a second, patches of impetigo on the face, and a third, impetigo of the scalp, with scattered septic spots on the skin. In the fourth, a child of 10, the only noteworthy fact in the history was that about a week before death, a small painless abscess had developed behind the right auricle, with no constitutional disturbance. This was surgically incised and drained 5 days later, and 2 days afterwards the child complained of pain in the back, and had several rigors, followed by vomiting, coma supervening shortly after. A fifth member of this group had cellulitis of the scalp for about 3 months before the onset of nephritis, which was incised surgically on two occasions,/

occasions, but continued to discharge. The sixth patient about 6 weeks ante-mortem, developed a "cold," followed by gingivitis and abscesses of the face, while much pus exuded from the gums and alveoli, and at post-mortem the whole lower jaw was necrotic, with loosening of the teeth. The pus showed streptococci and diphtheroid bacilli. Billings (1912) places septic conditions of the gums and alveolar sockets immediately after tonsillar infections in his list of foci of infection with an etiological relationship to nephritis. Various septic skin lesions, with a nephritic complication, have been recorded in the literature. Thus Prowse (1932) instances a case of nephritis following acute cellulitis of the hand, and Volhard and Fahr, and Addis and Oliver mention similar cases. Extensive burns and scalds are also mentioned by various authors - von Kahlden (1891), Edebohls (1904) - as preceding nephritis. Catteruccia (1931) states that skin diseases due to cocci can cause important renal complications, the most important etiologically, being impetigo. Capon (1926) describes a case of nephritis in a child of 3¼ years, following impetigo, and considered secondary to this, though otorrhoea and vaginitis were also present. Wyllie and Moncrieff (1926) include this same skin lesion in their list of infections having an etiological relationship to nephritis, and Langdon Brown (1929) saw two cases of scabies causing a staphylococcal skin infection followed by glomerulo-nephritis. This author states,/

states, "Since the skin is a part of the excretory apparatus; an association between diseases of the skin and the kidneys is not surprising. Extensive burns are well-known to cause nephritis, though here extensive sepsis is the chief factor."

Two cases in the present series remain to be considered, one following an attack of mumps 3 weeks before admission, while chicken-pox was followed by nephritic symptoms in the other. It is now recognised that almost any of the exanthemata of childhood can cause an attack of nephritis, scarlet fever, of course, being the most important, etiologically. A number of cases have been recorded traceable to the two infections mentioned above. Thus Miller (1905) reports a case of mumps in a boy of 4, the disease, however, being complicated by measles. He states that the nephritic complication of mumps, which tends to occur in early convalescence, is much more frequent in males than in females. His review of the literature on the subject reveals other 29 cases of nephritis secondary to mumps, and other writers mention, in addition, febrile albuminuria during the course of this disease. Foa (1930) records a case of nephritis associated with mumps in a boy of 9, but comments on the almost constant integrity of the renal function during parotitis. He states that when nephritis does occur it appears generally as a late complication, about 1 to 2 weeks after disappearance of the parotid swelling, though in a few instances recorded in the literature, the/

the two diseases ran a simultaneous course. In the case at present under discussion, the history states that the patient, a male child, 7 years of age, had mumps 21 days before admission, and 3 days later the eyelids became puffy. The case of nephritis following chicken-pox occurred in a male infant of 21 months. Cases of nephritis following chicken-pox are recorded by various authors, among them Waltner (1930) and Denny and Baker (1929). In the case described by the latter, the disease was complicated by an acute tonsillitis beginning two days before the chicken-pox eruption, and which might itself be considered the chief etiological factor. Ochsenius (1930) reports a familial outbreak of nephritis after chicken-pox, involving 3 children, and Murray Gordon (1924) describes a case where, after chicken-pox with a mild clinical course and rather scanty skin lesions, severe headache and polyuria with haematuria ushered in an attack of nephritis, this case being further complicated by encephalitis.

DISCUSSION ON THE ETIOLOGY OF ACUTE NEPHRITIS.

Kannenberg, as far back as 1880, recognised the fact that tonsillitis is a very common cause of nephritis. Until the beginning of the present century, however, little was added to our knowledge of the etiology of nephritis, and particularly in children the tendency was to regard it as generally/

generally due either to scarlet fever, or to cold and exposure. Recent investigations have shown, however, that either the acute exanthemata, naso-pharyngeal and other focal infections, and septic skin conditions are among the chief causes, while, though cold and exposure may play a part in precipitating an attack of nephritis, they do so merely by working in a round about way through bacterial infection. Langdon Brown (1929) does not believe that exposure to cold causes nephritis in healthy persons, though it may exacerbate an acute lesion. In the first winter of the war, epidemics of nephritis did not occur when the men were much exposed and badly housed, but it was prevalent in the spring of 1915, and there was no relation between low temperature and the incidence of nephritis. Lyttle and Rosenberg (1929) consider that the seasonal incidence of acute nephritis closely follows that of respiratory disease, the onset of about 75 per cent. of both occurring between the months of December and May (inclusive). They regard as unusual the absence of some previous infection in acute nephritis, and believe that upper respiratory tract infections predominate as the cause of all types. The importance of tonsillar disease has already been mentioned in dealing with the etiology of the series of cases forming the basis of this work. Among other authors who emphasize the etiological importance of diseased tonsils as foci of infection are Volhard and Fahr (1914) who attribute to them above one quarter/

quarter of all cases of known etiology, and state: "When we add that scarlet nephritis also results from scarlet angina, and that the primary cause of purpura, joint rheumatism and endocarditis is generally an angina, while in colds, flu-like diseases, rhinitis and otitis media, the infection as a rule starts from the lymphatic pharyngeal ring, we come to the remarkable conclusion that in almost three-quarters of all nephritides of known etiology the tonsils or the lymphatic pharyngeal ring form the portal of entry for the disease-producing organisms." A few of these authors' cases, however, followed damage to the skin, nephritis being due to a complicated fracture, for example, to some other infected wound, or to a disease such as eczema or scabies.

In the experience of Gainsborough (1932) most cases of nephritis are of scarlet or tonsillogenous etiology. In nephritis in children particularly, the etiological relationship to infection, according to the general opinion, is even more obvious than in adults, since any of the acute specific fevers may give rise to it, though the majority of such cases develop focal nephritis with recovery, unless where complicated by secondary infection (generally streptococcal), when true diffuse nephritis results, though this is comparatively rare, Hadfield and Garrod (1932). Gray (1928) is among those who find co-existing focal sepsis in nephritis easier to demonstrate in children than in adults. In an investigation of the case records of nephritic children in Aberdeen, he found among/

among 42 cases of acute nephritis 34 with definite focal sepsis, (81.0 per cent.), while in a control series of 50 cases of nervous diseases the incidence of focal sepsis amounted only to 28.0 per cent, and to 42.0 per cent. in 50 consecutive cases of all diseases excluding nephritis. In the opinion of Wyllie and Moncrieff (1926) tonsillitis with or without otitis is by far the commonest cause of nephritis in children, and Brown and Cummins (1916) find that a previous history of some disease, other than mere children's ailments, is about twice as common in nephritics as in non-nephritics. Pfaundler and Schlossman (1908) consider it rather unusual to be unable to assign a cause for an attack of nephritis. According to Paterson and Wyllie (1926) the belief is growing that nephritis is more often secondary to some naso-pharyngeal infection than to any other cause. Hill (1919) regards tonsillitis as the most frequent cause of nephritis in children, and rarely sees cases secondary to scarlatina in a general hospital. He believes that in cases of unknown etiology the trouble frequently begins with a mild tonsillitis missed, as nearly all children in his series had large and unhealthy tonsils. He includes cases secondary to otitis and cervical adenitis under the heading of throat infections. Osman (1925) also frequently finds in acute nephritis in children some acute inflammatory process in the upper respiratory tract, generally the tonsils or ears or both. Sautter (1922) and Kinney (1932) report cases of acute nephritis following acute mastoid infection/

infection. Garrod, Batten, Thursfield and Paterson (1929), in addition to diseases of the naso-pharynx, ear, or upper respiratory passages, mention as other prominent causes of nephritis in children, infected wounds, impetigo contagiosa, parotitis, cervical adenitis, erysipelas, pneumonia and empyaema, and even whitlow, the latter being in their opinion a not uncommon precursor of nephritis. Endocarditis is also frequently associated with nephritis. According to Baehr and Lande (1920), the former is one of the three diseases distinguished along with scarlet fever and streptococcal angina by the frequency with which it is complicated by acute and chronic nephritis. Various writers, Marriott (1924), Clausen (1925), Aldrich (1926), consider that in the parenchymatous type of nephritis where the lesion is mainly tubular, infection of the nasal sinuses is important etiologically. Apart from the diseases just mentioned, which are prevalent in Europe, writers from various countries abroad mention other etiological factors; thus Moncorvo (1902) considers malaria as important etiologically in Rio as scarlet fever in Europe, and found that of 35 cases of nephritis in young children, 26, or nearly 75 per cent., were associated with malaria. Surbek (1932) reports a series of cases of nephritis from South Sumatra, with malaria as the etiological factor, the severe chronic quartan type being most commonly associated with nephritis.

In Australia, M'Donald (1931) records a case of acute/

acute tubular nephritis in a child of 3 years and 11 months, following lead-poisoning, while Croll (1929) and Nye (1929) comment on the frequency in Queensland of chronic nephritis in children and young adults, the disease being familial and often affecting many members of a family. The prevalence of this disease in Queensland, these authors attribute to the fact that many of the wooden houses are painted with lead paint, which quickly dries in the sun and becomes reduced to a powder, with which children contaminate their fingers, and by nail-biting and thumb-sucking absorb sufficient lead over long periods to produce a slowly progressive chronic nephritis. Another fact that contributes to the greater prevalence of the disease in Queensland than in the rest of Australia, is that the wooden houses there are built on high blocks to prevent the activities of the white ant, and the verandas are provided with a gate, so that the children are confined within a narrow space and have a greater opportunity to absorb the powdered lead. Another way in which nephritis can arise is reported from Australia by Breinl and Priestley (1918) where, in the treatment of a protozoal infection with antimony (tartar emetic), the patient developed an acute interstitial nephritis.

A final way in which nephritis can arise, is through direct trauma. Schörcher (1931) and Koch (1931) report cases following a blow or a crushing injury in the kidney region.

In/

In such cases nephritis may be due to long-continued cramp of the renal vessels, to the formation of nephrotoxins from damage to renal tissue, to locally diminished resistance, or to a combination of all three factors.

A number of text-books on children's diseases divide nephritis into two main groups, according to the age of the child, placing the cases of infantile nephritis in a separate category from those in older children. As has already been mentioned, infants appear to have much less power of resistance than older children. Nephritis can appear at any age; thus Karsner (1908) reports the case of a nephritic infant dying 45 minutes after birth. Lapage (1932) describes a case in a new-born baby, and Ashby and Wright (1928) state that in rare cases infants are born with acute nephritis, while Ashby (1901) describes a case admitted to hospital the day after birth, with swollen face and marked oedema. No urine was passed and the child had convulsions, and died 24 hours after admission. An autopsy, marked proliferative changes were present in the interstitial tissue, and a cellular growth had surrounded the tubules and the glomeruli, and had put most of the latter out of action. Carpenter (1905) reports a case of interstitial nephritis associated with cirrhosis of the suprarenal capsules in an infant of 5 weeks. Ballantyne (1902), in his book on ante-natal pathology, mentions as a possibility the intrauterine origin of nephritis and reports 2 instances/

instances were in all probability the disease had begun before birth, one case being idiopathic, while in the other the mother had suffered from bronchitis and pneumonia shortly before the birth of her infant.

Pfaundler and Schlossman (1908) place gastro-enteritis first in their list of diseases associated with nephritis in infancy, followed next in order by the exanthemata, such as varicella and meningitis. They have also seen erysipelas, angina, tetanus neonatorum, impetigo contagiosa, aphthous stomatitis, and generalized eczema, followed by nephritis, some of the severest cases in their experience following streptococcal catarrh. Heubner, quoted by the above authors, also mentions the frequency of nephritis in infantile scurvy. They state further that infants are more readily affected than adults by external applications of toxic substances, such as iodine, tar, etc., and they include congenital syphilis among the etiological factors causing acute nephritis in infancy. Brüning and Schwalbe (1913) also stress the importance of gastro-enteritis in infantile nephritis. Abt (1923) agrees that nephritis in early infancy is generally caused by gastro-intestinal disturbance, though infections such as pneumonia, meningitis and erysipelas, diffuse skin eruptions, the acute exanthemata, as well as various toxic substances used as local applications may also determine an attack; and he also makes the important observation that congenital/

congenital defects of the renal structures are conducive to the onset of nephritis. He regards as predisposing causes, errors of diet, improper care of the skin, and hereditary factors. Well-authenticated cases are recorded where several members of the same family suffer from nephritis, and he assumes that in certain families inherent susceptibility to inflammation may be present. Thus, a mother with eclampsia may give birth to a child with diseased kidneys. Exposure to cold, Abt believes, probably renders the patient more susceptible to infection from other foci in the body. He quotes in this connection the experimental work of Helmholz, who failed in his attempt to produce pyelitis in rabbits by the intravenous injection of strains of colon bacilli, unless he damped their fur and chilled them by exposure to an electric fan. Simmonds (1896) believes that nephritis in marasmus is due not to gastro-enteritis, but to the otitis present in nearly all marasmic infants. Garrod, Batten, Thursfield and Paterson (1929), in general agreement with other writers, state that the characteristic signs of nephritis in infants may be easily overlooked, and symptoms may be mistaken for those of acute intestinal disturbance, with acidosis. These writers consider acute nephritis rarer in infancy than in later childhood, since infants are less liable to suffer from conditions likely to cause it. They regard congenital syphilis as a prominent etiological factor, most probably on account/

account of associated naso-pharyngeal sepsis, and in addition blame chiefly other acute specific or focal infections or skin sepsis, believing like Abt, that cold and exposure play only a part in precipitating an attack of nephritis. Blackman and Rake (1932), investigating a series of pneumococcal infections in young infants, found acute nephritis of considerable intensity in 9.5 per cent. of these.

While the general consensus of opinion thus regards nephritis as secondary to some focus of infection, it is agreed by some writers that true so-called primary nephritis does occur in a minority of cases. Thus Parsons and Barling (1933) state that in some instances the cause is unknown, the disease beginning during a period of good health. Still (1912) recognizes that many causes of nephritis exist in children apart from scarlet, but he believes that the majority of cases begin without any assignable etiological factor, and he concludes that there is a large group of cases where nephritis in childhood is apparently primary and idiopathic in the sense that we do not know its cause. Hill (1919) states that far more exudative than haemorrhagic cases are of unknown etiology, and Wyllie and Moncrieff (1926), and Paterson and Wyllie (1926) agree that foci of infection are more generally found in haemorrhagic than in tubular nephritis. The last-mentioned writers found in 22 cases of parenchymatous nephritis, 9 cases of quite obscure origin, while of 27 haemorrhagic cases, some focus/

focus of infection was observed in all but 2. In over 1/3rd of the cases forming the subject of this work, as we have seen, no factor with a possible etiological bearing was found, and this might seem at first sight to be at variation with modern views on nephritis. All cases, except 4, however, were of exudative type, and it is precisely in such cases that the authors last named found the largest percentage of idiopathic nephritis. Also, a number of patients were admitted moribund, with an insufficient history. While a writer like Hill, who made a special study of nephritis, might obtain a history of throat infection in a large proportion of cases, on making special enquiry with regard to this point, in a scattered series of cases such as the present, extending over a long period of time and where case particulars were obtained by many different, often harassed residents, it is very probable that no special enquiry would be made regarding recent sore throats or "colds." In the present series all that one is entitled to say is, that in over 1/3rd/ of the cases no primary focus of infection was discovered, not that a primary focus did not exist. It would be interesting to compare the present results with those of a series examined by one person, in a uniform way, paying due regard to the state of the tonsils, teeth, skin, and middle ears.

Having mentioned some of the current views with regard to the etiological factors associated with nephritis, the bacteriology/

bacteriology of such lesions will now be briefly discussed. Much attention has been devoted to this subject, and it is now generally recognized that streptococcal infections must be blamed in a large percentage of cases. Newburgh (1923) states: "One may expect the percentage of cases of acute nephritis demonstrated to be due to infection by streptococcus, to grow as our knowledge of medicine increases, but there will remain a few cases due to pneumococcus, B. diphtheriae, and perhaps staphylococcus." Volhard and Fahr agree that by far the greatest rôle is played by the streptococcus, with pneumococcus next in importance. The other infecting organisms, according to these authors, are insignificant etiologically, though B. influenzae may, at times, - and perhaps B. coli - cause true haemorrhagic nephritis. They quote Löhlein's view that streptococcus is alone responsible for nephritis, though the latter occasionally saw glomerulo-nephritis in pneumonia and tuberculosis, but considered nephritis a chance association in the last-named disease. In Gray's (1928) investigation in Aberdeen, mentioned above, the bacteriology of the lesion associated with nephritis was mentioned in 7 of the 42 cases, and was streptococcal in 5 of these. In Paterson and Wyllie, and Wyllie and Moncrieff's cases, the associated infection was generally streptococcal, though at times staphylococcal, or pneumococcal. Kolmer (1926) states: "Of all organisms believed responsible for focal infections, streptococcus/

streptococcus is the most important, followed next in order by staphylococcus aureus, pneumococcus, gonococcus and B. coli, the two former organisms certainly being of primary importance in this author's experience. The streptococco-pneumococcal group, according to Troisier (1932), possesses alone among the micrococci a certain renal affinity. Bumpus and Meisser (1921) find also that diseased teeth can not only harbour streptococci, with a selective affinity for the urinary tract, but that streptococcal strains isolated from the teeth, on being injected into rabbits, produced lesions localised to the kidneys in the great majority of these animals. Staphylococcus, in the opinion of recent American writers, is important etiologically in parenchymatous or tubular nephritis. Among other investigators, Marriott (1924), Clausen (1925), and Aldrich (1926) isolated staphylococci of aureus or albus type from the nasal sinuses in such patients.

The question whether in the non-suppurative type of nephritis organisms themselves or their toxins are responsible for the renal lesion still remains doubtful, except in the case of the embolic focal nephritis of Löhlein, where the lesion is due to the plugging of the capillary loops by emboli from heart valves the seat of bacterial endocarditis, the organism in question being generally streptococcus viridans. It has been suggested that in the acute haemorrhagic nephritis of children, the focal type of lesion, with the involvement/

involvement of relatively few glomeruli, is also due to emboli. Wyllie and Moncrieff (1926) & Ophüls (1917), believe that acute glomerulo-nephritis is due to the trapping of organisms in the glomerular capillaries, and that lysis of these organisms in situ, explains the severity of the glomerular lesion. Gray (1928) considers that the failure of various workers to obtain cultures from the kidneys at post-mortem in non-suppurative nephritis in non-septicaemic cases does not negative a bacterial origin, but what it does disprove is metastatic multiplication of bacteria in the kidneys. Hill (1919) and Kolmer (1926) are among those who are still doubtful whether the toxins of the organism causing the primary condition are responsible, or whether the kidney is itself invaded by organisms. Garrod, Batten, Thursfield and Paterson (1929), and Muir (1933), on the other hand, find no proof of actual bacterial invasion of the kidney, and consider that the interval between the original infection and the onset of nephritis favours a toxic, rather than a bacterial origin. The assumption that nephritis is due to bacterial infection is strengthened when, for example, nephritis immediately follows the onset of focal infection elsewhere, and clears up along with, but not before, it. Gray (1928), in his investigation of a series of 42 nephritic children, selected 16 as showing definite evidence of relationship between the renal lesion and some infective condition. Similar confirmatory/

confirmatory evidence is afforded when, as occasionally happens, co-existing focal sepsis is treated surgically after nephritis has subsided, and the latter flares up again. Lynch (1931) observed a number of patients with tubular nephritis, in all of whom tonsillectomy was performed, with a second flare up of nephritis in each instance. Hill (1919) describes 2 cases of nephritis, where there was a recurrence following tonsillectomy, which may have stirred up foci of infection, and Kolmer (1926) believes that, when extraction of a tooth, tonsillectomy, etc., is followed by exacerbation of secondary foci elsewhere, such a result is always strong presumptive evidence of relationship between primary and secondary foci.

ANAPHYLACTIC NEPHRITIS.

Having discussed the etiology of nephritis from both the pathological and bacteriological standpoint, reference should be made, before leaving the subject, to the anaphylactic theory of the causation of nephritis. The fact that this disease arises not immediately after an acute infection, such as tonsillitis, for example, but after an interval of some days, while in scarlet fever the onset of the typical glomerulo-nephritis is sometimes delayed until the third week, has suggested to some workers that in the interval the patient has developed hypersensitiveness during immunisation. Volhard/

Volhard and Fahr mention this possibility as early as 1914. Hadfield and Garrod (1932) believe that interaction of antigen and antibody produces substances with specific toxic action on the glomerular capillaries. The anaphylactic theory of nephritis appears to receive confirmation from the experimental work of Duval and Hibbard (1926), who showed that broth cultures of a haemolytic streptococcus scarlatinae were without apparent effect on rabbits, no matter how large the dose or the route of inoculation employed, as a result of the fact that the active principle of the streptococcus is endotoxic. A dose which, given previously, would have had no effect, will, however, produce symptoms in rabbits previously immunised. These authors consider this phenomenon due to the liberation of endotoxin from the injected organisms by specific bacteriolysins previously produced in the animals through the action of the specific antigen. Longcope (1929) concludes from a series of observations that a considerable number of cases of acute and sub-acute nephritis give exaggerated skin reactions to bouillon filtrates of haemolytic streptococci, and it seems to him that this pronounced reaction indicates the acquirement or possession on the part of the patients of a high degree of allergy towards some substance in the haemolytic streptococci or to their products of growth. This phenomenon is not temporary, but may persist through the attack of nephritis or even for several years after recovery.

10 WARD CASES.

Before leaving the subject of acute glomerulo-nephritis, a further series of 10 patients will be discussed, who failed to respond to medical treatment and were subjected to the operation of decapsulation of the kidneys. This group is kept separate from the other cases of acute glomerulo-nephritis, since, necessarily, in these patients it was not possible to carry out such a thorough examination of the macro- and microscopic pathology as in those coming to autopsy. On the other hand, clinical investigations were more extensive than in the latter series, as the former patients were all in the wards for considerable periods. These 10 form part of a series of 23 decapsulated cases, treated in the Royal Hospital for Sick Children, between June 1917 and January 1929, and reported by Campbell (1930). Histological material was available in 10 only, of whom 7 were male and 3 female, the ages varying between 21 months and 10 years. These patients had suffered from nephritis for varying periods, as indicated by the onset of renal symptoms, before decapsulation was performed, the shortest duration of the disease being 3½ weeks and the longest about 21 months. The condition which led all those children to seek advice was "swelling," either of the face or of the legs and feet, though in a few instances oedema first appeared below the/

the chin. With regard to etiological factors, one child had suffered for years from several annual attacks of tonsillitis, and though there was no history of such an attack immediately prior to the onset of nephritis, the tonsils were probably in an unhealthy condition. In the second, the disease began with sore throat and swelling of the neck (?glandular enlargement), followed in a few days by epigastric pain and puffiness round the eyes. A third had enlarged tonsils and impetigo of the face. A fourth gave a history of discharge from the right ear of 4 years' duration, and a fifth child of 21 months burned her hand severely about 3 months before admission to Hospital, and was unwell and irritable for about one month thereafter: orbital oedema being noted at the end of that time, though swelling was not generalised until 3 weeks later. The mother dated the onset of ill-health from the burn. In another child, there was a history of Bright's disease in the maternal grandfather. Though the patient himself had no history of infection or other illness prior to the onset of nephritis, it is possible he may have had an inherited predisposition to the disease. Thus some possible etiological factor was present in 6 cases. In the remaining 4, the disease began while the child was apparently in good health, though possibly some mild throat inflammation not mentioned in the history may have been present a short time before the appearance of oedema. During their stay in Hospital,/

Hospital, the prominent symptoms in these children were albuminuria and oedema, which failed to respond permanently to medical treatment, though oedema in some cases was of intermittent character.

At operation, both kidneys were decapsulated, either at the same time or at an interval of several days, a small portion being removed for histological examination at the time of operation. The appearance of the kidneys was mentioned in 5 instances in the surgical case-reports. Thus, in one case of 4½ months' duration, the kidneys were extremely avascular and each, particularly the left, showed a granular appearance, though the capsules stripped completely. In a second case of similar duration, the right kidney was small and granular, and the left large and granular and much more vascular than the right. (It may be mentioned that Edebohls (1904) found at operation, in a series of cases of chronic Bright's disease, that in about half the cases, only one kidney was obviously diseased, and to this fact he attributes the chronicity of such cases, the other presumably being involved only at a later date.) In a third case, the kidneys were described as dark-coloured and possibly enlarged 7½ months after the onset of the disease. The depth of colour may, however, be influenced by traction on the pedicle, while bringing the kidney into the wound. In a fourth instance, the organs were large, soft, friable, and very vascular after 9½ months' duration, and in the last case described at operation,/

operation, though the disease had lasted 12½ months, the kidneys were both enlarged, especially the right.

HISTOLOGY OF THE 10 WARD CASES.

On histological examination of the small fragments of renal tissue available, the most striking feature in the whole series was the fact that there was only comparatively slight evidence of proliferative change, even in the three most chronic cases, where the disease had lasted 14, 18, and 21 months respectively. In the case of shortest duration (under one month) the picture was that of a typical acute glomerulo-nephritis with enlarged, cellular, digitate, glomeruli, all in the acute inflammatory stage. The tubular epithelium showed marked catarrhal change, with abundant granular débris in the lumina, while a few contained rather scanty red blood corpuscles. The interstitial tissue showed only very slight cellular infiltration, with no connective-tissue overgrowth. A second case of 2½ months' duration showed glomeruli still acutely inflamed, large, swollen, and vascular. The tubular epithelium was the seat of marked degeneration, with swollen, granular protoplasm and shed epithelial cells, along with much débris in the lumina, while groups of convoluted tubules were distended with fresh red blood corpuscles. The interstitial tissue was oedematous, particularly in the right kidney, and was, at places, the seat of/

of slight early fibroblastic proliferation, with small foci of cellular infiltration.

Three cases of approximately 4½ months' duration showed closely similar histological appearances in the glomeruli, which in all 3 were enlarged, swollen and very cellular, endothelial proliferation causing them to appear rather avascular on the whole, though some capillaries were still patent, and distended with blood. Tubular changes were also similar, a granular, rather flat type of lining epithelium being present in each instance. In one of the 3 cases, red cells were present in the lumina of some of the convoluted tubules, but were not abundant in any of these, and in another there was some attempt at cell regeneration. Interstitial changes were practically absent in one case, another showed very slight peri-glomerular fibrosis and round-cell infiltration, while in the third areas of fibroblastic proliferation were present, associated with cellular infiltration, the tubules in these areas being compressed, atrophic and slightly dilated, the lumina containing colloid casts. In these 3 cases, though of approximately the same duration, while an acute lesion was still present in all, proliferative changes were not of equal extent, and were fairly advanced in one case after 4½ months; while in other cases (to be described later) of 14, 18, and 21 months' duration respectively, interstitial changes were still/

still very slight, and the glomeruli appeared not to have progressed beyond the acute inflammatory stage, except in one case, which showed transition to a more chronic type of glomerular lesion. Such findings bear out the fact already emphasized that no reliable information as to the duration of nephritis can be deduced on histological examination. Neither are the naked-eye appearances of help in determining the probable duration of the disease. Thus, small granular kidneys were described at operation, in one of the cases with a 4½ months' history, though in other 2 of 7½ and 9 months' duration, the kidneys, on naked-eye examination, were still enlarged and vascular. It would appear, therefore, that the macroscopic, and even the microscopic appearances are no certain criteria of the duration of a renal lesion. Volhard and Fahr mention a case where death occurred from meningitis 3½ years after the onset of glomerulonephritis. The kidneys were still at the "large white" stage, though in another patient scarring of the surface was marked 5 months after the onset of nephritis, so that the condition would have seemed of much longer standing in the latter case without a clinical history. Evidently a variable length of time is required in individual cases to produce scarring, and it is not possible to state the duration of a nephritis from the naked-eye appearances. The renal lesion may thus remain active for long periods without

any/

any marked degree of proliferation. Edebohls (1904) reports a case in a child of 4½ years, who developed acute nephritis after an extensive scald, with repeated acute exacerbations. At operation 2½ years later "large white" kidneys were present, each kidney being 3 times the normal size, with no mention of surface granularity. Capon (1926) also found the kidneys enlarged in one child, where decapsulation was performed 19 months after the onset of nephritis, and, in another instance, where the disease had lasted 11 months, the organs were of normal size. Experimental proof of the fact that a renal lesion may long remain in the acute stage is afforded by the experiments of Seegal (1927), who administered doses of N/10 hydrochloric acid and ammonium-chloride to rabbits over periods varying from 11 days to one year, and found at post-mortem only an acute degenerative process in the kidneys of these animals. No interstitial proliferation had taken place even in animals where marked albuminuria and all types of casts had been present for a year.

To return to the histology of the 5 remaining cases, which had lasted at the time of operation 7½, 9, 14, 18, and 21 months respectively, in 2 of these cases, of approximately 7½ and 9 months' duration respectively, the glomeruli on the whole were still enlarged, swollen, cellular and digitate, though a few showed degenerative changes, with atrophy of individual glomeruli. The tubular epithelium in both was markedly/

markedly flattened and granular, many cells showing pyknotic nuclei. The activity of the inflammatory process was illustrated in the second case by the presence of blood in groups of convoluted tubules. Both cases showed areas of fibroblastic proliferation and round-cell infiltration of the interstitial tissue, slightly more abundant and widespread in the case of longer duration. In the remaining cases of 14, 18, and 21 months' duration, the glomeruli in the first were very large, cellular, and digitate, filling the capsule of Bowman, while some showed albumin and a few red blood corpuscles in the capsular space. Some capillary loops still contained blood, but the majority were blocked by swollen, proliferated, endothelial cells. In the second, where some glomeruli still appeared to be in the stage of acute inflammation, all transitional stages to a chronic lesion were seen. In the case lasting 21 months, the enlarged, swollen glomeruli showed little evidence of fibrosis - polymorphs were numerous in the tufts - while the active nature of the lesion in this case was demonstrated by the presence of scanty red blood corpuscles in some capsules of Bowman. The tubular epithelium in these last 3 cases was the seat of degenerative changes, a marked degree of cloudy swelling being present in the case of longest duration. Tubular dilatation was lacking, and this can be attributed to the fact that interstitial proliferation was relatively slight in all 3 cases, and least marked in that of longest duration.

The/

The naked-eye appearances were not noted at the time of operation in any of these 3 cases.

CLINICAL INVESTIGATIONS AND RENAL EFFICIENCY TESTS.

Before decapsulation was resorted to in these cases, the patients were all observed for a considerable period. Oedema in each case was a marked, though variable feature, and the urine contained varying quantities of albumin. Blood was present at some time, either macro- or microscopically, in all except one case, and casts of varying type, - though not constantly present, - were observed in at least some specimens from each patient. The urinary out-put was low, or very low in 4 instances, fair in 3, and was not mentioned in the remainder. Before decapsulation was resorted to in these cases, various renal efficiency tests were performed, and the blood pressure was examined in the majority. Results are given in the accompanying table. With regard to normal figures, Crawford (1924) performed pigment excretion tests in 26 normal children, and found an average excretion in the first 2 hours of 67.0 per cent. of the dye. The urea concentration test, also performed in 26 normal children, after 15 gms. of urea per os yielded results varying between 2 and 6 per cent., anything over 2 per cent in the second hour being considered/

TABLE IV.
Decapsulated Cases.

Case	Age	Sex	Duration	Type of Lesion	Urea Conc. Test. %	Blood Urea. Mg.%.	N.P.N. Mg.%.	Pigment Test. %	Blood Pressure.	Result
1.	10 yrs.	M.	7½ mths.	Active glomerulonephritis with marked tubular degeneration.	1.4	27.9	-	58	64/40 107/78	Much improved though with moderate cloudofalbumin 2 years later.
					2.3	28.3	-	32-58	75/50	
2.	10 yrs.	M.	4 mths.	Active glomerulonephritis with marked tubular changes and early interstitial proliferation.	2.0-2.3	69	-	28-47	110/70 118/80	Practically well 5 weeks after operation. No oedema and only a trace of albumin.
3.	9 yrs.	F.	4½ mths.	Active glomerulonephritis with early interstitial proliferation.	2.0	-	-	65	110/80	Well nearly 2 years after operation.
					2.0-2.2	-	-	35-65	90/50-110/80	
4.	3 yrs.	M.	21 mths.	Mixed nephritis. Active glomerular lesion still present with marked tubular degeneration. Proliferation slight.	-	-	-	-	-	Much improved.
5.	5 yrs.	M.	3½ wks.	Acute glomerulonephritis with tubular catarrh and haemorrhage.	2.0	-	59.4	-	-	Removed 18 days after operation.
6.	8 yrs.	F.	18 mths.	Mixed nephritis with all stages between acute and chronic glomerular and interstitial proliferation.	-	-	-	-	90/45 100/80	I.S.Q. 2½ years after operation with slight recurring oedema, Albumin ++ and casts. B.P. 132/88.
					1.2	-	-	27.8	100/60	
7.	6 yrs.	M.	14 mths.	Active glomerulonephritis with much tubular degeneration and haemorrhage. Slight interstitial proliferation.	-	-	-	52	100/68-124/84	Temporary improvement but relapse, but 8 mths. after operation I.S.Q. with oedema and albumin ++.
					2.9-2.45	-	-	61-85	105/80-124/80	
8.	5½ yrs.	M.	2½ mths.	Acute glomerulonephritis with much tubular haemorrhage.	2.4	-	70.2	35.7	100/70-110/82	Appeared quite well 3 months after operation.
9.	3¾ yrs.	M.	9½ mths.	Acute glomerulonephritis with tubular haemorrhage. Interstitial proliferation.	2.7	-	-	70.0	-	Improved. General condition good 2 months after operation.
					2.7 (2x)	-	-	50.0	-	
10.	1¾ yrs.	F.	4½ mths.	Acute glomerulonephritis with tubular catarrh and haemorrhage.	1.5	-	-	18.8	-	Improved 3½ mths. after operation. Dismissed with measles.
					4.0	-	-	45.0	90/60-120/90	

considered within normal limits. The blood urea was estimated in 12 normal children, and varied between 20 and 51.6 m.g. per cent. The N.P.N. figure has already been mentioned, Harrison (1930) regarding as normal anything between 25 and 50 m.g. per cent. Judson and Nicholson's (1914) normal figures for the blood pressure between the ages of 3 and 10 years are 91.8 to 99.2 systolic, and 64.9 to 71.0 diastolic. As will be seen from the accompanying table, only moderate impairment of renal function was found in most of the cases examined, and the results were rather erratic in a number of instances. Thus, in case 1, urea concentration was low (1.4 per cent.), though pigment excretion was approximately normal (58.0 per cent.), and in case 8, the urea concentration was high (2.4 per cent.), with a pigment excretion of only 35.7 per cent. The blood urea was moderately raised in one instance, and the N.P.N. in other 2. Little, however, can be deduced from these scanty figures. Estimations are lacking in the cases of longest duration, and even in these lasting about the same time (nos. 2 and 3) there is discrepancy. Thus, case 2 appears to have fairly efficient kidneys, while number 10, of similar duration, shows both a low urea concentration and pigment excretion. Below the dotted line in the table are given the figures obtained after operation, where these are available. These again are erratic; thus, in case 9, the urea concentration remained

the same as before operation, while the pigment excretion had fallen from 70 to 50 per cent., though the patient's condition was improved. In case 3, the urea concentration rose from 2 to 2.2 per cent., and pigment excretion was at first considerably lowered, though it gradually rose to the figure obtained previously. The blood pressure showed only a slight or moderate rise, exceeding 120 in only one patient (No. 7). When more than one blood-pressure estimation was performed, considerable variation was noted in individual cases before operation, so that even an apparent fall after decapsulation may have little significance. The variation may be due, as Capon suggests, to emotional disturbance. On examining Campbell's (1930) larger series of renal efficiency tests, the figures here again show the same lack of agreement as in the present writer's smaller group, and Crawford (1924) was struck by the variable results of the different tests in any individual case, while Capon (1926) states that, in his experience, renal functional tests have not furnished any diagnostic information of value.

Results of Operation.

Regarding the results of operation in the series of 10 cases described above, immediate improvement followed operation in the majority of cases; thus oedema and albumin were considerably diminished, blood and casts were decreased in/

in amount or were absent, and the urinary out-put was improved in a number. One child was apparently benefited for a few days after operation, then relapsed and was taken home against advice 18 days after operation (case of 3½ weeks' duration). A second improved temporarily, but 8 months after decapsulation, oedema and albuminuria were as marked as before operation, while blurring of the optic discs and a diffuse apex beat were present in addition (case of 14 months' duration). A third, seen 2½ years after operation, suffered from slight recurrent oedema, with abundant albumin and casts in the urine, and a blood-pressure of 130 systolic (case of 18 months' duration). The child with a history of nephritis for 21 months before operation was reported as much improved one month after operation, but further information was not available. A fifth was considered improved 3½ months after operation, but was dismissed with measles. In a sixth the general condition was good 2 months after decapsulation, and a seventh appeared quite well 3 months after, an eighth 5 weeks after, and 2 further cases examined 2 years after operation were in good health, though in the urine of one of them a moderate cloud of albumin was present. On reviewing the results of operation, it can be stated definitely that 2 cases were not benefited; one was removed 18 days after operation unimproved, 2 remained well 2 years after operation, and the remaining/

remaining 5 were considered improved during the period of observation following decapsulation. The results of operation, on the whole, would appear to indicate that decapsulation had produced at least amelioration in the condition of most of the patients, though the period of observation in some cases was not sufficient to determine the final result. Campbell (1930) in his review of the larger series of 23 cases states that improvement was not permanent in a number of cases, recurrence of the disease sometimes taking place after dismissal from hospital. Ten of these 23 patients made an apparently complete recovery, the result was unknown in 2, the condition became chronic in 4, and 7 died, 3 of these having failed to recover from operation, 3 having died from nephritis, and one from an unknown cause. The 10 cases where recovery was judged complete had been traced for periods of 6 months to 6.2/3 years after operation. At the end of the respective periods, renal functional tests were performed. Though the children appeared well, the renal efficiency tests again gave very equivocal results, with very low figures in some cases, urea concentration being only one per cent., and pigment excretion 8 per cent. in one instance, and 1.2 per cent. and 25 per cent. respectively, in another. Campbell concludes that certain cases show definite improvement after operation. the improvement being reflected chiefly in the disappearance of/

of oedema, though the ultimate result in some cases of sub-acute nephritis is uninfluenced by the operation of de-capsulation. Many other authors have adopted this operative procedure in the attempt to cure nephritis. Edebohls (1904) was the first to attempt a cure of chronic Bright's disease by this means, the object being to create a new and liberal supply of arterial blood, thus permitting absorption of inflammatory products compressing the glomeruli and tubules, and allowing epithelial regeneration to take place. He describes an autopsy on a patient 4½ months after this operation, where extensive and abundant vascularisation was noted in the new capsule, which thus provided a new and increased supply of blood to the kidney. He considers that improvement in these cases is not due to mere relief of tension, since in chronic Bright's disease the capsules never compress the kidney, which has no tendency to bulge out of it. Harrison (1901), on the other hand, emphasizes the beneficial effects, in some cases of exploratory incision of the kidney, in patients suffering from albuminuria or other renal symptoms. He believes sudden distension of the kidneys subjects them to pressure by their capsules, relief being obtained by simple incision. The modern view, according to Campbell, is that the operation leads not to a cure of nephritis, but to improvement of the oedema, the operation acting in a purely mechanical fashion, allowing escape/

escape of fluid by the operation wound. Various other writers describe the results of decapsulation in recent years, among them Boyd and Beattie (1905), Morse (1917), Hill (1919), and Capon (1926). The first of these writers reports the post-mortem findings in a man with chronic nephritis, dead 4 months after decapsulation. They found a dense new capsule, which was very vascular, and contained vessels apparently anastomosing with those in the kidney cortex, but they believe that such vessels would do no more than compensate for those ruptured at operation, and in addition, formation of the new capsule was accompanied by fibrous prolongation into the kidney substance, thus increasing the interstitial fibrosis. Capon (1926), on examination of a kidney removed 3 months after decapsulation in a child of 6½ years, found no newly-formed capsule, with the exception of thin fibrous strands. The peri-renal fat contained abundant blood vessels, but it could not be shown that these passed into the kidney substance. Morse (1917) reports 2 cases of his own. In the first, a patient with uraemia and complete suppression of urine, death occurred 2 hours after operation: the second, a child of 10 years, had developed nephritis after tonsillitis, with suppression of urine and uraemia. A double decapsulation was done, the kidneys here being enlarged, pale, and bulging through the incision. Recovery ensued in this case. This author also culled/

culled from the literature other 3 cases in children with convulsions and uraemia, where operation was performed for relief of tension. He concludes that operation was the means of saving the lives of the last 4 children mentioned. Hill (1919) believes that operation should not be considered, except in extreme cases where the patient is oedematous and not responding to treatment, or in patients with uraemia and anuria. He reports 8 cases where decapsulation was done, all of severe exudative type, in 3 of which the patient's life was undoubtedly saved. In the fourth the child's life was saved temporarily. In the other 4 cases of acute or chronic nephritis, the operation did no good. Capon (1926) found some temporary improvement in 6 cases, with undoubted benefit in one of these. He regards the operation as worthy of further trial, and believes results would be better if the operation were performed earlier. From a general survey of the reported cases, it would therefore appear that acute nephritis with suppression of the urine is the type of case where most benefit ensues from decapsulation. Morse thinks that no child should be allowed to die without the chance afforded by operation, which, in more chronic cases, may prolong life, with improvement in the general condition, though seldom determining actual cure of the underlying disease.

An/

An alternative to decapsulation is suggested by Salvioli (1930) who advocates X-ray therapy in acute glomerulo-nephritis. So far it has been used, according to this author, only in anuric cases. Salvioli contends that the effects of X-ray therapy are almost similar to those of decapsulation, acting through the sympathetic nervous system, which stimulates diuresis by decreasing vascular spasm. He advocates irradiation in the region of the lower dorsal and upper lumbar vertebrae, and finds that this method of treatment gives good results in the acute stages of nephritis, determining in a great many cases increased diuresis, with sometimes decreased haematuria. Irradiation corrects the state of hypertension of the renal vaso-constrictor system, and the author suggests that X-ray therapy should first be tried in cases where operation is indicated, since surgery itself acts through the sympathetic system.

ACUTE INTERSTITIAL NEPHRITIS.

Since acute interstitial nephritis is one of the less frequently encountered types of renal lesion, this section will be introduced by Councilman's (1898) classical description of the naked-eye appearance of kidneys thus affected. He finds a variable degree of enlargement, but considers that in the most marked cases the appearances cannot be mistaken for anything else except leukaemic infiltration.

The capsules, which are distended, are thin and strip readily, and sometimes separate spontaneously on section of the kidney. The surface is pale-greyish and opaque, mottled irregularly, with hyperaemic points: the stellate vessels are injected, with, at times, punctate haemorrhages around them. In some cases the surface is irregular, due to the projection of small irregular nodules more opaque than the surrounding tissue. The cut surface is greyish and opaque, with scattered small haemorrhages, and the normal markings are obliterated with loss of demarcation between cortex and medulla, and the great increase in size is chiefly cortical. The tissue is soft, lax, friable and very moist. In many cases the changes are most evident at the base of the pyramids where granular opacity of the organ is seen. A very marked degree of microscopic change, however, may be present without producing macroscopic alteration in the appearance of the kidneys. Russell (1929) found acute interstitial nephritis a unilateral lesion in 4 of the 10 cases of this lesion described by her.

In the present series, the acute interstitial type of nephritis is represented by 4 cases, 2 of these showing widespread involvement of the kidneys, while in other 2, similar infiltration was much less extensive, still occupying, however, a large part of the interstitial tissue. Though, in 3 instances, this type of kidney lesion occurred in/

in association with another disease, tuberculosis in one case and congenital syphilis in the other 2, the associated renal pathology of these diseases being discussed later, the acute interstitial cases will be described together. Of the 2 children with a marked renal lesion, one was a female infant 6 months old, with a history of vomiting which began 4 weeks before admission, and was followed in a short time by a discharge from both ears. Two weeks afterwards, small whitish spots were noted in the mouth, affecting particularly the palate, marked palatal ulceration developing later, extensive sloughing of the tissues leading finally to gangrenous pharyngitis. During the course of the illness, the baby became very pale (red cell count 1,900,000, colour index of 0.7). Both kidneys could be palpated. No albumin was found in the urine, which, on microscopic examination, showed red blood cells, and casts of unspecified type. At autopsy, the kidneys were much enlarged, weighing together 155 gms. The capsules stripped with ease, leaving a pale, variegated surface, the seat of small haemorrhages. On section, the substance was soft, with marked mottling of the cortex, while the markings were fairly regular. Enlargement affected the organs as a whole, and not particularly the cortices. In addition to the renal changes described, the pancreas showed at autopsy an unusual abnormality in the form of a globular swelling at the head

of/

of the organ. In addition, early broncho-pneumonic consolidation involved the lower lobes of both lungs, while the left pleural sac contained a large amount of clear, straw-coloured fluid. Both ears contained abundant purulent exudate, films of which showed pneumococci and streptococci. A diffuse sloughing ulcerative condition was present in the pharyngeal tissues.

On histological examination of the kidneys, a striking feature was the presence of interstitial cell infiltrations, more focal in distribution in the cortical, and more diffuse in the medullary regions, sections being over-run by round and mononuclear cells, the latter showing an occasional very large hyperchromatic example. Plasma cells were also present, in addition to relatively scanty polymorphs. In the areas where these cell-infiltrations were very dense, the tubules were undergoing pressure atrophy. Here granular degeneration of the tubular epithelium was noted, and in the lumina of some tubules granular débris was present. Some of these structures were dilated and contained hyaline casts, a few showed red blood corpuscles, while the presence of leucocytes within the tubules was not a noteworthy feature, though, on careful search, a few cells appeared to be in the act of penetrating the walls from without. The glomeruli were well preserved and could be regarded as normal. On microscopic examination of the pancreas,/

pancreas, cellular infiltration was found as in the kidney, some atrophy of the pancreatic tissue resulting from pressure by the infiltrating cells. The second patient, a male infant aged 11 months, was admitted in March 1933, with a history of having had whooping cough in the previous December. Six weeks before entering hospital he developed an attack of pneumonia lasting 3 weeks, accompanied by crops of cervical abscesses. Swelling of the abdomen was noted 2 days before admission, and on examination, the liver and spleen were enlarged, and glandular masses were detected in the abdomen. The child was anaemic, the red cells numbering 2,730,000 per c.mm., the leucocytes 4,900, while the haemoglobin was reduced to 30 per cent. The Wassermann reaction was negative. No blood or albumin was found in the urine, the sediment containing urates only. The patient died 10 days after admission to Hospital. At autopsy, the kidneys were greatly swollen and thickened, being almost globular in shape. The capsules were thin and stripped readily, leaving a smooth surface. On section the cut surface was of a uniform pale-pinkish tint, while the markings, though fairly normal, were blurred and blotted out by what appeared to be a diffuse cellular infiltration. Enlargement affected all parts of the kidney. The appearances here agree closely with Councilman's description. The liver was the seat of a fine regular cirrhosis. The bowel showed

multiple/

multiple tuberculous ulcers, and the mesenteric glands were greatly enlarged. A miliary spread of tuberculosis was noted, but the brain was free from any evidence of tuberculous infection. On histological examination, the glomeruli were approximately normal. The tubules, some of which were slightly dilatated, showed degenerative changes, with flattening of the epithelium at places, though elsewhere the lining cells were swollen with granular protoplasmic débris within the lumina of the tubules. Some of the latter contained polymorphs and lymphocytes in small numbers, while occasionally a tubule was distended by a plug of these cells within its lumen. An interesting feature of these sections was the presence of active cell regeneration with abundant mitotic figures, particularly at the edges of the foci of cellular infiltration which overran the interstitial tissue, forming large collections chiefly in the cortex, the site of predilection being the superficial cortex, where definite cell foci were present immediately under the capsule. The cells consisted of lymphocytes, plasma cells, and large mononuclears, with very abundant polymorphs. In the areas where cellular infiltration was most marked, the normal renal architecture was quite lost. The leucocytes were not compactly massed together as in abscess formation, but were diffusely scattered throughout large areas. The naked-eye appearances were also suggestive rather of a diffuse infiltration than of a localised acute inflammatory process,/

process, generally surrounded by a zone of congestion which was entirely lacking here. No tubercles were noted in the kidneys, either on macro- or microscopic examination. No fat was found in frozen sections. Of the 2 cases associated with congenital syphilis, one occurred in a female infant of one month, and the other also in a female infant aged 4 months. The first patient had, on admission, oedema of the lower limbs, which had lasted 3 days, while snuffles, rhinitis and a vaginal discharge had been present since birth. Anti-specific treatment, sometimes blamed as the cause of renal damage in such cases, can be excluded here, as the single injection of neokharsivan was given only a few hours before the death of the child. At autopsy, the lungs were pale in colour and increased in consistence, apparently as the result of new connective tissue formation in the substance of these organs. The liver was hard and "rubbery," and the markings were obscured by overgrowth of fibrous tissue. The spleen was also enlarged and firm. No syphilitic bone disease was evident. In this case, the naked-eye appearance of the kidneys was not mentioned. The second syphilitic patient had a history of snuffles, with a nasal discharge since birth. A few days ante-mortem, a septic condition developed in the back of each hand. On admission, the nostrils were excoriated and eczema of the eyebrows was present, while the liver and spleen were enlarged./

enlarged. At autopsy, the kidneys appeared acutely congested with many petechial haemorrhages into the renal substance. The liver was enlarged and firm in texture, though on histological examination there was no evidence of interstitial fibrosis. The spleen was swollen, firm and congested. No evidence of syphilitic osteo-chondritis was detected in the femur examined. Histologically, these 2 cases are closely similar, so will be discussed together.

Each showed a mild acute interstitial type of lesion often described as characteristic of syphilitic nephritis in infants. In both patients foci of cellular infiltration were seen diffusely scattered throughout the cortices, and in one of these a cellular "mantle" surrounded some of the cortical vessels. The cells comprised chiefly lymphocytes and large mononuclears, many of the latter being very hyperchromatic. In addition, small numbers of polymorphs and a few eosinophils were found, these cells being most abundant in the case complicated by cellulitis of the hands. The glomeruli and tubules were essentially normal in appearance in one instance. In the other child, an infant of one month, an interesting feature was the appearance of a slight delay in development, since definite traces of a neogenic zone could still be seen immediately under the capsule. This aspect of the case will be dealt with more fully in the section on congenital syphilis.

The/

The first 2 cases (those of marked interstitial involvement) taken in conjunction are of interest as exemplifying two different types of acute interstitial nephritis as described in the literature. Some authors find polymorphs scanty as in the first case, while others consider this type of lesion closely related to an acute haematogenous infection, and the second case would appear to belong to this class, since polymorphs were abundant here, though diffuse and not focal in arrangement. Gray (1928) regards acute interstitial nephritis as a condition intermittent between non-suppurative and suppurative nephritis, some multiplication of organisms taking place in the kidney, though not to an extent sufficiently unrestrained to give a picture of frankly suppurative nephritis. Russell (1929) considers acute interstitial nephritis a descending haematogenous infection of exceptionally mild intensity, and shows in a series of such cases that, as the condition becomes more chronic, the character of the lesion becomes less and less purulent, mononuclear cells coming to predominate over polymorphs. Shaw Dunn (1924) also believes the condition not very far removed from that of pyogenic abscess formation, though non-granular leucocytes predominate in his opinion; while Kaufmann(1929) finds lymphocytes generally most abundant, though leucocytes may occasionally be numerous. With regard to the etiology of this type of renal/

renal lesion, most observers agree that it commonly occurs in association with acute streptococcal sepsis, particularly after scarlatina, severe angina, and sometimes also after diphtheria. Councilman (1898) found a varying amount of renal cellular infiltration in 24 of 103 cases of pure diphtheria, in 5 of 50 cases of pure scarlet fever, in 5 of 23 mixed scarlet fever and diphtheria, and in 2 of 5 cases of mixed diphtheria and measles. He also found a similar type of lesion in association with lobar pneumonia, pericarditis, and cerebro-spinal meningitis. This author investigated bacteriologically the kidneys in 42 cases of acute interstitial nephritis, occurring in the course of diphtheria, scarlet fever, etc. Though he isolated bacteria in some cases, similar cultures were obtained in these diseases from kidneys where interstitial nephritis was absent. Volhard and Fahr record a case of acute interstitial nephritis associated with tuberculosis, but consider the possibility of a streptococcal mixed infection here. These authors also saw a mild type of this renal lesion in measles, and once in a case of typhoid fever. They also mention pneumococcal infections as sometimes of etiological importance in its causation. Sutherland and Thomson Walker (1903) report 2 cases of acute interstitial nephritis in congenital syphilitics of 8 months and 16 months of age respectively. In the older child, one kidney was more severely affected than the other./

other. In the younger infant, a septic sore throat with much sloughing of the pharyngeal tissue complicated the case. The acute interstitial lesion complicating scarlet fever occurs early in the course of the disease, while the more usual glomerular type of renal involvement does not appear as a rule before the third week. Some writers regard acute glomerulo-nephritis and acute interstitial nephritis as two distinct processes. Reichel (1905) finds the acute interstitial focal type present in the early stages of scarlet fever, when it may be widespread in distribution without causing definite renal symptoms, though when of very severe degree it can lead to death in uraemia. It may also develop, according to this author, after the third week and need not be accompanied by glomerulo-nephritis. Friedländer (1883) describes three forms of scarlatinal nephritis: (1) initial catarrhal nephritis, (2) the interstitial septic type, and (3) glomerulo-nephritis (post-scarlatinosa). He considers that there is no evidence of a genetic connection between the three types. The septic interstitial form is rare, Friedländer having seen it only once in 229 cases of scarlet fever, and he regards it as associated particularly with very severe phlegmonous ulceration of the throat in scarlatina, though also occurring in severe, non-scarlatinal, septic throat lesions. He therefore believes it is only an indirect result of scarlet fever.

The/

The urine, he states, may remain normal throughout the course of this type of renal disease, while oedema is absent in such cases.

Councilman (1898) gives a minute description of the histological characters of this type of nephritis. In his experience there are 3 sites of predilection for cell infiltration: (1) the boundary zone of the pyramids, (2) the cortex, immediately under the capsule, and (3) the periglomerular tissue. The cells, according to his description, consist almost universally of lymphocytes, sometimes of large size, with 2 or more nuclei, and he believes that these are derived from the vessels by emigration. In many cases he found cells with a knob of protoplasm, as a result of fixation during amoeboid movement. Some writers also describe diapedesis of red corpuscles along with leucocytes. He even saw cells, half inside and half outside the vessels, in the process of emigration from the latter. Schridde (1913) agrees with Councilman that these cells are derived purely from the vessels, the first appearance of the disease being the heaping up of lymphocytes in groups around the capillaries, and also the arterioles in the medulla, the appearance suggesting lymphatic leukaemia, since lymphocytes often fill the vessels like a solid plug. A condition similar to this was seen in one of the present author's cases, where in a patient with pneumonia and a large septic burn, a glomerulo-

tubular/

tubular nephritis showed commencing cellular infiltration of the interstitial tissue, the vessels being packed with lymphocytes and appearing as dark streaks from this cause. In Schridde's next stage the vessels are less densely packed, and small infiltrations appear in the renal tissue. Lymphocytes are seen in the process of wandering through the capillary walls, and some cells penetrate into the lumina of the tubules. Later, plasma cells predominate over the original lymphocytes, and may be practically the only type of cell present unless for individual eosinophils and basophils. Finally, connective tissue cells appear to replace the special inflammatory cells, thus heralding the stage of scarring. Schridde (1913) believes that toxins, and probably streptococcal toxins, are eliminated by the glomeruli and concentrated within the lumina of the tubules, exerting a cyto-tactic effect, stimulating cell emigration from the vessels, and into the tubules. Later, destruction of tubular epithelium allows diffusion of toxin into the interstitial tissue, determining more widespread cell infiltration. Schridde has never seen marked participation of polymorphs in these cell infiltrations. Many authors express doubt regarding the end result of acute interstitial nephritis, but it is suggested by some, and Schridde's experience, since he saw connective tissue proliferation, would favour this view, that ultimately scarring may take place,/

place, resulting in one form of contracted kidney. Sawyer (1906) believes that a fibrosed kidney may have commenced as an acute interstitial nephritis, and Aschoff inclines to favour the view that some contracted kidneys may represent a later stage of this type of lesion.

CHRONIC NEPHRITIS.

Having dealt with acute nephritis, the sub-acute and chronic forms of the disease will now be discussed. These are represented by 9 cases in the present series, of which two were sub-acute and seven chronic, three of the latter being at an early chronic stage. Other 2 cases occurred in children who each possessed only one kidney, while chronic nephritis in the last member of this group affected kidneys the seat of extreme bilateral hypoplasia.

The Naked-eye Appearance of the Kidneys in Sub-acute and Chronic Nephritis.

The kidneys of the 2 children with a sub-acute lesion, aged 6 months and 6½ years respectively, were swollen and mottled, from intermingled fatty change and congestion. The cortices were deep, of pale-yellowish colour, with fairly regular markings. In one of these cases the capsules were very slightly adherent. Of the patients with a single kidney, one was a male child, aged 18 months. The left kidney and ureter were absent, and the right kidney was much larger than normal, and the seat of hydronephrosis, with a very wide ureter, though no valvular or other obstructive lesion could be found to account for this. In the other patient, a girl of 13.1/3 years, the right kidney was missing, though the right suprarenal was in the normal position. The left kidney

was decidedly hydronephrotic, only a thin rim of renal tissue remaining. The kidney and pelvis showed no naked-eye evidence of an inflammatory lesion. The left ureter was dilated, but no apparent cause for this was discovered. A small ureter, ending blindly at the pelvic brim, was found on the right side. These 2 cases along with that of renal hypoplasia, where both kidneys were only the size of haricot beans, will be discussed fully in the section dealing with congenital renal anomalies. In the remaining 4 children, the chronic lesion was at an early stage in 3 and more advanced in the 4th. The naked-eye appearances of the kidneys in these 4 children did not at all correspond to the lesion found on microscopic examination, an acute type of disease having been diagnosed even in the cases where histologically marked proliferative changes and even dense fibrosis were found. The organs in three of the four cases were swollen, oedematous, and irregularly mottled on section, and the capsules were only very slightly adherent, and, on stripping, left a surface free from any noteworthy irregularity, the glomeruli in one appearing as transparent points. In the fourth case, that of an infant aged 4 months, the kidneys were small and the surface irregularity was apparently due to persistent foetal lobulation very commonly seen in infants. The capsules in this case were slightly adherent, and the kidney substance was deeply congested, the subcapsular stellate veins being injected./

injected. On section, the markings were considerably distorted, with ill-marked distinction between cortex and medulla resulting from irregular congestion affecting both organs.

Microscopically, the 2 sub-acute cases showed enlargement of the glomeruli, some being still in the acute inflammatory stage, though, in the majority, the capsule of Bowman showed very definite crescent-formation along with fibrosis of the tufts, and adhesions between capsules and tufts. Relatively few glomeruli were completely fibrosed. The most striking feature in the tubules was haemorrhage, many of the convoluted tubules being filled with red blood cells, the latter indicating the presence in the glomeruli of a still active lesion, Addis and Oliver (1931). The secreting epithelium showed very marked cloudy swelling in one case, while in the other many cells were vacuolated, apparently from the dissolving out of fatty globules, while granular débris and many hyaline casts were found in the lumina, in addition to the red cells, in both cases. Some tubules were dilated, with flattened epithelium. The interstitial tissue in both was only slightly increased, with early fibroblastic peri-glomerular proliferation, and scanty foci of round-cell infiltration in the cortex. No significant changes were apparent in the vessels. Frozen sections were stained for fat in one instance, when many convoluted tubules were found loaded with fat droplets, while/

while some cells had ruptured, setting free their fatty contents in the lumina of the tubules. Some of the ascending loops of Henle also contained fat, while small fat globules were seen in the epithelium of the collecting tubules. A fair amount of the fat was doubly refractile. The four chronic cases showed varying degrees of proliferation in the glomeruli and interstitial tissue. In all 4, practically all the glomeruli were diseased, some being still in the acute inflammatory stage, the presence in each instance of red blood cells in groups of convoluted tubules confirming this fact. Glomerular fibrosis was generally of extra-capillary type, with adhesions of varying degree between tuft and capsule. Peri-glomerular fibrosis was well-marked and some glomeruli in all sections were completely hyalinised, though only in one of the 4 cases were glomeruli the seat of such extensive damage found in large numbers. In this last case, proliferative interstitial changes were also marked, though the regular distribution of fibrosis and the absence of dense scar formation with contraction would explain the lack of nodularity on naked-eye examination, the kidneys in this case being still swollen and smooth at autopsy. Cellular infiltration was evident in this case, and was both focal and diffuse in arrangement. The tubules in these 4 chronic cases showed varying degrees of distortion, many being greatly dilated. The/

The even, diffuse distribution of the interstitial fibrous tissue overgrowth in all did not, however, separate large groups of tubules with the production of "islands" of tubular hyperplasia, but these structures tended rather to be isolated in small foci. Some tubules were collapsed, shrunken, and atrophied, though the epithelium varied from a flat to a high cubical, apparently hyperplastic type. One case in particular showed marked tubular regeneration, with irregular epithelial proliferation, the hyperchromatic cells often being heaped up at one side of the tubule. Though the nuclei of such regenerating cells were large and irregular, mitotic figures were rare. The altered tubules enclosed various abnormal contents. Fresh red blood corpuscles, as stated, were fairly abundant, or casts derived from these. Hyaline, granular and colloid casts in varying numbers were all present in addition, as well as swollen desquamated epithelial cells. In no case were the blood vessels, large or small, the seat of any noteworthy pathological change. At autopsy, various acute inflammatory complications were found in the sub-acute and chronic cases. One of the 2 patients with a sub-acute nephritis died of streptococcal peritonitis, this case being further complicated by severe purpura. In the other, nephritis was the only lesion found at autopsy. Of the four chronic cases, one showed broncho-pneumonic consolidation with foci of suppuration,/

suppuration, another, early broncho-pneumonia, a third, gastro-enteritis, while the fourth patient died in a convulsion, the brain in this case showing marked oedema and congestion. With regard to oedema, in one of the sub-acute cases there was oedema of the sub-cutaneous tissues and of the liver; in the other, oedema of the feet and ankles only; while more or less extensive dropsy involved the sub-cutaneous tissues and the various serous sacs in 3 of the 4 chronic cases under discussion. The remaining patient showed no evidence of dropsy. The brain was examined in this series only in 2 of the patients with an early chronic nephritis. In both instances it was oedematous (one case mentioned above). The heart was hypertrophied in 2 of the 4 chronic cases, and was normal in the 2 patients with a sub-acute lesion.

Clinical Findings in Sub-acute and Chronic Nephritis.

In some of these children there was nothing in the history or on clinical examination to suggest the presence of nephritis. Thus the patient with the most chronic type of renal lesion (aged 6 months) was admitted with cervical adenitis and a discharging sinus in the right side of the neck. Sinus forceps were inserted, when a second deep abscess was opened. The child appeared well for about 12 hours thereafter, but about mid-night he became very restless./

restless. Tracheotomy was performed at 3 a.m. and the breathing was relieved, but the child died 12 hours later. (Broncho-pneumonia was the only lesion found post-mortem in addition to the nephritis in this case.) The urine was not examined. Of the other 3 patients with a chronic nephritis, one, a male infant of 4 months, was healthy until about 4 weeks prior to admission when screaming attacks began, followed two weeks later by a swelling round the eyes, and two days before admission by swelling of the neck. The urine contained abundant albumin and blood, while granular and cellular casts, along with red and white blood cells were found on microscopic examination. In another patient, a girl aged 7 years, there was a history of angina seven weeks before admission, followed 2 weeks later by puffiness of the face and oliguria, the urine being red in colour. The whole body was oedematous on admission, and the urine constantly contained abundant albumin and blood, specimens being examined daily for a month. Blood, granular, epithelial and hyaline casts were also found microscopically. The urine was cultured on two occasions, the first specimen yielding a mixed growth of coliform bacilli, staphylococcus and streptococcus, and the second, a coliform growth only. The remaining patient, aged 1 year and 11 months, was dead on admission, and no definite history was obtained (male child).

Of the 2 sub-acute cases, one occurred in a male infant/

infant of 6 months, who was healthy till the age of 6 weeks, when he had chicken-pox, after which the stools became green. His feet began to swell and oedema spread to involve the legs and abdomen, and oliguria was noted during this time. Blood and albumin were found in the urine on admission. The oedema decreased in hospital, but diarrhoea persisted and the patient gradually became weaker, death resulting about 6 weeks from the time of onset of nephritic symptoms. The second patient with a sub-acute lesion was a girl aged 6½ years, who developed pain and swelling of the feet and ankles 3 weeks before admission, purpuric spots appearing in the skin shortly after, accompanied by haemorrhages from the stomach, bowel and bladder. The urine thus contained blood along with albumin.

Etiology of Sub-acute and Chronic Nephritis.

In this group, 2 factors must be taken into account: (1) the chronic proliferative lesion, (2) the acute element present, as indicated by the presence of blood in the renal tubules. (Of the total 9 patients in this group, only the 2 sub-acute and 4 chronic cases are discussed here, the 3 with/severe anatomical renal abnormality being dealt with elsewhere).

In the first sub-acute case, the onset of nephritis probably dated from the attack of chicken-pox. In many acute/

acute fevers where nephritis is focal in distribution, the renal disease is silent clinically until an acute exacerbation directs attention to the kidneys. The gastro-enteritis possibly accounted for the acute element in this case. The second patient with sub-acute nephritis had pain and swelling of the feet and ankles three weeks before death, followed by purpura. The crescent formation which involved a large proportion of the glomerular capsules was suggestive of an older lesion, and the purpura was possibly responsible for the acute exacerbation, since purpura of rheumatic type is sometimes associated with acute nephritis.

Of the 4 chronic nephritic cases the first, an infant aged 4 months, was apparently healthy until about one month ante-mortem, when he developed the symptoms of acute nephritis, and in such a young infant the disease might possibly progress to a proliferative stage in a very much shorter space of time than in older persons, where regenerative processes are slow, and where there is also a greater resistance to degeneration. Democh (1902) considers that three weeks in a young infant would suffice to produce a contracted kidney. The second patient, aged 7 years, gave a history of acute tonsillitis 11 weeks before death, puffiness of the face developing 2 weeks later. Here, on histological examination of the kidneys, much haemorrhage into the tubules was found, but well-marked proliferative/

proliferative changes were also present in the interstitial tissue and in the glomeruli, some of these being completely hyalinised. As this patient had unhealthy cryptic tonsils and many carious teeth, the possibility remains that a previous tonsillar infection had inaugurated the nephritis in a mild form without obvious clinical symptoms.

In the third child, who died after tracheotomy within 24 hours of admission, the history was inadequate, and there was nothing to indicate whether the cervical adenitis present was a chronic focus of suppuration which had originally damaged the kidneys, or if this was a recent complication merely causing exacerbation of a pre-existing renal lesion. The last patient in this group was dead on admission, and no history was obtained.

CHRONIC NEPHRITIS.

Discussion.

From a survey of the literature, chronic nephritis is distinctly less common in children than in adults. Brüning and Schwalbe consider it rare in the former, when it is generally the result of acute nephritis, though more rarely spontaneous. These authors are of the opinion that chronic nephritis in children differs little from the same form of the disease in adults. In the opinion of Blackfan and Hamilton (1925) the chief distinction between adult and juvenile nephritis is the fact that in the former chronic forms predominate, while acute forms are almost exclusively seen in paediatric clinics. Various writers have traced cases of acute nephritis in children for months or years, after the acute attack to find the percentage terminating in chronic disease. James (1921) investigated a series of 67 children with acute nephritis between the ages of 2 and 12 years, and found that 9 or 13.3 per cent. of these developed chronic nephritis, though in only two cases was the disease considered severe. He concludes that the great majority of children recover completely from acute nephritis, since a number of those re-examined by him at varying intervals after the original attack had passed through acute infectious diseases with no sign of renal involvement, and he agrees with Hill (1919) and Guild (1931) that if recovery from an acute attack of nephritis is complete, the/

the patient shows no more tendency to subsequent renal involvement than children who have never had nephritis. In this connection Gray's (1933) findings may be of interest. He examined the kidneys of 3 relatively young individuals, who had passed through an attack of acute nephritis with recovery a short time before death. One was a child who recovered from acute nephritis, about 2 months prior to death from rheumatic carditis. Another, a young man who died as the result of an accident 3 months after recovery from acute nephritis. In both cases the nephritic process was of approximately 3 weeks' duration. No evidence of renal disease was found in either of these cases. The third patient was a man aged 32 years, who died of pulmonary embolism after operation for hernia when apparently in perfect health, the urine showing no abnormality. A year previously he had had an attack of nephritis lasting 2 months. The kidneys in this case were of normal size, and the capsules were not thickened, but were slightly adherent to a very slightly granular surface. The cut surface showed no evidence of abnormality. Histological examination revealed a mild degree of post-nephritic change, consisting of hyalinisation of glomeruli, with crescent formation, along with tubular atrophy in small scattered foci. Of the 3 cases, therefore, only in the patient where nephritis had lasted for two months was there any permanent structural alteration in the kidneys. Guild(1931) gives acute nephritis a good prognosis/

prognosis in children, the better the younger the patient, and finds that when the urine fails to clear completely albumin may be present for years without impairment of the general health. MacAdam (1933) quotes the opinion of Evans, that residual albumin from a previous renal lesion may have no more significance than the scar of a perfectly-healed skin lesion. Wyllie and Moncrieff, on the other hand, emphasize the importance in post-nephritic patients of even a faint trace of albumin associated with excess of cells in the centrifuged sediment, which they consider definitely of pathological significance. Lyttle and Rosenberg (1929) followed 58 members of a series of 99 children with acute nephritis for periods varying from 1 to 7 years, and found a chronic lesion in 9 of these (15.5 per cent.), chronicity resulting as often from a mild as from a severe initial lesion. They conclude that probably some persistent or recurrent focus of infection prevents the renal inflammatory condition from healing. Osman (1925) finds a higher percentage of persistent impairment of renal function than most authors - 35.7 per cent. in a series of 56 juvenile cases. On comparing the prognosis of nephritis in children with that in adults, Hume and Nattras's (1927) figures are of interest. These writers, investigating the outcome of 281 cases of acute war nephritis, found no definite evidence of renal disease in 45.5 per cent., thus leaving 54.5 per cent. with evidence of chronic nephritis, advanced in 9.5 per/

per cent. and gradually progressive in 45 per cent. These figures are much higher than those in the statistics just given for children.

The incidence of chronic nephritis after an acute attack developing in the course of scarlet fever has been widely studied in various countries. Rosenfeld and Rechtenstamn (1912) re-investigated at intervals between 9 months and 10 years, 93 children of whom 52 had albuminuria on dismissal. No single case showed a severe degree of nephritis, though 10 children had albuminuria, accompanied in 7 instances by cells in the sediment, and in one case by high blood pressure. The severity of the original disease as deduced from uraemic symptoms had no influence on the development of a chronic renal lesion. Sörensen (1891) agrees that the great proportion of cases of scarlatinal nephritis end in cure. In his opinion the severity of the renal lesion can be correlated with the severity of the throat complications in scarlet fever. According to Hansborg (1924) also, the general view that scarlet fever often leads to contracted kidneys is incorrect, since in his investigation of 284 children who had suffered from scarlatinal nephritis 1 to 10 years previously 259 were normal. One had chronic albuminuria lasting for 5 years after acute nephritis, with no other signs of renal involvement, and in only one patient had chronic nephritis developed, though even this case the author does not regard as/

as a result of scarlatinal nephritis. Twenty-three patients in this series had orthostatic albuminuria, but Hansborg finds that scarlet fever is not more frequent in the history of patients with this type of albuminuria than in normal persons, so believes that orthostatic albuminuria in these patients cannot be attributed to scarlatina.

In the haemorrhagic type of nephritis so common in childhood there are some differences of opinion as to the final result. While all authors agree that this type is rarely fatal, complete cure, according to Paterson and Wyllie (1926), takes place in less than half of the cases, (44.4 per cent.), and Hill (1909) agrees that ultimate impairment of renal function is more frequent than the mildness of the original disease would lead one to expect, though Wyllie and Moncrieff (1926) find that, as a rule, the primary attack heals without sequelae. Failure of the renal lesion to clear appears to be due in some cases to the persistence of some focus of infection. Lyttle and Rosenberg (1929) and Alport (1932) believe that residual foci may be found in the tonsils, antra, sinuses, teeth, or even in the bowel, though the last structure is not often suggested as a site of focal sepsis in nephritis, and Guild (1931) finds that, though a number of her patients recovered entirely in spite of neglect of foci of infection, some patients with persisting urinary abnormalities showed such foci. Addis and Oliver (1931), on the other hand, believe/

believe that the continuance over years or decades of a slow disintegration of the renal architecture may be the result of structural disorganisation produced in the initial stage of the disease, and that it would not be necessary to hypothecate the continued action of any toxin. The endotoxin of scarlet fever might act only for a day or an hour, in the opinion of these authors, and yet its effect on the kidney might not reach full fruition until the death of the patient in uraemia 20 or 30 years later. Similarly, Volhard and Fahr trace a typical case of secondary contracted kidney to an attack of erysipelas 22 years previously. Bell and Hartzell (1922) again, consider that the progressive nature of the lesion is due to repeated acute exacerbations of glomerulo-nephritis. Though evidence for associated streptococcal infection is very convincing in acute cases, fairly good in sub-acute, and not at all in the chronic group, it does not appear to these authors that such data exclude a primary infection, since clinical histories are often unsatisfactory, and patients may have forgotten a mild infection years before. Emerson (1921) distinguishes in chronic renal disease two components; the underlying permanent element, and the superimposed acute exacerbation. He believes that chronic nephritis is not a progressive disease varying in severity at different periods, but rather a succession of slight distinct acute diseases which are distributed over years, each adding a little to the permanent/

permanent damage of the kidney as a whole. He believes that the patient does not suffer from one attack of nephritis, but from a thousand and one. Mitchell and Guest (1931) agree that bacterial infections, especially of streptococcal nature, may cause chronic as well as acute nephritis. These authors stress the importance of hereditary and familial predisposition to nephritis. Such a factor is well recognised in both the acute and chronic type of lesion, and to it may be attributed some of the juvenile cases where chronic nephritis has an insidious onset, with no demonstrable general or focal infection as a possible source. In adults, the same explanation may serve but one must also take into account, as Bell and Hartzell suggest, the fact that some mild infection, though forgotten by the patient, may have proved the starting-point of the disease, or a focal type of lesion resulting from some infectious fever and clinically silent, may have led to a slow insidious type of contraction, the "nephritis rèpens" of Russell (1929). That chronic nephritis may be found in young children and even in infants has been amply demonstrated in the literature, while in some cases it would appear to date even from intra-uterine existence. Thus, Carpenter (1905) describes a case of interstitial nephritis with cirrhosis of the suprarenal glands in an infant aged 5 weeks, who was healthy for 10 days after birth, but became very oedematous thereafter. At post-mortem, chronic nephritic changes were found/

found in the renal interstitial tissue, while the glomeruli were atrophied and the small arteries thickened. The supra-renal glands were also the seat of chronic inflammatory change. Hellendall (1897) reports death from chronic nephritis in two children, one aged 2 years and the other 6 months. The mother herself suffered from chronic nephritis, which, in the author's view, began before the birth of the first of the two children mentioned here, though she had scarlet fever in childhood and had always been sickly. Hellendall believes that nephritis in the case of these 2 children began in foetal life, since both the inheritance of the disease and the disposition to acquire it can be transmitted to the offspring. In this article another feature of interest is the fact that relatives of both the parents of these two children suffered from nephritis. Syphilis could be excluded as an etiological factor in the case of these infants. Democh (1902) reports another classical case in an infant healthy at birth, but who died with signs of renal disease at the age of 2 months. This case, however, is regarded by various authors as possibly of the nature of a pyelonephritis with scarring, since the lesion was much more pronounced on the right than on the left side. Frölich (1906) records other 2 cases of chronic familial congenital nephritis in infancy, where there was no history of nephritis in the mother during pregnancy. The first of these two children was quite healthy after birth, but failed to thrive and at the age/

age of 4½ months, albumin and casts were present in the urine, and persisted until the death of the child at 11 months. The second patient, also normal at birth, began to sicken at the age of 14 days, and albumin and casts appeared in the urine and persisted until the death of the patient at the age of 15 months. Autopsy showed typical contracted kidneys. These cases appear to resemble closely a series more recently described by various writers in this country, Morley Fletcher, Barber, Paterson, Miller and Parsons, and Naish. Morley Fletcher (1910) reports the case of a child with polyuria, the result of chronic renal disease, who had not grown since the first year of life, and who suffered from polyuria and polydipsia. Genu valgum developed at 5 years of age. The case was regarded as one of infantilism associated with, or due to, chronic renal disease, dating from intrauterine existence. Miller and Parsons (1912), and Naish (1912) describe other similar cases, in some of which polydipsia and polyuria had been present since birth, with impairment of growth since infancy. Congenital syphilis could be excluded as the etiological factor. Paterson (1921) reports another similar case in a child born with abnormality of the hands and feet from twisting of the wrists and ankles. Barber (1926) published a collected series of 17 cases. All these patients were dwarfed in stature, - the height at puberty being generally about 10 inches less than the average. Only three of these 17 children died without/

without bony deformities. Autopsy in 8 revealed small kidneys with pure chronic interstitial nephritis. On microscopic examination, the smaller arterioles showed some thickening, but clinically there were no obvious arterial changes, and in only one instance was the blood pressure raised. Bony deformities in the other 14 were generally of the nature of a genu valgum, though the wrist- and ankle-joints were also affected in some. The earliest age at which some bony deformity was noted in this group was 7 years, the usual age of onset being between the ages of 11 and 14 years. Blood urea was high in all these patients, reaching 300 m.g. per cent. The first stage of this disease is seen in young children who fail to develop, suffer from thirst and polyuria, the condition being insidious and resembling diabetes. Later, bony abnormalities develop towards puberty, the children being typical renal dwarfs with late rickets. Three children died at the age of 14, 15 and 22 years respectively, without bony deformities, though symptoms of interstitial nephritis had been observed for several years. Death in the great majority of such cases, in the author's experience, takes place before the end of the second decade. Parsons (1927) from a study of the bone changes concludes that they are of true rachitic type, and that the primary cause is the inability of the kidneys to excrete phosphorus, the blood calcium being kept at a comparatively high level by mobilisation of calcium, the latter being mobilised/

mobilised from the bones to prevent the onset of tetany, the bone deformities associated with renal infantilism being those of true low-calcium rickets. The blood shows marked lipaemia, nitrogen and phosphorus retention, and acidosis is also a feature of such cases, indicating failure of the diseased kidneys to excrete acid end-products of metabolism.

Another type of chronic renal disease of rare occurrence in childhood is that resulting from arterial disease, primary or genuine contracted kidney according to the older nomenclature, but now generally known as malignant nephrosclerosis. Cases of this type have been reported among others by Glaser (1918), by Schwartz (1924), by Ask-Upmark (1929), and by Gray (1933). Glaser's case concerned a female child of 10 years, whose mother died of renal disease during childbirth, and whose sister died at 2½ also from nephritis. The patient herself was healthy during the first year of life, but at 15 months polyuria and polydipsia appeared, with a trace of albumin in the urine. The child was in a state of mental deficiency amounting to idiocy. At 10 years of age she had hard arteries, a systolic blood pressure of 160, and hypertrophy of the left ventricle, with accentuation of the second aortic sound, in addition to albuminuric retinitis. The Wasserman reaction was negative. Diphtheria was the immediate cause of death. At autopsy, both kidneys were small, with a granular surface, and primary contracted kidney was diagnosed./

diagnosed. In a case of Heubner's quoted by Glaser, an exactly similar type of renal lesion occurred in a mentally deficient child. The latter believes that this condition is probably due to hypoplasia of the renal vessels, and that the mental condition of the patient might also be associated with under-development of the vascular system. Ask-Upmark's (1929) article also deals with malignant nephrosclerosis. Of his 8 cases, 6 occurred in the second decade, the two youngest both being about 12 years old at the time of death. A feature in this group was the association of unilateral hypoplasia with deformity of one or both kidneys, which showed a peculiar abnormality in the form of a long narrow process reaching from the pelvis to the superficial cortex, where an indentation of the surface marked the end of this elongated calyx. A sure criterion of primary hypoplasia, according to this author, is reduction in the number of renal elements, one of the kidneys in his series having only 2 pyramids. The arteries in these patients were markedly abnormal, with splitting and hyperplasia of the elastic lamina and increase in the interstitial tissue. He concludes that this type of kidney, with renal hypoplasia and deficiency in renal elements, is often affected in youth by disease processes running the course characteristic of malignant nephrosclerosis, and that the more pronounced the malformation the greater the predisposition to renal disease. This view is supported by other investigators who find this true/

true also in the case of a solitary kidney. Thus Pepper and Lucke (1921) report a case of chronic glomerulo-nephritis in a single kidney with death at the age of 14, following scarlet fever 7 years previously, resulting in chronic ill-health. Anders (1910), on collecting the statistics of various authors, concludes that more deaths are due to kidney disease among subjects with a congenital single kidney than among normal individuals, and that either acute or chronic nephritis gives a worse prognosis where renal agenesis exists that where both kidneys are normally developed. According to this author 46.5 per cent. of all single kidneys show morbid changes, and 42.3 per cent. some form of chronic nephritis, while Rolleston (1916) considersdystopic kidneys peculiarly liable to disease, especially if the misplaced organ be single. The explanation generally given is that such organs cannot react to any excessive strain, and this is supported by the experiments of Bell and Hartzell (1922), who found that removal of three-quarters of the renal tissue produces renal insufficiency, the kidney remnant undergoing degeneration apparently as a result of excessive functional strain. Developmental renal abnormalities favour not only the development of nephritis, but render such an organ prone to other infections. Thus, Browning et al (1933) state that in chronic urinary carriers of B. Typhosus, where the bacilli are restricted to the urine from one ureter, a unilateral developmental abnormality may be/

be the cause determining localisation of the bacilli to one kidney. Schwartz (1924) describes 3 cases of malignant nephrosclerotic type, the first in a male child of 3½ years, with a complaint of sharp epigastric pain and headaches. The skin was dry and wrinkled, and the temporal arteries were plainly visible. The systolic blood pressure was 250, and the diastolic 195. Retinitis was present with narrow arteries, and also old and fresh haemorrhages. The urine showed a trace of albumin and a few red and white cells. Haemorrhage from the bowel ushered in the fatal termination. The second case concerned a female child of 11½ years, in whose family there was no history of renal disease. The systolic pressure here varied between 180 and 240, and albuminuric retinitis was present. During the last week of life the child passed a clot of blood per rectum, and purpura appeared. At autopsy the left ventricle was immensely hypertrophied, with patches of atheroma on the aorta, and nodules at the orifices of the intercostal arteries, with irregular thickening of the systemic vessels. The right kidney here showed congenital hypoplasia, with dense fibrosis surrounding the glomeruli and atrophic tubules, and the thickening of the arteries which showed enormous hyaline swelling of the intima, with narrowing of the lumina. Ulceration of the ileum accounted for the intestinal haemorrhage in this case. A third female child was also 11½ years old, with no family history of nephritis, when swelling appeared/

appeared round her eyes and shortly thereafter she had a sudden convulsive seizure, followed by coma. The systolic blood pressure in this case rose to 215. and she died in a convulsion. In this group of 3 cases no definite etiological factor was present. A history of scarlet fever was present in one patient, but was absent in the others. Nitrogen retention in this group was only moderate. Gray's (1933) case was that of a female child aged 8½ years and backward mentally, admitted to hospital unconscious, with a long-continued history of severe frontal headaches. The blood pressure was 160 systolic and 120 diastolic, and the heart was over-acting. Retinal lesions were found on ophthalmoscopic examination. The urine contained a marked trace of albumin, in which a few cells were found on microscopic examination. Repeated attacks of unconsciousness occurred in the ensuing 11 months before the patient's death in uraemia. At times the urine became red, an acute exacerbation thus being suggested. The blood-pressure rose gradually, reaching 250 systolic just before death. The blood urea remained only slightly above normal, until a uraemic element developed shortly before death. At autopsy, arteriosclerosis was found in the coronary arteries, and the abdominal aorta showed definite nodular atheroma for about one inch. The heart was much enlarged, the left ventricle in particular being greatly hypertrophied. The kidneys showed irregular congestion, and on section the left cortex

was/

was very narrow and the organ was only about half the size of that on the right, the latter being smooth and very pale, with some petechial haemorrhages. Histologically, arterial changes were striking, the medium-sized arteries displaying hypertrophy of the media, while the smaller vessels showed various changes, sometimes extreme hypertrophy of the media alone or combined with thickening of the intima, hyaline or fatty change being present, and the lumen being almost occluded in some instances. There was no proliferation of elastic tissue. These severe changes affecting the small and smallest vessels recall Volhard and Fahr's essential vascular lesion in their cases of adult malignant nephrosclerosis. In Gray's patient there was little evidence of an inflammatory lesion in the glomeruli, the majority showing hyaline changes of ischaemic nature. Some interstitial fibrosis was present, but there was no marked cell infiltration. In the right kidney changes similar to those described were present, but to a less severe degree. The arteries in the liver, spleen, pancreas, heart, and voluntary muscles showed medial hypertrophy alone or combined with hyaline degeneration of the intima. Such cases as these just described show that malignant nephrosclerosis or primary contracted kidney, with a vascular lesion as the essential component, can occur even in young children, and in them the condition, though very much rarer than in adults, appears to be of exactly similar type, though with the important/

important difference, namely, that while in adults the proportion of males to females is about 2 to 1, in children this proportion is reversed - the disease preponderating in the female sex. In young subjects, in addition, some renal mal-development or hypoplasia is present in a strikingly large number of the reported cases. It would appear, therefore, that malignant nephrosclerosis in children attacks kidneys already handicapped in development, presumably by defective arteriogenesis, the mal-developed arteries themselves readily undergoing degenerative changes.

The study of chronic renal disease in children cannot be left without mentioning another type, first called by Heubner (1908) "Paedonephritis," and since described by various writers. This is a mild type of renal lesion often discovered only on examination of the urine, since it can last for years without producing oedema or any of the usual sequelae of nephritis, such as rise in blood pressure, cardiac hypertrophy, retinal changes, or uraemia. Paedonephritis may be due to hereditary predisposition or may result from one of the infectious fevers, or from angina. In the urine is found a moderate amount of albumin, with hyaline casts, epithelial cells, and only scanty red blood corpuscles in the sediment. Since the albuminuria is often of orthostatic type, paedonephritis has been regarded by some investigators as orthostatic albuminuria of unusually severe type, though Heubner/

Heubner objects that in paedonephritis, formed elements are present, while these are absent in orthostatic albuminuria. The type of child with paedonephritis tends to be sickly, easily tired, with headaches and indefinite pains. In many instances albumin is discovered by chance on routine examination, or appears insidiously after some infectious disease. This type of renal lesion would appear to be closely related to some of the other albuminurias of childhood or adolescence, - orthostatic or cyclical albuminuria. Capon (1926) believes that Heubner's paedonephritis is the same condition as Volhard and Fahr's "focal" nephritis. Long (1928) agrees that in this type of lesion hereditary tendencies play an important rôle. He records the case of a mother with a cloud of albumin in the urine and abundant hyaline and granular casts. Her children appeared healthy, but examination of the urine of each showed a trace of albumin in association with hyaline casts. Four generations of her family had suffered from Bright's disease. Several other patients, he mentions, were rejected for life insurance on account of albuminuria, and the urinary sediments of these patients also contained hyaline casts and a few red blood corpuscles. In the majority of such patients a focus of infection was found in the tonsils or nasal sinuses, and on removal of the latter the urine became normal. It should be mentioned, however, that Addis and Oliver (1931) found traces of albumin and even casts and scanty/

scanty red blood corpuscles in the urine of apparently healthy young adults, and this fact led them to regard Bright's disease as a condition differing from the normal not qualitatively, since albumin, blood and casts can be present both in healthy persons and in nephritic subjects, but quantitatively, Bright's disease being a lesion where more albumin, blood and casts are present than in healthy individuals. MacAdam (1933) also comments on the fact that 5 per cent. of 60,000 men physically fit, investigated during the war, showed albuminuria. Such individuals were no more liable to develop nephritis than those with no trace of albumin in the urine. MacAdam thinks that unless an excess of casts is found in the urinary sediment, this mere fact of the finding of a trace of albumin should not be considered as indicative of a renal lesion.

BLOOD DISEASES COMPLICATING CHRONIC NEPHRITIS.

A final aspect of chronic nephritis calls for a brief note - namely, the tendency to anaemia and haemorrhages associated with this type of renal disease. Thus in two of the 9 cases of sub-acute and chronic nephritis, severe purpura occurred 2 to 3 weeks before death in each instance, with haemorrhages into the skin and severe bleeding from the stomach, bowel, and bladder. Garrod, Batten, Thursfield, and Paterson (1929) find nephritis, generally of haemorrhagic type, a rare complication of purpura, especially of Henoch's type, characterised by severe/

severe crises of abdominal pain, often accompanied by vomiting and diarrhoea with blood in the stools. Sometimes severe arthritis is also present. Ramond (1929) agrees that the type of purpura with a tendency to renal involvement has three essential features: (1) purpuric eruptions, (2) painful joints, (3) gastro-intestinal upset. On the other hand, purpura may be secondary to nephritis, appearing at times in chronic Bright's disease as a manifestation of the underlying cachetic condition. In the two cases mentioned above, one of sub-acute nephritis, and one of chronic nephritis occurring in a single kidney, purpura in the former would appear to be primary, since a purpuric eruption followed pain and swelling of the feet, though in this case abdominal pain was absent until peritonitis developed as a terminal event. The acute exacerbation with abundant tubular haemorrhage of the underlying sub-acute renal lesion was possibly secondary to the purpura. In the other instance where chronic nephritis occurred in a single kidney, there was a history of listlessness for a year before admission to hospital, and purpura appeared with no antecedent rheumatic or gastro-intestinal disturbance. Bleeding from the bowel was severe and might be regarded as part of the haemorrhagic tendency, associated with chronic Bright's disease as, for example, in two of the cases described by Schwartz. Cabot (1932) reports a case somewhat similar to that just described in a female child aged 15 years, admitted/

admitted as a case of severe purpura, with blood oozing from the mouth and nose. At autopsy, the kidneys showed severe chronic nephritis, the purpura in this case being regarded by the author as secondary to the renal lesion. Severe anaemia, sometimes so profound as to suggest the pernicious type, is another blood disease frequently associated with chronic nephritis. Naegeli (1923) states that some French writers consider chronic nephritis as one possible cause of pernicious anaemia. In the present investigation, blood counts were done in only 2 chronic cases, one being the child with the single kidney mentioned above, whose red cells fell to 1,770,000 per c.mm. Severe haemorrhages, were however sufficient to account for marked anaemia in this case. In the other patient with chronic nephritis, the red cells numbered 2,790,000 per c.mm. Various writers mention the association of severe anaemia with chronic nephritis. Scarlett (1929) found that in 51 cases of chronic nephritis the red cells averaged 2,780,000 per c.mm., and he believes that anaemia may be the only clinical manifestation of chronic nephritis. He states further that the presence of severe anaemia serves as an important point of differentiation between chronic glomerulo-nephritis and malignant hypertension, the blood count not being lowered in the latter. According to Brown and Roth (1922) the anaemia of chronic Bright's disease may simulate the primary type. In their study of 187 cases of chronic Bright's disease at the Mayo/

Mayo Clinic, 105 had severe anaemia, excluding all cases with macroscopic loss of blood. The average red cell count in these 105 patients was 3.31 millions, as against 4.22 millions in the remaining cases. The platelet count in 8 of these anaemic patients averaged only 152,000 per c.mm., and Brown and Roth consider that the low platelet content of the blood may have some bearing on the tendency to haemorrhage shown by some cases of chronic nephritis. They regard the anaemia as due to inadequate haematopoiesis, the bone marrow suffering damage concomitantly with the renal and cardio-vascular tissues. Ceconi (1905) believes that the action of the toxins present in chronic nephritis has a paralysing effect on haematopoiesis, resulting in insufficient production of cells.

CONGENITAL RENAL ABNORMALITIES.

On searching the post-mortem records in the Royal Hospital for Sick Children for the last 15 years, the period during which the cases of nephritis in the present series were collected, 26 instances were found of some developmental renal abnormality, exclusive of horse-shoe kidneys and minor degrees of hydronephrosis. Of these 26 patients, 14 were male, 11 female, and in one instance the sex was not stated. The ages varied from 26 days to $13\frac{1}{3}$ years, though in 22 cases the children were under 1 year of age, and in the remaining 4 the ages were 15 and 18 months, $2\frac{2}{3}$ and $13\frac{1}{3}$ years respectively. The types of developmental anomaly can be grouped as follows:- 10 cases where one kidney was absent; 9 cases where one kidney was hypoplastic;/

hypoplastic; 7 cases with miscellaneous abnormalities. One additional kidney removed at operation is described in this section. In the first group of 10 subjects with a single kidney, the left organ was lacking in 8 male patients, and the right in 2 female children. The fact that the absence of one kidney was generally left-sided and in male patients is in agreement with the findings of other authors. Brüning and Schwalbe quote Klebs' statement, that it is generally the left kidney that is absent, while a single kidney is found twice as often in males as in females, and Dorland (1911) also finds a great preponderance of renal abnormalities in male subjects, only 28 per cent., according to this author, occurring in females. With regard to the presence of a ureter, in 4 instances the ureter as well as the kidney was completely absent on one side, in 5 cases this structure was not mentioned, and in one patient the ureter could be traced two inches up from the bladder, becoming lost thereafter in fibrous tissue. Brüning and Schwalbe state that where one kidney is absent, either the ureter is altogether lacking or the vesical end may be present. These authors believe that on microscopic search of the tissues in the normal kidney region, traces of renal elements may be found, and that entire absence of one organ is very rare. Naked-eye examination of the single kidney in the 10 cases of the present series showed simple hypertrophy in 4 instances, in one of which the right kidney was as large as 2 organs combined/

combined, while the ureter was dilated. In other 2 instances, the single kidney was enlarged and hydronephrotic, also with a very wide ureter. These two cases are included in the sub-acute and chronic group of this investigation and have been already mentioned, but the histological characters will be fully described later in this section, as it was thought advisable to place them along with other developmental abnormalities. One occurred in a girl aged 13½ years, with chronic glomerulo-nephritis, and the other in a male child aged 18 months, with a similar renal lesion, much tubular hyperplasia being present in the latter as shown by the projection of raised nodules of renal tissue from the sunken fibrous-tissue background. No obstruction was found in these cases to account for dilatation of the ureter. In other two of the 10 cases the single kidney present was at a lower level than normal, once at the pelvic brim, and the seat of malformation in this instance, only 4 calyces being present. In the other case, the enlarged single organ was the seat of cortical abscesses. Of the last two single kidneys, one was described as showing nothing of note, while the other was enlarged and pale. Thus of the 10 single kidneys, apart from mere hypertrophy noted in four of the organs, two showed severe chronic nephritis, one was the seat of abscess formation, and two were in abnormal positions, one of these being malformed in addition. The fact that disease was present in several of these single kidneys also appears to correspond with the generally accepted

view/

view that a single kidney is peculiarly liable to pathological change, and this can happen even in young children, since one of the patients with a chronic nephritis was only 18 months of age. The second group of 9 cases, with one hypoplastic kidney, includes 4 male and 4 female patients, and one whose sex is not stated. The abnormal kidney was represented in 3 cases merely by a vestigial cyst-like structure, described in one instance as the size of a raisin. The ureter in this case, on being traced up from the bladder, ended as a delicate fibrous cord, extending up to this small structure. The right kidney here was enlarged, with marked cloudy swelling and fatty change. In the second instance, the right kidney was represented by a small cystic mass with four lobes, the left kidney being larger than normal, and the seat of congestion. In the third case, the left kidney appeared as a small fibrous mass in which were embedded several small cysts, this structure showing nothing suggestive of renal tissue on naked-eye examination. The right kidney was normal in size and appearance, both macro- and microscopically. In these three instances, therefore, only one kidney was present from the functional point of view. In the other six cases in this group, the size of the abnormal kidney varied from that of a chestnut to half or one-third of the normal organ, the ureter being occluded in two instances. The small kidney in some of these cases showed marked foetal lobulation, and in two instances the/

the abnormal organ was lower than usual in position, lying at the pelvic brim. In the case where the right kidney is described as chestnut-sized, this vestigial organ was in the normal position, while the left kidney, of normal size, was lower than usual, displaced towards the right side, and connected to the right kidney situated immediately above it by a narrow band of fibrous tissue. In another instance, the small kidney at autopsy appeared to be fibrosed, and on microscopic examination a cavernous haemangioma was present, large blood-filled spaces being present embedded in a fairly dense fibrous stroma. In the remaining group of miscellaneous congenital abnormalities, numbering 7 cases, extreme hypoplasia of both kidneys was found in one patient. The noteworthy feature in two instances was the abnormal position of one of the organs. In one of these cases, the right kidney lying just above the pelvic brim was the seat of pyelonephritis, while the left kidney was in the normal site. In the other, the left kidney was situated on the anterior aspect of the sacrum just below the bifurcation of the aorta. A fourth case showed congenital cystic disease of the left kidney, with a ureter present both at the pelvic and the bladder end, though both portions ended blindly in fibrous tissue. In a fifth instance, the right kidney was hydronephrotic, only a thin rim of renal tissue remaining, though the ureter on this side was not dilated, while the left kidney showed a less marked degree of hydronephrosis./

hydronephrosis. Minor degrees of maldevelopment were found in the two remaining cases, one aged 10 and the other 14 days. In the latter, a male infant, the right kidney cortex was extremely narrow in comparison with the medullary portion, which was the seat of malformation, one large calyx occupying the upper pole of the kidney and three small calyces the rest of the organ. In the left kidney the distribution of the calyces was normal. On histological examination of this kidney there was no evidence of any pathological change, and fat was negligible in amount, both in cortex and medulla. In the former, a female infant aged 10 days, both kidneys appeared rather larger than normal, with extremely narrow cortices, though these showed no evidence of any inflammatory or other lesion, and the cortical markings were quite regular. This infant had a history of complete anuria with convulsions for 3 days prior to admission. On catheterisation one drop of urine containing albumin was obtained. No gross oedema was present. No obstructive lesion was found anywhere in the urinary tract at autopsy. On histological examination, the kidneys were of normal infantile type, with prominent Malpighian bodies, which appeared closely packed together, from lack of tubular development. There was no evidence of any inflammatory lesion, the only abnormality detected being the presence of abundant fat, chiefly in the convoluted tubules. Albuminuria may be present without for 1 to 2 weeks after birth/

birth any pathological significance. Indeed, according to Ribbert (1884) albumin is present in the majority of infants in the first few days of life. He believes that all the albumin is derived from the glomeruli and is merely a continuation after birth of an embryonic process, since foetal glomeruli are known to be permeable to albumin from lack of development of the capillary walls, though, in addition, the increased metabolism at birth represents an important factor in the process. According to the views of other investigators the mechanical irritation of uric acid infarcts frequently found at the apices of the papillae shortly after birth may be of itself sufficient to cause albuminuria in young infants.

Histological examination was possible only in a few cases of congenital deformity, in addition to the two just described, and was carried out in the cases of chronic nephritis occurring in a single kidney, in the case where both kidneys were the seat of marked hypoplasia, and in another instance where bilateral hydronephrosis was present in association with a vaginal cyst, and finally in a case with one vestigial and one normal kidney. A further case of unusual interest was that of a kidney removed surgically, the seat of lymphoid hyperplasia, which will be included in this group, though not forming part of the series just described.

The two instances of chronic nephritis occurring in a single kidney will first of all be dealt with. It is a matter/

matter of common experience that a solitary kidney is particularly prone to develop nephritis. Cases are described by Rolleston (1916) and Pepper and Lucke (1921), while Anders (1910) states that of single kidneys 42.3 per cent. show some form of chronic nephritis. The first of these two patients was a male child aged 18 months, brought to hospital with no history of renal disease, but with a severe angina of Vincent's type of two weeks' duration. On admission, the child's gums were in a sloughing condition, smears showing abundant fusiform bacilli and spirochaetes. He died 2 days after admission and the urine was not examined. At autopsy in this case, the left kidney and ureter were entirely absent. The right kidney was much larger than normal and the seat of hydronephrosis, with a very wide ureter. Rolleston (1916) describes dilatation and hypertrophy of the ureter in a single kidney, the seat of nephritis, though in his case an obstruction was found at the vesical end of the ureter. In the present case no obstructive or other lesion was discovered to account for this dilatation. The kidney substance was pale, with marked surface irregularity, light yellowish nodules projecting from a sunken,darker-coloured background. No gross lesion was found at autopsy in any of the other organs, in this case, and there was no effusion into the serous sacs. On histological examination all stages of glomerular involvement could be traced from an acute lesion, with congested, cellular glomeruli,/

through various stages of proliferation with extensive adhesions between capsule and tuft, to complete fibrosis and shrinkage of the latter. Groups of tubules were greatly dilated, with flattening of the epithelium and various abnormal contents in the lumina, many being filled with fresh red blood corpuscles, while hyaline casts were also abundant. In a few tubules small ingrowing papilliform processes were noted. These areas of dilated tubules corresponded to the nodules on the surface of the kidney and were separated by dense strands of fibrous tissue, while a diffuse but delicate fibrous-tissue network ramified between the individual tubules in the areas of hyperplasia. This type of lesion contrasts well with the group of cases of chronic nephritis described in a previous section, where the proliferated fibrous tissue was diffusely distributed, the surface of the kidney remaining smooth.

The second patient with chronic nephritis in a single kidney was a girl aged $13^{1}/3$ years. The right kidney was absent, though a ureter was found on the right side ending blindly at the pelvic brim, and the right suprarenal gland was in its usual position. The left kidney was extremely hydronephrotic, only a thin shell of renal tissue being present, so that in this patient, in view of the severe chronic nephritis with destruction of many renal units, an extraordinarily small amount of functioning renal tissue remained at the time of death. The left ureter was dilated, but/

but a probe could be passed along it and into the bladder without any evidence of obstruction. Regarding other abnormalities found at autopsy, the pericardial fluid was increased and was slightly turbid with fibrinous exudate on both pericardial surfaces. The infecting organ was a streptococcus. Both ventricles, particularly the left, were the seat of hypertrophy. The other serous sacs showed no abnormality. The organs were pale as a result of anaemia and the liver and spleen gave a marked iron reaction. A large amount of blood was present in the stomach and bowel, apparently as part of the purpuric condition since no ulceration or other lesion was present to account for its presence. The uterus was of bicornuate type. According to Dorland (1911) congenital renal defects are not infrequently associated with maldevelopment of other pelvic structures. The kidney on microscopic examination showed an extremely abnormal picture. Glomeruli appeared very scanty, apparently from the fact that a very large proportion of these structures had been reduced to mere hyaline balls. Some of the remaining glomeruli were greatly enlarged, while a few showed marked cellularity and freedom from fibrosis, and were apparently still acutely inflamed. Others showed commencing adhesions between tuft and capsule. In others the process had advanced to marked fibrosis, and all the intervening stages could be traced to shrinkage and complete hyalinisation. The tubules also appeared/

appeared scanty and greatly hypertrophied and dilated, while many had abnormal contents including hyaline and granular casts, with frequent clumps of polymorphonuclear cells. Haemorrhage into the tubules was not a feature in this case. The epithelium as a whole was flat, and isolated tubules were the seat of hyaline droplet degeneration. The interstitial tissue was greatly increased and diffusely distributed so that a large part of the scanty renal tissue remaining had its "nobler" elements replaced by connective tissue. Many glomeruli showed a special zone of peri-glomerular fibrosis. Throughout the interstitial tissue cellular infiltration was abundant, polymorphs, lymphocytes, and plasma cells all participating. The arteriolar walls appeared slightly thickened, hypertrophy affecting both the media and the intima. A few scattered structures apparently of the nature of primitive glomeruli were seen in various sections.

The next case to be considered in detail is that of a male infant aged 5 days, admitted with a history of loose green stools for two days. At autopsy intense gastro-enteritis was present as well as early broncho-pneumonia. The right kidney and ureter in this case were normal in position, size and shape. The left kidney was represented by a small bean-shaped structure in which macroscopically there was nothing resembling kidney tissue, the appearance being that of a small fibrous mass in which several tiny cysts were/

were embedded. A ureter was present, which, though narrow, was patent throughout its length, and appeared to end normally in the bladder. On histological examination the right kidney was essentially normal, the glomeruli showing merely slight congestion, and the epithelium of the convoluted tubules having rather a vacuolated appearance. Traces of a neogenic zone were still present, but, as has been previously shown, isolated embryonic structures are not uncommon in the kidneys of infants for some months after birth. The rudimentary structure representing the left kidney was largely composed of dense fibrous tissue, in which were embedded here and there small groups of primitive renal structures. All the glomeruli represented were very small and imperfect, and some of these showed fibrosis with definite capsular proliferation, while areas of hyalinsation were present in others; thereby, along with similar findings in the kidneys of the 2 cases next to be described, affording confirmation of the view expressed earlier in this paper, that immature glomeruli are specially prone to become diseased. The tubules in the rudimentary kidney were represented by small groups of imperfect convoluted and collecting tubules. In the fibrous stroma were also present larger tubular structures, representing probably primitive ducts of Bellini, and some of these tubular structures were surrounded by primitive connective tissue concentrically arranged. In the fibrous tissue were also embedded large blood-filled/

blood-filled spaces with flat endothelial lining.

The next patient was a female infant aged 4 months, admitted with a history of swelling of the abdomen since birth. The child developed a terminal hypostatic pneumonia and died 3 days after admission to hospital. This case has been included in the group of septic cases to be described later, on account of infection of the abdominal cyst. At autopsy the right kidney was extremely hydronephrotic, only a thin rim of kidney tissue remaining, but the right ureter was not dilated. Hydronephrosis of less marked degree affected also the left kidney. A large cystic structure with contents infected with B. lactis aerogenes, occupied the greater part of the abdomen, originating apparently from the vagina, with which a dilated thin-walled uterus communicated through a wide cervix. The only other lesion of note found at autopsy in this case was the presence of a terminal broncho-pneumonia.

On histological examination of the left kidney acute nephritis was present, the glomeruli as a whole being definitely enlarged, swollen, cellular and congested, with complete loss of the covering epithelium. In addition red corpuscles were present in isolated convoluted tubules, in amount sufficient/

sufficient to distend these with blood. Many primitive glomeruli or glomerular anlage were present, a number of these imperfect structures being sclerosed, with surrounding cell infiltration. The vessels were thick-walled, especially the small arterioles, while the thickened intima encroached on the lumen of some. Sections of the right kidney, the more hydronephrotic of the two, showed lesions essentially similar to those just described, though fibrosis and general departure from the normal renal architecture were still more striking in the latter. In one area of the cortex, the seat of fibrosis and cell infiltration, was noted a group of vessels with particularly thick walls.

The two cases next to be described have been published by Blacklock (1933). The first concerned a female infant aged 25 days who was three weeks premature at birth and weighed 7½ lbs. Shortly after birth twitching of the eyes, mouth and tongue was noted. On admission to hospital at the age of 23 days, her weight was only 4 lbs. 13 oz. Nothing abnormal was found in the circulatory or nervous systems. The breathing was slow and gasping, and cyanosis was marked in the periods between respirations. The small amount of urine that could be collected contained albumin and blood. At autopsy the kidneys were each about the size of a haricot bean, the right being rather smaller than the left, the vertical diameter being 1 cm. and the horizontal 0.8 cm., while the left kidney

was/

was about 1.5 x 1.2 cm. Each kidney had a small subcapsular cortex (0.25 cm. in the left and less in the right) but there was no interpyramidal cortex in either. Scattered throughout the cortices of both kidneys irregular vascular areas were noted, and the normal markings were indistinct. Each kidney had a small pelvis. The normal size of the suprarenal glands made the kidneys seem still smaller by comparison. On histological examination these organs were very immature, persistence of a definite neogenic zone being noted immediately under the capsule, the appearance thus corresponding with that of an early stage of foetal development. Some of the primitive glomeruli showed definite capsular thickening. Primitive tubules were also seen throughout sections, recognised by the high columnar type of epithelium, with abundant protoplasm and darkly-staining nucleus. Some of these tubules were surrounded by a concentric zone of spindle-cell connective tissue. The interstitial tissue was definitely increased, areas of fibroblastic proliferation being present, with foci of cell infiltration at places, round cells predominating, with a few eosinophils. The glomeruli, apart from these immature examples, were as a whole enlarged, congested, and cellular, with loss of the covering epithelium. Some glomerular tufts showed early adhesions to their capsules. In others, the capsular epithelium filled the capsule of Bowman, while some of the tufts were the seat of early fibrosis. The majority

of/

of the tubules were dilated and the epithelium of an abnormally low type, while many contained blood, hyaline casts, and desquamated cells. Some tubules formed cyst-like spaces, as a result of fibrous-tissue obstruction. Little fat was found in the tubular epithelium or in the interstitial tissue. In this case the striking features were first, delay in development, and second, nephritis of a proliferative rather than of an acute type, though an active process was still present, as indicated by the increased cellularity of many glomeruli, and haemorrhage into some glomerular capsules and tubules. Another noteworthy point was thickening of the vessels, the small arterioles in particular showing slight concentric thickening of all coats, and appearing unduly prominent in sections. This infant was the 8th child and there was no suggestion of syphilis either in the patient or in the family history. The only feature of note in this case was the fact that the mother had been exhausted throughout the pregnancy and had suffered from headaches, sickness and vomiting during the last 3 months. At autopsy in addition to the renal lesion described above early broncho-pneumonic consolidation was present, while some mucoid secretion was found in the right middle ear.

With regard to hypoplastic nephritis in the literature, Coplin (1917) describes a case where unilateral hypoplasia and dysplasia were apparently the result of an associated defective/

defective arteriogenesis. He considers that this type of renal abnormality renders inevitable some form of nephritis. One kidney may be less than a quarter the size of the other, and may in fact weigh even less than 1 gm. Bilateral hypoplasia is rarely observed, according to this author, but the case just reported would appear to form one of these rare instances. An associated genital anomaly may be present, according to Coplin, usually on the side of the affected kidney. He also quotes Besançon's view that subnormal arterial function has a damaging effect on the kidney, increasing its susceptibility to toxic bodies. Coplin believes that nephritis, toxaemia, or uraemia, appearing in young patients without adequate cause, should arouse suspicion of the presence of renal hypoplasia. Babes (1905) in the course of three years saw 6 young patients, mostly under 30, who, during some slight illness, were suddenly seized with symptoms of severe nephritis, falling into coma and succumbing within 24 hours. Such patients were generally anaemia and weak, though with no previous renal symptoms of note. At autopsy a similar type of renal lesion was noted in all, the kidneys, or at least one kidney, being smaller than normal, and lower in position, with the corresponding renal artery of much narrower diameter than usual, coming off the abdominal aorta lower down. In Babes' series one kidney was almost agenetic in one instance, being replaced by a kind of membranous sac (similar to one of the/

the cases described above), and in another one organ was extremely small, granular and indurated. On microscopic examination, the glomerular arteries were hypogenetic in the latter and the glomeruli ill-developed, sclerosed, or atrophied, generally without much thickening of the capsule of Bowman, of which the epithelium was often embryonic. The interstitial tissue was extremely thick with the homogeneous character of the interstitial tissue of the foetal kidney, with some tubules of embryonic type. The author concludes that this is not an ordinary type of sclerotic kidney, but a particular renal condition, constituted by certain foetal factors, - an arrest of development, hence true hypogenesis.

Hutinel (1922) describes a type of case where development of the kidney is arrested and very imperfect, the organ then being very small and represented only by a fibrous structure, in which are still recognisable some excretory tubules, cysts, and rudimentary glomeruli. Here also the condition is not one of atrophy, but of arrested development. One of the organs can be completely suppressed. This author finds that vascular aplasia is not constant and he considers it difficult to prove that it is primary. In his opinion, it generally runs parallel to renal aplasia, and may be contemporary with or even secondary to the latter. The causes of this aplasia are variable the most common being hereditary influence. In certain cases the parents are too old, exhausted by fatigue, with some infection/

infection or intoxication, or else suffering from some organic or endocrine-glandular lesion. The author found renal aplasia in a child whose mother had albuminuria before birth, but in the majority of these aplasias congenital syphilis certainly occupies the most important place in Hutinel's opinion. Of interest in this connection is a case of Rathery, Thoyer and Waitz (1930), that of a syphilitic patient aged 24 years, in whom, at autopsy, the kidneys were very atrophic showing marked endo- and peri-arteritis with fibrosis and haemorrhage at places. Islands of small embryonic cells were present, such cells being most abundant round the altered vessels.

The last case to be described in this group has also been reported by Blacklock (1933). The patient was a female child aged 18 months, who, subsequent to an attack of scarlet fever at the age of 15 months, suffered from painful micturition with attacks of pyrexia. Dilatation of the left renal pelvis and ureter was found on examination, and a trace of albumin was present in the urine, along with pus cells and coliform bacilli. The left kidney was excised surgically. The organ was slightly enlarged, the cut surface showing several areas of suppuration in both cortex and medulla. The whole organ was paler than normal, and there was a very slight degree of hydronephrosis. Histological examination revealed a very extraordinary/

extraordinary picture. Well-formed lymphoid follicles were present, a definite reticulum separating the germ cells. These follicles were scattered throughout both cortex and medulla, though more abundant in the former. Normal glomeruli were seen lying beside these lymphoid structures. Sub-acute abscesses were also present in the cortex and medulla with foci of cell infiltration, and pus cells in some tubules. The presence of this lymphoid tissue would appear to be associated with the occurrence of chronic inflammatory change in the kidney substance, as this type of tissue is sometimes present in abnormal situations in organs the seat of inflammation, the gall-bladder in typhoid carriers for example. No reference to a similar condition has been encountered so far by the writer in the literature on nephritis, though in a single case belonging to the present series, an appearance was noted which vaguely recalls these lymphoid structures just described. The patient in question was a female infant aged 23 weeks, with von Jaksch's anaemia. At autopsy purpuric spots were scattered over the trunk, and a large haemorrhage had occurred into the substance of the thymus. Small cysts of apparently congenital nature were present in the substance of the left kidney, but were absent in the right kidney, and the organs showed nothing else of note beyond extreme pallor. Microscopically both kidneys appeared normal for the most part, though sections showed, here and there, foci of cell infiltration, mainly of lymphocytic type. These lymphocytes/

lymphocytes had infiltrated the renal tissue diffusely for the most part, though at places they were closely massed together, showing an attempt at follicle-formation, with even a suggestion of a germ centre, though the structures were very imperfect, unlike the well-formed, typical follicles in the preceding case. In these areas of lymphocytic infiltration in the case under discussion, very primitive glomerular structures were present, some of which were undergoing fibrosis. The arterioles in these areas were narrowed as a result of concentric thickening of their walls. Such foci would appear to represent delay in development with secondary lymphocytic infiltration, and an imperfect attempt at follicle formation.

Congenital Defects associated with Renal Anomalies.

In 9 of the 26 cases with kidneys the seat of developmental abnormalities various other congenital defects were present in addition. These included, in one child, congenital abnormality of the cranial bones and of the right lung, where the middle lobe was lacking. In another were found imperforate anus, ectopia testis, hypospadias and hypertrophy of the bladder. A third had congenital heart disease with an abnormal type of ossification of the skull. A fourth patient had hypertrophic pyloric stenosis, cleft palate and a right inguinal hernia. In a fifth, congenital heart disease was present. The sixth had a bicornuate uterus. In a seventh were found/

found talipes and undescended testicles, while the eighth had an abnormally long mesentery which had caused a volvulus of the small bowel. Finally, in the ninth patient a large vaginal cyst, communicating with the uterus, filled the greater part of the abdomen. In this case in addition accessory digits were present on the hands and feet.

The existence of such developmental defects in association with mal-development of one or both kidneys confirms the findings of other investigators. Kaufmann states that unilateral malformations are found in the female and sometimes in the male genitalia. Rolleston in several instances found mental deficiency in patients with renal dystopia and considers that this was not a chance association, but that both defects were stigmata of degeneration. Glaser reports one juvenile case of contracted kidney due to hypoplasia of the renal arteries, in a mentally deficient child, and mentions another of similar type. Dorland also finds not infrequently associated defects in other organs - including rectum, bladder, uterus, vagina, ovaries and lower spermatic tract, and believes that the female genitalia are particularly apt to be defective, almost invariably on the side of the renal abnormality.

SECONDARY NEPHRITIS.

Various investigators have found nephritic lesions at autopsy in a variety of septic conditions, though a renal lesion had not generally been suspected during life, owing to the fact that the primary disease had dominated the clinical picture, the nephritis also in some cases being only focal in type.

Ophüls (1908) on macroscopic and microscopic examination of the kidneys in 640 post-mortems discovered well-marked nephritis in 67 cases (= 10 per cent).

Gray (1928) analysed a consecutive series of 170 autopsies and found marked septic or infective factors in 91 of these, 4 cases of haemorrhagic nephritis being detected in the latter group. None of these had been diagnosed during life. In the 4 cases of nephritis a streptococcal infection was present in 3 and probably in the 4th.

Shaw Dunn and Thompson (1921) found acute nephritis in 13 instances in a series of 660 post-mortems, the majority of the kidneys in these cases showing enlargement, pallor, or punctate cortical haemorrhages. The primary disease in all these 13 cases was some severe septic infection, the infecting organism being a streptococcus in 8 (2 of these strains being haemolytic), pneumococcus in 1 and staphylococcus in 1. Acute nephritis was diagnosed in only one of these cases during life, and was then considered of secondary development

in the course of a septicaemia.

Blackman and Rake (1932) found that a mild acute and subacute nephritis could be demonstrated in about 40 to 50 per cent. of patients dying from pneumococcal lesions.

The present writer, with a view to discovering the incidence of nephritic complications in various septic and toxic conditions in children, examined the kidneys macroscopically and microscopically in a series of cases dying from various acute and chronic inflammatory processes, such as septicaemia, bacterial endocarditis, meningitis, pneumonia, tuberculosis, the whole series amounting to 163 cases.

Nephritis in Septic Conditions.

This group includes 33 cases of various extensive suppurative lesions with or without septicaemia, and 6 cases of general peritonitis, the latter having been included here since infection of the peritoneal cavity represents a widespread septic process which, like other septic conditions, allows of much toxic absorption.

Of these 39 combined cases 24 were of the male and 15 of the female sex, 11 were aged 6 months or under, and 7 were between 6 months and 1 year of age. Rather less than half of the infections to be described, therefore, occurred in the first year of life. Other 14 cases were under 5 years, and the remaining 7 between 5 and 10 years of age. The septic conditions included 14 cases of septicaemia, 11 streptococcal, 1 staphylococcal/

staphylococcal, 1 coliform, the result of a ruptured bladder with pelvic cellulitis, and in the remaining case culture of the spleen pulp yielded no growth. The rest of the septic lesions consisted of more or less extensive suppurative processes, including sloughing wounds and cellulitis, septic sores or burns, pneumonia associated with empyema, peritonitis or pericarditis, severe septic tonsillitis with follicular abscesses, osteomyelitis, periostitis, one case of exfoliative dermatitis, and one of a large abdominal cyst with infected contents. Bacteriological examination performed in 23 of the whole series of 33 septic cases yielded streptococcus in 13 instances, staphylococcus aureus in 4, pneumococcus in 1, and a coliform bacillus in 2, while in 3 cases a mixed infection was present, staphylococcus and streptococcus together being found in one case, pneumococcus and streptococcus in the second, and in the third a rich mixed bacterial flora (Case of septic tonsillitis).

With regard to the 6 patients with peritonitis, the infecting organism was pneumococcus in 3, streptococcus in 2, and in the remaining case the report states merely that cocci and bacilli were abundant in the peritoneal pus.

In the combined 39 cases, therefore, streptococcus was present in 15 instances, pneumococcus in 4, staphylococcus in 4, and a mixed infection in 4 including the last mentioned case of peritonitis.

Of the 33 septic cases, nephritis had supervened in 7, while a nephritic complication was found in 3 of the 6 peritonitis/

tonitis cases. In the combined series of 39 cases, therefore, 10 showed an acute inflammatory renal lesion.

Of the 7 cases comprised in the septic group, 4 of the children were under 1 year, and the other 3 were aged $4\frac{1}{2}$, $8\frac{2}{3}$ and $10\frac{2}{3}$ years respectively, while of the peritonitis group, one was aged 6 months, one $3\frac{1}{2}$ years, and one 9 years.

Of the 7 cases included in the former group, 4 were associated with streptococcal septicaemia, and in the 5th with an axillary abscess which, along with a septic rash, followed vaccination. In this case a carbolic dressing had been applied, but the urine became dark in colour, so the carbolic dressing was discontinued. The 6th case of nephritis occurred in a patient with an extensive sloughing wound following an appendix operation, and the 7th in a female infant with a large abdominal cyst, the contents of which were infected with B. lactis aerogenes.

Of the 4 septicaemic cases, one was complicated in addition by a streptococcal meningitis, one by double empyema, pericarditis and peritonitis, and one was secondary to Vincent's angina with cellulitis of the neck.

Of the peritonitis cases, one was streptococcal, one pneumococcal, and one occurred with the mixed cocco-bacillary infection.

Regarding the kidneys in the 7 septic cases, on naked-eye examination these were enlarged and swollen in 3 instances, one case being described further as bulging out of the capsule on incision/

incision of the latter, and another as thick, mottled, and firm in texture with irregular markings, the appearance suggesting a subacute type of lesion. In the other 4 cases the kidneys were not enlarged, but were intensely congested with much fatty change or cloudy swelling in 2 of these, while fatty change was extreme in a third. In the 4th instance, that of the infant with the abdominal cyst, double hydronephrosis was present. This case has been already described in detail in the section dealing with congenital renal abnormalities.

Of the 3 nephritic lesions developing in the peritonitis cases, the kidneys were not enlarged in any instance, and on naked-eye examination the appearances suggested merely cloudy swelling of marked degree.

Histologically, taking first the 6 septic cases (exclusive of that associated with the infected cyst already described), in the 3 patients under one year of age a striking feature in sections was the loss of the prominent plump cubical epithelial layer covering the tufts. In these 3 cases the glomerular lesion was of moderately severe diffuse type, with some exudate of albumin in the capsule of Bowman. The tubular epithelium showed degenerative changes of relatively mild type, consisting of cloudy swelling and granularity of the epithelium with, in one instance, hyaline droplet degeneration in isolated tubules. Scanty red cells were found within the lumina of the tubules in 2 of these cases, but were absent in the third. The interstitial tissue was oedematous in 2, and small foci of cellular infiltration/

tion were present in one of these. No interstitial abnormality was noted in the third. Of the 3 older children with nephritis secondary to a septic condition, the kidneys in one showed a rather mild type of glomerular lesion, while in the other 2, both cases of streptococcal septicaemia, the most striking feature in sections was the presence of streptococcal plugs in the glomerular capillaries as well as in other capillaries in the kidney substance. In isolated instances the glomerular afferent arteriole could be seen distended with a plug of streptococcus which filled the arteriole and passed into its divisions as it ramified within the glomeruli. A large proportion of the glomeruli were involved in each case. The condition appeared more or less diffuse, with generalised swelling of the tufts though streptococcal plugs were not seen in all, though possibly they were present in many, but were absent in the particular plane in which sections were cut. Some glomeruli showed an older lesion in the form of small areas of hyaline necrosis involving individual glomerular loops, and indicating the site of an older bacterial embolus. The glomeruli in addition were the seat of abundant polymorphonuclear infiltration and endothelial proliferation, with albuminous exudate in some glomerular capsules. Regarding the tubules in the last 3 cases, in the first case with a mild glomerular lesion, the epithelium was of flattened granular type while the scanty tubules were the seat of hyaline droplet degeneration. A few small foci of round-celled infiltration were noted in this case

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in association with early fibroblastic proliferation, chiefly just under the capsule. On cutting frozen sections fat was scanty, occurring in the form of fine droplets in isolated convoluted tubules. In the 2 cases with embolic glomerular lesions, the tubular epithelium was the seat of cloudy swelling. In addition, in both cases red blood corpuscles and polymorphs were present within numerous tubules. The interstitial tissue was normal in one instance, and in another showed oedema and slight cellular infiltration. Apart from acute congestion and embolic bacterial plugs as described, no lesion was found in connection with the vessels. In the 3 nephritides secondary to peritonitis the glomeruli were all closely similar, showing enlargement and increased cellularity, while in some glomerular capillaries the lumina were occluded from endothelial proliferation. No bacterial emboli were noted in any of these cases. Marked haemorrhage into the tubules was a feature in 2 instances, but was absent in the third. Cloudy swelling of the epithelium was noted in all 3, products of cell disintegration being found within the lumina of some tubules. Slight oedema was the only interstitial lesion in all, and the vessels were normal apart from vascular engorgement.

Of the various septic lesions (33) 26 were free from a nephritic complication. In these, various degrees of degenerative tubular changes were present which could be graded into 13 of mild, 8 of moderate, and 5 of severe degree. The mild and moderate degenerative changes consisted of cloudy swelling, catarrhal/

catarrhal or vacuolar degeneration of the epithelium, while the more severe cases showed hyaline droplet degeneration, with much cell necrosis. The last group with severest tubular lesion comprised a case of umbilical sepsis with purulent infiltration of the surrounding tissues, a septic burn, septicaemia following cervical adenitis, septicaemia with a sloughing skin lesion, and osteomyelitis with septicaemia, lung abscesses and infection of the serous sacs. The infecting organism in these 5 cases was streptococcus in one instance, pneumococcus and streptococcus together in a second, staphylococcus in a third, while the organism was not determined in the other 2. Thus of the streptococcal infections (13) 4 gave rise to acute glomerular lesions, and 2 (one along with pneumococcus) to the most severe tubular damage; thus about half the streptococcal infections produced a severe renal lesion.

Of the 3 non-nephritic peritonitis cases the only degenerative change in the tubular epithelium consisted of cloudy swelling, mild in one instance, more severe in the other 2.

All varieties of septic lesions have been considered the etiological factor in the production of nephritis. The part played by tonsillitis and by skin lesions has already been described in the chapter on Etiology. Gray (1928) believes that though nephritis may be a rare complication in septicaemia, it may be more frequent in the streptococcal variety, and this would appear to be borne out in the small series described above. Russell (1929) finds in some bacteraemias that the majority of cases give microscopic evidence of nephritis, sometimes focal though more frequently general, and then of intense type. Brüning and Schwalbe (1913) report a case of nephritis in an infant after vaccination and mention similar recorded cases. Prowse (1932) and Addis and Oliver report nephritis following staphylococcal cellulitis. Volhard and Fahr (1914) found it developing after septic skin lesions the result of a small wound, after complicated fractures or other infected wounds. In the case in the above series where the infant developed nephritis after axillary abcess following vaccination it is possible that the carbolic dressing played a part in the production of nephritis since the kidneys of children and particularly young infants are prone to suffer damage from toxic substances used as external applications. (Abt, 1924.)

Nephritis in
Rheumatic Endocarditis (9 cases)
Ulcerative Endocarditis (1 case).

The kidneys were examined in 10 cases of endocarditis, 9 rheumatic and 1 ulcerative. 4 of these patients were of the male and 6 of the female sex, the ages varying between 3 years and 3 months and 10 years and 10 months. In 6 of these children a complicating nephritis was present, all in the rheumatic group. In these 6 cases at autopsy the heart was more or less enlarged, and vegetations were present on the mitral and tricuspid and sometimes on the aortic valves, various degrees of thickening and distortion of these structures being present, while the vegetations were of the typical small firm fibrous variety. In the case of the child with ulcerative endocarditis, the vegetations were large and florid and had spread to involve the wall of the left ventricle. Pericardial adhesions were found in some instances. In two cases pneumonia was a terminal event,and in another tabes mesenterica was present with a caseous glandular mass in the abdomen, but no sign of miliary spread. The macroscopic appearances of these 6 nephritic kidneys were rather variable. In one case they were slightly enlarged throughout, extremely firm in texture, with a deep red medullary portion and a paler cortex. Case 2 showed pale kidneys with firm cortices. Case 3 had slightly enlarged red firm kidneys with regular cortical markings and very slightly adherent capsules. Case 4 had rubber-like kidneys with deep red, rather wide cortices, with

no/

no distortion of the renal architecture and a smooth surface, from which the capsule stripped with ease. In case 5 the kidneys were the seat of typical cloudy swelling, and in case 6 swollen kidneys were found with wide cortices, which showed marked fatty change. The capsules in this case stripped readily.

Microscopically the lesion in all 6 instances was essentially the same, and was present in the form of a diffuse glomerulo-nephritis of only moderately severe type. There was no suggestion in any of these cases of the embolic focal type of lesion so frequently described in association with bacterial endocarditis. The glomeruli were all enlarged, lobulated and very cellular, both from endothelial proliferation and from polymorph infiltration. The tufts were rather bloodless on the whole, though in the 2 cases where chronic venous congestion was present intense congestion was noted in the majority of the glomerular capillaries. A striking feature in 4 of these cases was the presence in the capsule of Bowman of abundant albuminous exudate sometimes in sufficient amount to fill the capsule and apparently compress some of the glomeruli. The tubules in these cases were the seat of fairly well-marked degenerative changes, sometimes of the nature of cloudy swelling, and sometimes the epithelium was rather flattened and granular in appearance. Granular casts were seen in the lumina of some of the tubules. No haemorrhage was detected in any. The only interstitial change was occasional slight oedema with no proliferation or cell infiltration. The vessels were normal

apart/

apart from congestion. Frozen sections were stained for fat in 2 instances. In neither was it abundant, though small fatty droplets were seen in some of the tubules, (chiefly proximal convoluted) and in some ascending Henle loops in one instance, and in the other a slight sprinkling of small fatty particles was present in the distal convoluted tubules and in some collecting tubules. No doubly refractile lipoid was found in either instance. The urine was examined in 5 of these patients. In one instance a trace of albumin was present with no casts. In another albumin and blood were practically constant on daily examination for nearly 4 weeks, hyaline casts and some epithelial cells being found on microscopic examination. The third showed albumin and casts but no blood, although there was a history of passing "dark" urine. This patient had an attack of scarlet fever about 10 months ante-mortem, and was dismissed from the fever hospital with "diseased heart and kidneys." A 4th patient had been passing scanty dark-coloured urine before admission, but no further information is forthcoming on this point. The last case had albuminuria and haematuria on admission, the latter clearing in a few days, though the albuminuria persisted. Oedema was present in 4 of these patients, and was of cardiac type, though 2 in addition were puffy round the eyes, and in a third the oedema developed in the tissues of the chest wall and in the right arm and hand. In a few of these children, therefore, the urinary findings and the distribution of the oedema pointed to the presence of a nephritis.

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In the 4 remaining cases, including the one instance of ulcerative endocarditis, where nephritis was not found, histologically the kidneys were the seat of slight chronic venous congestion and the glomeruli were normal or slightly engorged with blood, the only noteworthy lesion being a moderate degree of catarrhal change in the secretory epithelium with slight oedema of the interstitial tissue in one instance.

Baehr and Lande (1920) state that 3 diseases are distinguished from all others by the frequency with which they are complicated by acute haemorrhagic glomerulo-nephritis -scarlet fever, acute and chronic streptococcal angina, and subacute streptococcal endocarditis, and they emphasize the frequency of diffuse glomerulo-nephritis as a complication of subacute endocarditis due to streptococcus viridans. In a series of 77 cases of this disease, 9 patients (11.5 per cent.) died in uraemia from an intercurrent acute or chronic glomerulo-nephritis. Acute nephritis in their cases occurred only in the stage when streptococci were still in the circulating blood. This is the period at which embolic glomerular lesions are also found, and the authors believe that the latter themselves render the glomeruli more susceptible to the engrafting of an intercurrent acute glomerulo-nephritis.

Baehr (1921) describes another group of 6 cases in the above series of 77, where as many as from 60 to 90 per cent. of the glomeruli were involved in the embolic glomerular process

not
in each kidney, the histological picture being/unlike an acute glomerulo-nephritis at first sight, though closer examination showed the lesions were almost all of embolic type, Even where almost all glomeruli are more or less damaged by the embolic process, the function of the kidney may be unaffected, since unlike true glomerulo-nephritis, in the uninvolved portions of the damaged glomeruli blood continues to circulate through the capillaries, thus sufficing to maintain renal function. Baehr concludes that the development of renal insufficiency in patients with subacute endocarditis is evidence of a diffuse glomerular lesion.

Goldring (1931) reports 2 cases where rheumatic fever was complicated by acute diffuse glomerulo-nephritis, though he believes this type of renal lesion a rare complication of the disease.

Volhard and Fahr (1914) consider that if larger arterial twigs are blocked by bacterial masses miliary abscesses form, and if a suppurative process remains absent, it is only on account of the slight chemiotactic action of the bacteria, and the small numbers in which they are present, transition readily taking place from an embolic non-purulent to an embolic purulent lesion. These authors also describe the occurrence of mixed forms of nephritis. Thus in one case amyloid change was present along with nephritis of embolic type, and also true inflammatory processes were present in glomeruli not the seat of emboli. Volhard and Fahr consider

embolic/

embolic focal nephritis the only haematogenous renal disease of quite definite etiology, but not the only result of this particular etiological factor, since with infective endocarditis all other possible renal changes can occur, though they believe that the eminently chronic course of infective endocarditis is hardly influenced by the renal condition, which is only one of the complications possible.

Gray (1931) like Volhard and Fahr, in his experience of endocarditis finds not only the type of lesion due to infarction by vegetations described by Löhlein as embolic non-suppurative focal nephritis, but also the more ordinary focal bacterial lesions seen in focal nephritis in general, the latter being more common than Löhlein's type with small infarcts.

Councilman(1897) similarly found in staphylococcal infarctions that an intense focal inflammatory reaction may be seen round emboli of bacteria, while in addition a diffuse lesion may be present as a result of soluble toxins present in the blood-stream.

Russell (1929) also in describing a series of cases of acute infective endocarditis found in a number pyaemic abscesses arising from glomerular and other capillaries while some glomeruli showed nephritis of acute or "acris" type. This author also investigated 31 cases of subacute bacteraemic endocarditis, and found a focal type of lestion in 17 cases, and a diffuse nephritis in 12.

Addis and Oliver (1931) believe that toxic substances may produce/

produce by means of capillary thrombosis lesions in the glomerular tufts which are essentially similar to those due to the actual presence of bacteria, and they consider further that in bacterial endocarditis as in any septic infection the bloodstream is flooded by toxic products, and it is therefore not surprising that a diffuse glomerulo-nephritis is frequently found; or that mixed cases also occur where, besides focal embolic nephritis with necrosis of some loops, in other tufts is present diffuse nephritis of intra- and extra-capillary type.

Nephritis associated with Congenital Syphilis (5 cases).

The 5 cases of congenital syphilis in this group all occurred in young infants, 2 being 1 month, 1 6 weeks, one 2 months, and 1, 4 months of age, while 4 of these patients were of the female, and 1 of the male sex. One case showed no noteworthy renal lesion, either on naked-eye or on histological examination and need not be further discussed; while other 2 cases with a mild acute interstitial lesion have already been described in the section dealing with this type of lesion. An acute glomerular lesion was present in the two remaining cases, associated in one of these with small interstitial abscesses. At autopsy the kidneys in the latter were congested with small haemorrhagic points, and in the former the organs were pale but otherwise healthy, and on histological examination, showed intense congestion of the glomerular capillaries which were intensely engorged while albuminous exudate was present in the capsule of Bowman, with loss of the epithelium covering the tuft. The secreting epithelium was the seat of cloudy swelling with some granular débris in the lumina of a number of tubules. In the other case, the glomeruli appeared swollen and cellular though not all equally enlarged. In isolated instances the glomerular capillaries were greatly distended with blood, with, in very rare glomeruli rupture into the capsule of Bowman, the latter being distended by haemorrhage.

Groups/

Groups of convoluted tubules in this case were filled with red blood corpuscles and cloudy swelling was the chief epithelial change. In the interstitial tissue were present small abscesses in which were seen plugs of cocci of undetermined type and the tubules in these regions contained collections of polymorphs, the lesion here apparently being of embolic focal type with abscess formation where the cocci were most abundant. No bacterial emboli were seen in the glomeruli. In these 2 instances the type of lesion had nothing specially characteristic of congenital syphilis and might be related to the respiratory or skin lesions in one case or to extensive excoriation about the mouth and nose in the other. Of the 2 cases with acute interstitial nephritis, one may be dismissed as this was the only lesion present. In the other, a female infant aged 1 month in addition to the acute interstitial nephritis there was present an apparent slight delay in development since here definite traces of a neogenic zone could still be seen immediately under the capsule, being present in the form of scanty tubules with a foetal type of epithelium while a few primitive glomeruli at different stages were also found. Various writers have described developmental delay in the kidneys of congenital syphilitic infants, though the subject is controversial as other authors maintain that development does not cease at birth, but can go on to the third month of extra-uterine existence, Mayer (1903) though this author agrees that syphilis plays an important rôle in developmental delay.

Stroebe (1891), Stoerk (1901) and Cassel (1904) have all studied the renal lesion in syphilitic infants. The first-mentioned writer describes the case of a congenital syphilitic infant living only half an hour after birth. The skin was covered with a pemphigoid eruption and the lungs were the seat of syphilitic interstitial pneumonia with the inclusion of remnants of foetal tissue. The kidneys were of normal size and appearance, with marked foetal lobulation, and the capsules stripped easily without loss of the underlying substance. Microscopic examination showed marked increase of nuclei compared with control kidneys of the same age, along with interstitial fibrous proliferation following chiefly the course of the interlobular arteries. In addition, peculiar folded and coiled hollow structures lay in a continuous layer directly under the capsule though present elsewhere in the cortex in isolated patches. These structures represented the "neogenic zone" of which the author found no trace in normal kidneys of children of the same age, where the glomeruli were ripe, though some of these structures and the tubules were still rather small. In the case in question Stroebe believes that the kidney would correspond in development only to that of a 4 months' embryo. He explains delay in development on the grounds of interstitial overgrowth resulting from the action of the syphilitic toxin.

Stoerk/

Stoerk (1891) investigated the kidneys of children with congenital syphilis, and as a control about 3 times the number of non-syphilitic infants. He finds as a distinguishing feature between the 2 groups, delay in development in the syphilitic cases. He believes that normally by the 9th or 10th lunar month a neogenic zone is no longer demonstrable, the foetal connective tissue having disappeared and the primitive glomerular anlage having ripened until finally, closely-packed young glomeruli are seen under the capsule, with only isolated embryonic structures. The present writer's experience agrees with this last fact, since she found that in young infants during the first few months of life, the newly ripened glomeruli are closely packed in a zone under the capsule, where isolated glomerular anlage are still to be seen.

Stoerk finds in some syphilitic cases a partly diffuse, and partly focal round-celled infiltration throughout the whole kidney substance and these cells are accompanied in some instances by red blood corpuscles, suggesting diapedesis from the vessels.

Cassel (1904) also finds some delay in renal development in congenital syphilis, the neogenic zone in his opinion vanishing normally at the end of the 9th month of foetal life. He describes in such cases along with delay in development inflammatory instertitial proliferation of varying degree though often quite/

quite slight. On naked-eye examination such kidneys rarely appear abnormal, and clinical symptoms of nephritis are seldom present.

In the clinical history of the 4 syphilitic cases with associated renal lesions in the present investigation, oedema was noted in only one instance, that of the patient with the remnant of the neogenic zone along with the interstitial cell infiltration. In this case the lungs in addition were the seat of new connective tissue overgrowth recalling Stroebe's case, just mentioned. The quantity of urine was diminished in this child, though no other information is available with regard to the urinary findings, and the naked-eye appearances of the kidneys are not mentioned here. In the other patient with an acute interstitial lesion the kidneys were acutely congested. The child with the haemorrhagic type of lesion had kidneys suggesting, on naked-eye examination, an acute nephritis and a trace of albumin was present in the urine, a few red and white cells being present on microscopic examination. In the other two syphilitic patients, no urinary abnormality was found.

Hutinel (1922) agrees that small infants with a syphilitic renal lesion show practically nothing of note clinically, and without doubt in his opinion, it is to the persistence of small latent foci of infection in the kidneys of these young infants that most of the recrudescences of specific infection in the kidneys of older children are due, spirochaetes remaining dormant but capable of awakening under/

under the influence of various stimuli. He finds that albumin is sometimes present in the urine of syphilitic infants, especially in association with modifications of the glomeruli and tubules.

Warthin (1922) believes that spirochaeta pallida is excreted in the stage of syphilitic septicaemia both in congenital and acquired syphilis, but as the organisms are largely destroyed few may reach the urine.

Miller and Hay (1930) have also demonstrated spirochaetes in the kidney tubules in a man of 47, with a history of venereal infection 20 years previously, and consider the presence of the spirochaetes unusual after such a long interval.

In later childhood syphilitic nephritis sometimes has an acute course and behaves like ordinary nephritis on a specific foundation. Sometimes the course is subacute and sometimes chronic.

Weiss (1931) insists on the fact that naked-eye examination of the kidneys in syphilitic infants is quite inadequate in determining the true state of these organs. He distinguishes between foetal and infantile syphilis, the first being characterised by persistence of the neogenic zone, the latter by proliferation of the interstitial tissue with perivascular infiltration, the renal parenchyma rarely being attacked, so that clinical evidence of renal disease is rarely forthcoming though since syphilitic infants are specially prone to super-added infection and to digestive troubles, such non-specific factors/

factors can frequently cause a pathological condition of the urine which has no relation to the primary renal disease.

In a further article (1932) this author states that where the renal parenchyma was extensively involved in the disease process, he saw marked albuminuria, though the striking feature of such cases was the abundant blood in the urine, which he never failed to find, and he regards erythrocyturia as the hall-mark of all clincally manifest cases of congenital syphilis in infancy. White blood corpuscles, casts and abundant detritus are also often present. Hydropic manifestations are often found among other renal symptoms, though he attributes this in part to the associated marasmic condition, death in such cases generally being due, not to the renal complication but to the underlying disease. He considers that in congenital syphilitic infants an interstitial renal lesion is the only pathognomonic type of congenital syphilis.

Ballantyne (1902) quotes Hecker who saw acute lesions in every one of 10 dead-born syphilitic foetuses, and also found that the earliest abnormality was a small-celled infiltration round the smaller vessels of the cortex and sometimes round the larger vessels in the medulla with a frequent co-existing proliferation of the interstitial connective tissue and an endo- or peri-arteritis of the smaller vessels of the cortex.

According to Hutinel sclerosed kidneys in childhood awaken the idea of specific disease, but renal atrophy can have other origins. In the type due to congenital syphilis the dominant/

dominant lesion is a sclerosis more or less advanced in which can be seen here and there young elements and heaps of round cells which appear to result from acute exacerbations. The fibrous tissue predominates round the vessels, and endarteritis obliterans and peri-arteritis are present with fibrous bundles radiating between the tubules and glomeruli.

A subacute type of Nephritis with alterations in the secreting epithelium, as well as an interstitial lesion, is also described by Hutinel in older children and this approaches a variety of syphilitic renal disease found in adults. Munk (1913) reports 14 cases of the latter type where clinically oedema, anaemia and weakness were associated with abundant albumin and casts chiefly of lipoid type, and along with red and white blood-cells in the urine, while the kidneys at autopsy were of the "large white" variety with much lipoid in the tubules, the glomeruli and interstitial tissue being intact. This lesion can be cured, can last for months or years with no marked change in the general condition, or can become subacute or chronic, while any of these stages can be associated with amyloid disease.

Sawyer (1903) regards adult renal syphilis as a nephrotic type with abundant albumin, all kinds of casts, only a small amount of blood, and much oedema.

The characteristic type of syphilitic renal lesion in the young infant would appear to be an acute interstitial nephritis, and sometimes at least such kidneys show delay in development/

development, the kidneys at birth still representing a considerably earlier developmental stage, while in older children tubular lesions tend to predominate as in adults, with a syphilitic renal involvement.

Nephritis in
Meningitis (11 cases).

In this group of meningitis cases,7 males and 4 females, the ages varied between 8 weeks and 4 years. A meningococcal infection was present in 5 (3 being of posterior basic type), 4 were of pneumococcal, 1 was of influenzal and 1 of streptococcal type. Nephritis occurred in 4 of these combined cases, in 2 patients with a meningococcal infection and 2 with a pneumococcal infection. In the first 2 children, aged 20 weeks and 8 weeks respectively, the kidneys showed an appearance suggestive of cloudy swelling in the first and congestion in the second on naked-eye examination. Histologically in the case of the first-mentioned infant the glomeruli were enlarged, swollen and congested, with complete loss of the epithelium covering the tufts so conspicuous at this age. An occasional red blood corpuscle or desquamated epithelial cell was found in the capsule of Bowman, and red blood corpuscles were also seen in small numbers in the lumina of some tubules, which showed degenerative changes in the secreting epithelium, the cells being swollen, granular and vacuolated with loss of many nuclei. The instertitial tissue showed no lesion of note. In the second case the glomeruli were also enlarged and swollen with definite proliferation of endothelial cells, many showing large irregular hyperchromatic nuclei and slight polymorph infiltration. The covering epithelial layer had disappeared also in this case. In this patient the kidneys appeared to be rather under-developed,

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an unusual number of immature glomeruli being seen just under the capsule. A few of these appeared as cystic structures with the remains of small flattened tufts. Some of these primitive glomeruli were apparently undergoing atrophy of ischaemic type, as if the arterioles supplying these were also defective, small groups of glomeruli supplied by the same arterial branch being similarly affected. It would appear that this kidney was of rather under-developed type and hence a more ready prey to an acute inflammatory complication. The tubules here showed no noteworthy lesion, and the interstitial tissue was normal apart from the areas round the sclerosed glomeruli described above, where patchy interstitial fibrosis was noted with slight cellular infiltration. It is of interest that of these 2 patients the first showed evidence of septicaemia, a purpuric eruption being present with a purulent arthritis of the left ankle joint, pus from which yielded meningococci in films and on culture. In the second patient the lesion was of a more chronic type, with abundant and extensive adhesions around the base of the brain, meningococci being present in some of the pus cells. No oedema was noted in either of these infants. The urine of one contained a trace of albumin; in the other the amount obtained was insufficient for tests.

Of the 2 pneumococcal meningitis cases associated with nephritis one concerned a child of 2 years and 8 months and the other a child of 3 years and 4 months. In the first patient meningitis resulted from a fall, and in the second

an/

an otitis media was present with discharge from both ears. In both instances the kidneys were swollen and in one numerous petechial haemorrhages were present along with generalised congestion, while the other showed mottling but no distortion of the renal architecture. The usual appearances of diffuse acute glomerulo-nephritis were present in both on histological examination, while both had abundant blood in the convoluted tubules and both fresh blood corpuscles and blood casts in the collecting tubules. In each a very slight cellular infiltration was present in the interstitial tissue. No oedema was noted in either patient during life. The urine of both children contained albumin and blood, and blood and epithelial casts on microscopic examination. (In the second case abundant blood was present in 10 specimens examined). In this patient also the Non-Protein Nitrogen was 76 mg. per cent., and the blood pressure was raised, varying from 104 to 128 systolic and from 70 to 88 diastolic. Urea excretion was within normal limits. In this case, therefore, the urinary findings were suggestive of the presence of a complicating nephritis though oedema was absent.

Blackman and Rake (1932) mention pneumococcal meningitis as one of the pneumococcal lesions complicated by nephritis in infancy, though in adults the kidneys are less susceptible to damage by pneumococcal toxins.

In the remaining 7 meningeal cases, 3 meningococcal, 2 pneumococcal, 1 influenzal, and 1 streptococcal, the last following otitis/

otitis media and mastoiditis, well-marked cloudy swelling was the only lesion seen in 5 instances and in the other 2 hyaline droplet degeneration affected a few isolated tubules.

Masterman (1932) mentions a case of meningitis associated with hematuria in a child aged 3 years who developed acute tonsillitis. Shortly thereafter, oedema was noticed in the face and eyelids, and herpes appeared round the mouth. Abundant blood and albumin were present in the urine, and the condition was thought to be haemorrhagic nephritis associated with tonsillitis. About 10 days after the onset of nephritic symptoms the child became very irritable, with flexed limbs and rigid neck muscles, while the cerebrospinal fluid appeared to be under increased pressure and contained abundant leucocytes. The condition improved but there were periodic relapses, and the cerebrospinal fluid contained numerous polymorphs, though it was always sterile. Finally about 3 months after the onset of meningeal symptoms, ventriculography was performed and internal hydrocephalus diagnosed. Masterman believes that the onset resembling acute haemorrhagic nephritis was probably a manifestation of meningococcal septicaemia which ran a prolonged course and improved after ventriculography. In favour of a meningococcal meningitis were the labial herpes at the start, the nuchal rigidity and the large numbers of polymorphs in the cerebrospinal fluid. Though no meningococci were seen in films or on culture it is a well-known fact that meningococci can be very scanty in some cases.

Wallgren (1920) reports 3 cases of meningococcal meningitis/

meningitis, 2 in adolescents and one in a child aged 5 years. The meningitis in all 3 cases was preceded by nephritis, the cerebral symptoms suggesting uraemia. The last mentioned patient, 5 years old, had always been well until oedema was noted in the face and eyelids, and was so marked in the latter that the patient could not open his eyes. Blood, albumin, and granular cysts were present in the urine. After a few days' illness intense headache began with malaise and the child was admitted to hospital as a case of haemorrhagic nephritis with uraemia. As a positive Kernig's sign was present a lumbar puncture was done when meningococcal meningitis was diagnosed. Despite treatment with anti-meningococcal serum the child died, and at autopsy meningitis was found with much pus at the base of the brain and in the dilated ventricles. The kidneys on histological examination showed glomeruli infiltrated with red cells and the tubular epithelium was the seat of degeneration with scanty red blood corpuscles in the lumina. It appeared that the nephritis and meningitis owed their origin to the same source -- a blood infection with meningococci. Many textbooks state that in epidemics of meningitis, haemorrhagic nephritis appears as a complication in some instances. It is also known that meningococci can exist in the blood causing a septicaemia sometimes before the onset of meningitis, and to this blood infection Wallgren attributes the haemorrhagic nephritis preceding meningitis in his cases. He also states that meningococci have been isolated from various unusual sites including joints, and this is confirmed by the present/

present writer's case first described where meningococci were isolated from the swollen left ankle joint. An extensive purpuric skin eruption was also present, so this case would appear to resemble those described above by Masterman and Wallgren, though here the nephritic element was obvious only on histological examination, when haemorrhage was found in some tubules along with swelling and increased cellularity of the glomeruli.

Nephritis in Diphtheria.(3 cases).

Only 3 cases of laryngeal diphtheria are included in the present series, and of these one, a female child aged 23 months, showed early glomerulo-nephritis of mild type, the kidneys on naked-eye examination being dark red and swollen, with yellowish mottling of the cortex, and blurring of the markings.

Histologically the glomeruli were slightly enlarged and digitate, with some cellular increase, chiefly from endothelial proliferation, though, in addition, slight polymorphonuclear infiltration was present. The epithelium covering the tufts was lost. Abundant albuminous exudate was present in the capsule of Bowman, appearing in some of these as a crescentic layer, abundant enough in some instances to compress the tuft and extending into the neck of the related convoluted tubule, where this was seen in sections. The tubular epithelium showed cloudy swelling. The interstitial tissue showed no evidence of cellular reaction, and apart from intense congestion of the intertubular capillaries the vessels were normal. The urine in this case was not examined, as the child died on the day of admission to hospital. In the other two children severe cloudy swelling of the tubular epithelium was the only lesion noted.

More than one type of nephritis is recognised in diphtheria. Feldmann (1921) observed 123 cases of diptheria and/

and found nephrosis in 15 of these (12.2 per cent.), and von Kahlden, Pfaundler and Schlossman, Volhard and Fahr, and Brüning and Schwalbe all mention diphtheria as a disease which frequently gives rise to a degenerative lesion in the renal tubules. Acute interstitial nephritis, as was shown in the appropriate section, is frequently associated with diphtheria. Thus Councilman (1898) found a varying degree of interstitial involvement in 24 of 103 cases of pure diphtheria and also saw this type of renal lesion in cases where diphtheria was combined with one of the other exanthemata. Muir (1933), among other authors, has described true glomerulo-nephritis in diphtheria, like the case mentioned above.

Nephritis in Pneumonia.

The renal lesion has been studied in 28 cases of pneumonia between the ages of 2 weeks and 9 years. Of these children, 7 were under 6 months and other 11 were under 1 year of age, while 19 were of the male, and 9 of the female sex. Broncho-pneumonia was the type of lesion present in all but 3 cases, and of these exceptions 2 had lobar pneumonia, and one had a chronic interstitial pulmonary lesion. Several cases were complicated by mild gastro-enteritis or by otitis, while in one patient a small right-sided interlobar empyaema was present. In another patient pneumococcal meningitis/

meningitis complicated the pneumonia, in another a large septic burn resulting from a poultice, while in a final case pneumonia followed the operation of appendicectomy and here marked fatty degeneration was present in the liver and kidneys, suggesting delayed chloroform poisoning. These last 3 cases as well as one of the two lobar pneumonias were complicated by nephritis. The kidneys in all 4 nephritis cases were described at autopsy as being extremely pale and mottled, and in 2 cases swelling was present which involved all parts of the kidney, though particularly the cortices. Histologically, the glomeruli in all cases showed varying degrees of inflammatory change, though in no instance was the lesion of a very intense nature. In one case the glomeruli were congested and very cellular, with numerous polymorphs in the tufts. In another albuminous exudate in the capsule of Bowman was the most striking feature, and in addition the capillaries appeared to be largely occluded by endothelial proliferation. A third showed marked glomerular enlargement with much cell increase and polymorphonuclear infiltration of the tufts,with, in addition, hyaline necrosis of an occasional loop. The fourth case was of a type similar to this last, but of a less severe degree. The tubules in all 4 showed degenerative changes. In the case following appendicectomy the secreting epithelium was granular and vacuolated, apparently from solution of fat droplets, (no frozen/

frozen sections were available here), with extensive areas of cell necrosis, the nuclei having disappeared and the cells having desquamated into the lumina of the tubules. Bile pigment was also abundant in this case, both in the secreting and the collecting tubular epithelium. In two other instances cloudy swelling was the chief epithelial change, with red blood corpuscles and polymorphs in the lumina of some convoluted tubules. In one of these fat was present in groups of convoluted tubules and in the débris within their lumina. No anisotropic lipoid was found. Various types of casts were noted in the lumina of some tubules in all cases. The patient with the large septic burn showed fairly widespread hyaline droplet degeneration of the epithelium, and here also cellular infiltration of the interstitial tissue was a noteworthy feature, the cells being present both in small compact foci, and distributed more diffusely, the appearance suggesting a very early acute interstitial lesion, though secondary to the glomerular and tubular changes described above. An interesting feature of this case was the presence in the small capillaries of the cortex and medulla, of a great increase in the number of leucocytes, lymphocytes predominating, which were apparently the source of the cell collections in the interstitial tissue (Schridde and Councilman). Very slight diffuse cell infiltration was observed in another of the 4 nephritis cases, and/oedema interstitial occurred in the last two instances.

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In the remaining 24 patients no noteworthy glomerular lesion was found beyond slight albuminous exudate in the capsule of Bowman, in some, but the secreting epithelium showed varying degrees of tubular degeneration, "acute nephrosis" Gray (1933). In 14 instances the tubular lesion was slight, consisting generally of cloudy swelling, sometimes of minimal degree. In the remaining 10 patients, degenerative tubular lesions were more severe, the secreting epithelium showing marked cloudy swelling or vacuolar degeneration of the cell protoplasm, or being of flat granular type. In one case only, early hyaline droplet degeneration was noted. Hyaline and granular casts were present in some instances, but there was no noteworthy haemorrhage in any, and leucocytes were absent from the lumina of the tubules. The only interstitial change was a slight degree of oedema in some kidneys. It would appear from this series of cases that in children pneumonia, at least the broncho-pneumonic type, is not prone to lead to acute inflammatory lesions in the kidneys. Broncho-pneumonia is frequently a terminal event, but in the cases selected for this study, broncho-pneumonia was the primary lesion, and consolidation was generally fairly extensive. No uncomplicated case of broncho-pneumonia in this series was associated with nephritis, 3 of the 4 instances where nephritis occurred being associated with some other lesion, pneumococcal meningitis, septic burn, delayed chloroform poisoning and in the/

the fourth case lobar pneumonia, or at least pneumonia of lobar distribution, was present. This child was only 2 years old, and true lobar pneumonia is still rare at this age. Von Kahlden (1891), studying the renal lesion in both lobar and broncho-pneumonia found nephritis in the latter as well as in the former, though less severe in type in the broncho-pneumonic cases. The ages of the patients with nephritic complications were 2 years, 3 years, 3½ years, and 9 years respectively. In the 11 infants under 1 year of age, no special severity was noted in the type of epithelial lesion, even in a number of babies a few weeks old. Special attention was paid to this point, since Blackman and Rake (1932) found that young infants are particularly susceptible to pneumococcal infection, and in a series of 95 cases investigated by them, almost 10 per cent. showed severe nephritic changes histologically, though on naked-eye examination no gross abnormality was detected in the kidneys.

Blackman, Brown and Rake (1931) also succeeded in producing acute and sub-acute changes, comparable to nephritis in man, in a series of rabbits, by injection of an autolysate, obtained from pneumococci, and also by intradermal injections of pneumococci of types I, II, and III. In all of these animals pneumococci could be demonstrated in the capillaries of the kidneys, as part of a general septicaemia, though the effects of the autolysate alone prepared from type I pneumo-

cocci/

pneumococci were shown by hyaline and fibrous thrombi of the glomerular capillaries, with blood and fibrin in the tubules, and epithelial damage in the latter.

Oedema was not present in any of the 4 nephritic patients on clinical examination. The urine is mentioned in the case records in only 2 members of this group, albumin alone being present in one, and albumin with casts of unspecified type, and red and white blood corpuscles in the other. The majority of authors find that pneumococcal lesions are comparatively rarely followed by nephritis, and Volhard and Fahr consider it noteworthy that so few pleuro-pulmonary diseases which provide so many hospital cases, lead to nephritis. Von Kahlden (1891) quotes the collected figures of various investigators who studied the renal lesion in adult patients with pneumonia, and found the incidence of nephritis low. Thus Nauwerck in 550 cases of pneumonia found nephritis in 13 (2.4 per cent.), Rosenstein in 130 cases saw nephritis only twice (1.5 per cent.), while Wagner in 150 patients found nephritic complications in only 4 (2.6 per cent.). In Russell's (1929) series of 25 cases of lobar pneumonia nephritis occurred only in 4, and this incidence corresponds with that in the series of broncho-pneumonia in children under discussion. In Russell's group, parenchymatous degeneration was found in 18, and the kidneys were normal in 3 instances. Gray (1933) in 6 patients with lobar pneumonia, found tubular degeneration of/

of moderate or extreme degree, accompanied in one case by slight focal glomerulo-nephritis. In 8 patients with broncho-pneumonia this author found in the majority, only an insignificant degree of tubular degeneration, with no evidence of acute inflammation. The pneumococcus is considered, however, of some etiological significance, ranking next in importance to the streptococcus, in the opinion of some investigators, including Volhard and Fahr and Aschoff, though the virulence of the pneumococcus is much less than that of the streptococcus.

Nephritis in Gastro-enteritis.

Cases of gastro-enteritis were investigated to the number of 27, 14 of these being of the male, and 13 of the female sex, while the ages varied from 5 days to 7 years, 14 being under 6 months and other 5 between 6 months and 1 year of age. In this group acute nephritis was present in 3 instances. The first of these patients was a male child, aged 4 years, with a history of vomiting for 3 days, the second a male infant of 4 months, who had suffered from diarrhoea and vomiting for 10 days, and the third a female infant aged 27 weeks. In this last case a terminal broncho-pneumonia was also present, but the child had had previous intermittent attacks of vomiting and diarrhoea, and had been in hospital on several occasions on account of this condition in the last

few/

few months of life. No noteworthy abnormality was seen at autopsy in the kidneys of any of these children, except in the first case where the cortex was mottled as a result of fatty change in the tubules. Histologically in the first case the type of glomerular involvement was focal, some glomeruli being greatly enlarged, swollen, and bloodless, with marked cellular increase including polymorphonuclear infiltration. Others were only moderately enlarged, with well-filled capillaries. The tubular epithelium was the seat of marked cloudy swelling. In the other 2 instances a rather mild degree of diffuse glomerulitis was present, with enlargement and increased cellularity of the tufts, loss of the covering epithelium, and congestion of the capillaries. Cloudy swelling was noted in the secreting epithelium of both these cases with early hyaline-droplet degeneration in one, and a striking feature in both was the presence of haemorrhage into isolated convoluted tubules. The interstitial tissue and vessels were free from any noteworthy lesion. No oedema was noted clinically in any of these three children. A trace of albumin was found in the urine of the 4-year old patient, while pus was present in specimens from the other two children, and a coliform culture was obtained from the urine of each, though at post-mortem no sign of an acute inflammatory lesion was seen in the kidneys, renal pelves, ureters, or bladder of either. With regard to the remaining kidneys/

kidneys in this series (24), no abnormality was detected on naked-eye examination of any of these. Histologically, no glomerular lesion was detected in any, beyond slight congestion of the capillaries, or a little albuminous exudate, with or without a few degenerated epithelial cells in the capsule of Bowman. The secreting tubular epithelium was the seat of degenerative changes of varying degree, being severe or extreme in 8 cases, and mild or moderate in 15. The last case deserves special mention on account of almost complete aplasia of one kidney. This case has been previously reported in the section dealing with congenital abnormalities. Of the 8 children with severe degenerative changes, the most extreme degree was present in a female child aged 15 months with abundant albumin in the urine, who died after 3 days' illness, when generalised catarrh of the stomach and small and large bowel was found at autopsy, together with a left-sided pyelitis. The kidneys at post-mortem were extremely pale and fatty, the cut surface of the cortices being mottled from intermingled areas of fatty change and congestion, while the superficial stellate veins were engorged.

Microscopically the glomeruli appeared essentially normal, but the secreting epithelium showed almost complete coagulative necrosis with swollen, dead, structureless cells projecting into the lumina of the convoluted tubules, thus reducing them to mere slits. The normally stained nuclei in the collecting tubules and in the glomeruli contrasted markedly

with the eosinophil-staining, structureless, secreting epithelium, where only the basement-membranes and the cell outlines were visible. Such severe tubular changes are sometimes designated by the name of acute tubular nephritis, but the writer prefers Gray's (1933) term, "acute nephrosis", as in the case just described, there was no evidence of anything in the nature of an inflammatory reaction. Another case showed marked tubular degeneration with extreme cloudy swelling, and actual necrosis of a fair proportion of cells, many of these having desquamated, thus producing marked structural distortion. In another instance early hyaline-droplet degeneration involved a number of convoluted tubules. In frozen sections of this kidney a ring of fat droplets was present next the basement-membrane, in the majority of the convoluted tubules. In the remaining five cases of this group of 8, severe cloudy swelling or vacuolar degeneration of the secreting epithelium was evident, though with little actual cell death, much protoplasmic débris being present in the lumina of many tubules, in the form of droplets or casts. In the other 15 patients no lesion was detected beyond slight degenerative changes of the secreting epithelium, which was generally the seat of cloudy swelling though sometimes rather flattened and granular. Frozen sections of one of the kidneys in the above group of 15 were examined for fat, but this was negligible in amount.

The importance attributed by some of the text-books

on/

on Paediatrics to gastro-enteritis as an etiological factor in the nephritis of infancy, has already been mentioned, in the section dealing with etiology. Among other writers on the subject, Koplik (1902) believes that nephritis as a complication of gastro-enteritis is much more frequent than generally recognised, often appearing early in the course of this disease. In mild cases, albumin may be the only evidence of renal damage, though uraemic manifestations and oedema of the extremities may supervene in severe cases. The prognosis, according to Koplik, is generally good. Czerny and Moser (1894) believe that various forms of nephritis complicate gastro-enteritis, when not only albumin but hyaline and granular casts, and red and white blood corpuscles are found in the urine, while blood is occasionally present in amount sufficient for macroscopic recognition. These authors rarely observed oedema in such cases. As, however, they frequently saw masses of micro-organisms in sections, associated with foci of cell infiltration the possibility is that some of their cases were of the nature of pyelonephritis. Felsenthal and Bernard (1894) found varying amounts of albumin in the urine of the majority of children with gastro-enteritis, though this was abundant only in the more chronic cases. They never saw gross haematuria in such patients though red blood corpuscles were sometimes present on microscopic examination of the sediment. Oedema was often seen in the face and lower limbs, but they emphasize the importance of distinguishing nephritic/

nephritic from marantic oedema. Though in most of the cases they describe histologically, tubular degenerative changes predominated, in at least 3 instances glomerular involvement was evident with marked haemorrhage into the tubules, and one of these cases showed, in addition, interstitial cell-infiltration. In nephritis associated with gastro-enteritis the underlying factor would appear to be toxic absorption from the alimentary tract. Nephritis in adults has also been described in severe gastro-intestinal lesions with marked toxaemia. Thus Brown, Eusterman, Hartman, and Rowntree (1923) report a series of cases of nephritis associated with pyloric or duodenal obstruction, in some of which, along with glomerular involvement, foci of round-cell infiltration were noted as in Felsenthal and Bernard's case mentioned above. Zeman, Friedman and Mann (1924) diagnosed toxic degenerative nephrosis in 4 cases of pyloric obstruction where histologically an extreme degree of cell necrosis was evident, the lesion here closely resembling that of the child in the present series with extensive coagulative necrosis of the secreting epithelium, though the dead cells in the adult kidney showed deposits of calcium salts not present in the child. Fox, Mantel and Rabens (1931) also report renal involvement in an adult with strangulation of a loop of small bowel in an inguinal hernia.

Renal damage from absorption of toxins elaborated in the bowel, would therefore appear to result both in children and/

and in adults, though in the former, a relatively mild catarrhal condition of the gastro-intestinal mucosa apparently suffices to determine either a true nephritis or an acute nephrosis with almost total necrosis of the secreting epithelium, while in adults a similar degree of renal damage is seen only in severe obstructive lesions. This severe renal involvement in children, in view of the relative mildness of the underlying inflammatory lesion, would bear out the fact that the kidneys in young subjects have a minimal power of resistance.

Nephritis in Tuberculosis. (12 cases).

12 cases of tuberculosis were investigated, 6 of these in male and 6 in female children, between the ages of 5 months and 10 years. 3 cases of nephritis occurred in this group, one of which has been already described (acute interstitial nephritis associated with tabes mesenterica), and will not be further mentioned here. In another patient the kidneys were the seat of an early sub-acute nephritis associated with slight amyloid degeneration. In the 3rd early acute glomerulo-nephritis was present. The case of sub-acute nephritis occurred in a male child aged 10 years, with marked kyphosis. Pott's disease had been present since the age of 2, and a discharging sinus had developed in the right thigh about

3/

3 years ante-mortem. The child was admitted suffering from oedema, with a history of passing blood per rectum. The urine, which was diminished in amount, contained abundant albumin and fairly numerous casts of epithelial and granular type with, in addition, many epithelial cells and leucocytes. There was no mention of haematuria while the child was in hospital, though the urine was "dark" before admission to the wards. The renal efficiency was impaired in this patient, the result of the pigment test being low, only 32 per cent. of pigment being excreted in 2 hours, though excretion of urea was approximately normal - 2.4 per cent. in 2 hours. Pneumococcal peritonitis proved a fatal complication. The kidneys at autopsy were slightly enlarged, with swollen cortices, fatty and catarrhal tubular changes giving the cut surface a mottled appearance. On microscopic examination the glomeruli were swollen throughout, with an increase of cells in the tufts, the capsules in some instances showing epithelial crescents while varying degrees of adhesion were noted between capsules and tufts. In addition, amyloid degeneration of slight degree was seen in the capillaries of some glomeruli, the afferent glomerular arterioles also being affected, and to a slight extent the basement membranes. The renal tubules were lined by a flat granular type of epithelium, and much débris was present in the lumina. Many convoluted tubules also contained casts, chiefly of hyaline type. The interstitial tissue was oedematous, with foci of round-cell/

round-cell infiltration. Amyloid degeneration is of rare occurrence in childhood. According to Brüning and Schwalbe, it occurs as in adults, in cases of cachectic disease such as tuberculosis, syphilis, and bone suppuration. In one of Eckstein's cases previously mentioned, amyloid degeneration was well marked in the kidneys of a child with a mixed tuberculous and luetic infection, while Addis and Oliver report a case in a child of 10 with tuberculous disease of the spine, and a draining sinus, as in the case at present under discussion. The 3rd case of nephritis in this series occurred also in a male child aged 10 years with extensive tuberculosis of the lungs and thoracic glands, widespread miliary tuberculosis and tuberculous meningitis with tuberculomata in the cerebellum. The kidneys in this case were enlarged, with broad cortices of rather mottled appearance, in which were found scanty miliary tubercles. Sections showed diffuse swelling of the glomeruli, the noteworthy feature of which was extensive engorgement with blood, though no haemorrhages were seen into Bowman's capsule. In the tubules, marked cloudy swelling was the only lesion found, and the interstitial tissue was normal apart from slight oedema. The intertubular capillaries were all intensely congested. Fat was negligible in amount in frozen sections. There was no history of oedema in this case, and specimens of the urine examined contained no albumin or blood, while microscopically, only a few leucocytes were seen.

The remaining 9 cases of this series showed only varying degrees of epithelial degeneration, chiefly of the nature of cloudy swelling of mild or more severe degree, though miliary tubercles were abundant in some of these kidneys. In one instance, in an infant aged 10 months, with tuberculous ulceration of the bowel, and tabes mesenterica, with generalised miliary spread, slight cellular infiltration of the interstitial tissue was present, small areas of round, plasma, or large mononuclear cells being diffusely scattered both in the cortex and at the cortico-medullary junction, while similar cells occurred also in small foci often periglomerular in distribution, while some of the larger vessels were surrounded by a "cell mantle", thus indicating diapedesis from the vessels. In this case no large or striking cell masses were present as in the case of acute interstitial nephritis belonging to this group and already reported, though possibly a similar condition was present here at a very early stage. The kidneys in this case at autopsy were not enlarged, the only abnormality being extreme pallor of the organs.

Nephritis is occasionally mentioned in the literature, in association with tuberculosis. Volhard and Fahr, as already stated, found acute interstitial nephritis in a tuberculous patient. These authors believe that the toxins of the tubercle bacillus are perhaps responsible for the inflammatory renal lesion sometimes associated with this disease, and the breakdown/

breakdown of caseous material for the degenerative processes, though they are not prepared to state how far the specific tuberculous toxins produce degenerative changes, or to what extent associated streptococcal infection is responsible. They would be inclined to stress this last possibility, were it not for the fact that various investigators have shown that tuberculin injections can produce haemorrhagic nephritis. Jasienski (1930) found symptoms of nephritis only exceptionally in tuberculous patients. He believes that the kidney can excrete with the urine, tubercle bacilli toxic for guinea pigs, without itself developing a tuberculous lesion. He mentions instances where animal inoculation with the urine of phthisical patients confirmed the presence of tubercle bacilli though no sign of tuberculous involvement was seen at autopsy in the kidneys or genital organs of these individuals. In other cases, kidneys the seat of neoplasm or calculus formation eliminated tubercle bacilli, though on removal at operation no sign of renal tuberculosis was found. Holten (1924) describes haemorrhagic nephritis alone, or with amyloid disease in tuberculous patients. He regards the former as a not very rare complication, sometimes arising after pleurisy or haemoptosis, and occurring at all stages of phthisis, the prognosis of the case depending on that of the pulmonary condition. He regards amyloid disease as the most frequent complication of tuberculosis, haemorrhagic nephritis coming next in order of/

of frequency, and other forms of renal inflammation being rare. Anderson (1932) reports a case of tuberculous meningitis in a patient aged 26 years, tubercle bacilli being found in the cerebrospinal fluid, along with an increase in the lymphocytes. Some weeks after the patient was admitted to hospital, the face and eyelids swelled, and albumin was found in the urine. The patient was dismissed but was re-admitted later with acute nephritis, persistent albumin and abundant blood being present in the urine. Here, however, a mild attack of influenza intervened between the meningitis and the onset of nephritic symptoms, so the former cannot be excluded as a possible etiological factor. Gray (1933) found in 3 cases of acute miliary tuberculosis acute nephritis of very low grade and of focal distribution, in one instance in addition to tubular degeneration. Nephritis, however, would appear to be only a rare complication of tuberculosis in children, only a slight degenerative tubular lesion being noted even in kidneys the seat of multiple miliary tubercles.

Nephritis in Blood Diseases (9 cases).

Naegeli (1923) considers that anaemia in rare instances may induce the onset of nephritis, so the kidneys of patients with various blood diseases were investigated for any possible nephritic complication. This group comprises 2 cases of lymphatic/

lymphatic leukaemia, one of von Jaksch's anaemia, one of Banti's disease, with haematemesis and anaemia, 2 of anaemia gravis, and 3 of melaena neonatorum. The ages in this group varied from 3 days to 6 years, 6 patients being under 1 year of age. Of these 9 children 3 were of the male, and 6 of the female sex. Nephritis was not present in any instance, but features of interest were found in some, of which a brief description will be given, first dismissing the cases with no noteworthy lesion. The 3 cases of melaena neonatorum, and the one of Banti's disease showed merely a mild degree of tubular catarrh. In a further case of anaemia gravis the epithelium was rather flattened and granular, with a good deal of cell necrosis, and desquamation. The 4 remaining cases, 2 of anaemia and 2 of lymphatic leukaemia are of some interest. The case of von Jaksch's anaemia occurred in a female infant dying at the age of 43 weeks. Purpuric spots were present on the trunk, and a large haemorrhage had occurred into the substance of the thymus. The red cells were reduced to 2,310,000 per c.mm.; the haemoglobin to 36 per cent., while the blood platelets numbered 36,000 per c.mm. At autopsy scanty small cysts which appeared to be of congenital origin were confined to the left kidney. Both organs otherwise appeared normal except for extreme pallor. Histologically, foci of embryonic tissue were found along with lymphocytic infiltration and an imperfect attempt at follicle formation. The microscopic characters of this kidney have already/

already been fully described, in the section of congenital abnormalities. The other anaemic child, aged 14 months, had kidneys which appeared normal at autopsy, except for pallor. On histological examination, sections on the whole presented an appearance normal for the child's age, the glomerular epithelium having lost the characteristic appearance of the infantile kidney. In a few areas, however, the appearances were exactly those of a kidney immediately after birth, the glomeruli being small, with a prominent covering epithelium, and crowded together from lack of expansion of the tubules; in such foci glomerular anlage were present. A few of these primitive glomeruli were the seat of sclerosis with thickening of the capsule, and adhesions between capsule and tuft. Throughout this investigation it has been shown that primitive glomeruli are specially prone to degenerate. Of the two remaining cases of lymphatic leukaemia, one occurred in a girl aged 6 years, with marked general glandular enlargement and infiltration of the liver and spleen, while button-like nodules of lymphoid tissue were present in the bowel wall. The red cells numbered about 2 million per c.mm., while the leucocytes reached the high figure of 118,000 shortly before death, nearly 100 per cent. of these cells being lymphocytes. The other patient was a male child aged 2 years with an aleukaemia type of leukaemia, the leucocytes in this case numbering only 1,400, and the red blood cells half a million, while the haemoglobin

was/

was reduced to 10 per cent. shortly before death. No noteworthy glandular or tissue involvement was noted post-mortem in this case. In the first case the kidneys were swollen, with abundant petechial haemorrhages in the subcapsular cortices, which were slightly broadened and pale, with well-defined pink medullary regions. There was no suggestion on macroscopic examination of massive lymphocytic infiltration of these organs, though a patch of leukaemic infiltration into which haemorrhage had occurred was present in the right renal pelvis, and the left pelvis showed petechiae, the blood present in the urine evidently coming from these pelvic haemorrhages. The appearance of the kidneys post-mortem was not mentioned in the other case.

Microscopically, the kidneys in both cases showed well-marked leukaemic infiltration, much more marked in the first patient, where the glomerular capillaries appeared to be filled with lymphocytes, and the vessels throughout sections were seen as dark streaks, from their abundant lymphocytic content. These cells appeared to be present almost to the exclusion of red blood corpuscles. Foci of cell infiltration were found immediately under the capsule, but were most abundant at the cortico-medullary junction, where larger cell masses were present. Sections of the liver, spleen, bowel, and glands showed similar lymphocytic infiltration.

In the aleukaemic case, small patches of cell infiltration were found, chiefly at the cortico-medullary junction, the/

the cells being mainly large lymphocytes. The spleen, liver, glands and bone marrow similarly showed foci of lymphocytic infiltration.

Nephritis in Jaundice.

A few cases of jaundice were available for study. Of these children 3 had congenital atresia of the bile-ducts. The 4th had severe jaundice 2 days after birth, though no gross hepatic defect was found at autopsy. Other 2 patients suffered from delayed chloroform poisoning, 2 from acute yellow atrophy of the liver, and 1 from hepatic cirrhosis. (A case of malignant hepatoma has been included in the section on tumours). The ages in this group varied from 2 days to 10 years, and 5 were of the female, and 4 of the male sex. A mild early nephritis occurred in 2 members of this group, one being an infant aged 6 weeks with congenital atresia of the bile ducts, and the other a child of 9 years with delayed chloroform poisoning. In the infant the kidneys were deeply bile-stained, while the older child showed extreme fatty degeneration of the kidneys, as well as of the liver and heart muscle, the result of delayed chloroform poisoning, following operation for a perforated gangrenous appendix.

Histologically, the infantile kidneys showed fairly diffuse/

diffuse glomerular involvement with swelling, intense congestion of the capillaries, and desquamation of the covering epithelium, though a few glomeruli remained normal and formed a striking contrast to those involved in the inflammatory process. In the tubules marked catarrhal changes were present in the secreting epithelium, which was the seat of marked vacuolar degeneration, many cells having lost their nuclei. Rare tubules contained red blood corpuscles, while in others, débris or granular casts were present. Sections showed less bile pigment than the gross appearance of the kidneys would have suggested. No lesion was noted in the interstitial tissue.

In the 2nd case the glomeruli were swollen and bloodless from endothelial cell proliferation, with, in the capsule of Bowman, much albuminous exudate, which could be seen in some instances extending into the neck of the corresponding tubule. Severe tubular degeneration was evident, with marked cell necrosis, groups of convoluted tubules having lost their lining epithelium, which had desquamated into the lumina. Elsewhere cloudy swelling was so extreme as almost to block the lumina, and many cells were vacuolated, apparently from the dissolving of fat droplets in the process of paraffin-embedding. Much bile pigment was also deposited both in the secreting and collecting epithelium, and many granular casts were found in the collecting tubules. Interstitial oedema was marked. Examine of the urine in the first of these 2 cases showed/

showed no abnormal constituent except bile, and in the 2nd there was no note with regard to the urine beyond "pain on micturition". Several of the other patients in this group showed very severe tubular degenerative changes, particularly the child with cirrhosis of the liver, where many epithelial cells had lost their nuclei and had desquamated into the lumina of the tubules. The protoplasm throughout the secreting epithelium was granular and vacuolated, and large granules of bile pigment were present in the cells, next the basement membrane. In another child with acute yellow atrophy of the liver, the condition was very similar. In a 2nd case of acute yellow atrophy with marked catarrh of the tubules, frozen sections showed abundant fat in the secreting epithelium, chiefly in the proximal convoluted tubules, and in the thick Henle loops, where fatty droplets coalesced to a large size. The fat was all isotropic. In another patient, an infant with congenital atresia of the bile ducts, and a terminal streptococcal peritonitis, early hyaline droplet degeneration was present in groups of convoluted tubules, while in the infant jaundiced at birth and dying 2 days thereafter epithelial necrosis was extensive. In the 2 remaining cases only slight cloudy swelling was noted in the tubular epithelium, with bile pigment in one. Epithelial degeneration in this group thus appeared to be of exceptional severity. Gray (1933) found in a series of six cases of deep jaundice in adults, extreme nephrosis in 3, severe nephrosis in/

in 2, and moderate nephrosis in one. A low-grade acute nephritis accompanied one of the cases with extreme tubular degeneration. Russell (1929) in 13 cases found microscopic changes in all. 5 of 7 cases of severe jaundice had nephritis of low grade ("mitis" type according to this author). In other 2 instances the inflammatory lesion was still less severe, while in 6 parenchymatous changes alone were present. Russell believes that jaundice gives rise to nephritis through endogenous toxins, either from bile itself or from perverted metabolic products.

Von Kahlden (1891) reports an adult case of jaundice in a patient with malignant hepatoma. Albumin and casts had been present intermittently in the urine during life. At autopsy the renal tubules were the seat of marked fatty degeneration, with much cell necrosis and bile pigment in the epithelial cells. The glomeruli were essentially normal. He never saw red blood corpuscles in the urine in such cases, though scanty casts, and bile-stained pus or epithelial cells were often found. Thus jaundice would appear to lead to severe degenerative tubular changes with an occasional mild inflammatory glomerular involvement both in adults and in children.

Nephritis in Malignant Tumours. (5 cases)

A further group of 5 children dying of malignant disease was examined, since in these neoplasms extensive necrosis/

necrosis sometimes takes place, with resulting toxic absorption. No nephritic complication was, however, observed in any member of this group. The tumours comprised 3 sympathicoblastomata with very extensive hepatic involvement, and widespread glandular metastases, the tumour tissue being extremely soft and necrotic. In two instances the kidney on the same side as the tumour was invaded at the hilum, but appeared normal outside the tumour area, except for slight pallor. The 4th tumour was a malignant hepatoma, the 5th a cerebral glioma. The sympathicoblastoma cases were aged 2 years and 11 months, 3 years, and 3½ years respectively. In all cases, the only lesion noted histologically, was cloudy swelling of moderate degree, in the secreting epithelium. In one instance frozen sections stained for fat showed the presence of a very small amount, an occasional group of convoluted tubules in the cortex containing small droplets, with a powdering in some of the collecting tubules. The patient with the cerebral tumour, an 8 year old boy, showed merely slight catarrh of the secreting epithelium. The child with extensive malignant disease in the liver and secondary nodules in the lungs - a female infant of 8 months - had severely damaged kidneys. At autopsy the organs were the seat of marked fatty change, and histologically, severe degenerative changes were present in the secreting epithelium, particularly in the thick limbs of Henle's loops, where much cell necrosis was evident. The glomeruli were normal. In this case jaundice was probably the factor determining the/

the severity of the renal lesion though bile pigment was not abundant in the sections examined.

Nephritis in Marasmus. (4 cases)

The kidneys were investigated in a final group of 4 cases of marasmus, 2 of these children suffering from tetany in addition.

The first two patients without tetany were infants aged 30 days and 10 months respectively. The first case was complicated by gastro-enteritis, and the second by otitis media. Simmonds (1896) in 60 cases of pure marasmus, excluding lues, pneumonia, acute infections, purulent conditions, tabes mesenterica, and severe gastro-enteritis, found fatty degeneration of the tubular epithelium, and hyaline casts in their lumina, while albuminous exudate was present in the capsular spaces. In 29 of these cases the middle ears were examined, when exudative otitis media was found in 28 instances. In another series of 133 autopsies on marasmic infants the middle ears were free from exudate only twice. Simmonds concludes that nephritis in marasmus is due not to the mild gastro-intestinal catarrh present in some of these infants, but to the accompanying otitis media, not necessarily purulent. In neither of the cases mentioned above was nephritis present, the kidneys being normal on naked-eye examination in both, and/

TABLE V.

Nephritic Complications in various acute inflammatory lesions.

Disease.	No. of Cases.	No. of Nephritic Complications.	% of Nephritis.
Suppurative lesions with or without septicaemia.	33	7	21.21
Peritonitis	6	3	50
			35.60
Pneumonia	29	4	13.79
Gastro-enteritis	27	3	11.11
Tuberculosis	12	3 (2 acute glomerulo-nephritis. 1 acute interstitial nephritis.)	25
Meningitis	11	4	36.36
Rheumatic + Ulcerative Endocarditis	9	6	66.66
	1	-	-
Jaundice	9	2	22.22
Congenital Syphilis	5	4 (2 acute glomerulo-nephritis. 2 early acute interstitial nephritis.)	80
Diphtheria	3	1	33.33
Blood Disease	9	-	-
Marasmus	4	-	-
Malignant Tumours	5	-	-
Total:	163	37	Average % Nephritic Complications = 22.70

and histologically showing only cloudy swelling with hyaline casts in the lumina of some tubules. Both children with a history of tetany had had numerous fits since birth. The elder, aged 7½ years, was markedly rachitic, and fits towards the end became very frequent. Broncho-pneumonia was a terminal event, and the child died in coma. A trace of albumin was present in the urine. The kidneys at autopsy appeared to be the seat of cloudy swelling, and this was confirmed on histological examination, when slight tubular degeneration was the only lesion found. The other patient with tetany, a child aged 2½ years, was admitted to hospital suffering from severe convulsions, and unconscious. A left otitis media was present along with a terminal broncho-pneumonia. Albumin was present in this case with an occasional cast (type not specified), and swelling of the hands and feet accompanied the convulsions. Histologically, some glomeruli appeared slightly congested, and a small amount of albuminous exudate was present in the capsule of Bowman in a few instances. The secreting epithelium showed a mild degree of cloudy swelling, the thick Henle loops being most severely involved. In this group no nephritic complication was found.

The varying percentages of nephritic complications in these 163 combined inflammatory lesions are seen from the accompanying table. Nephritis on an average was present in 37 cases or 22.70 per cent. of the whole series. Naturally

in individual groups the numbers are too small to be of any value, but congenital syphilis, and rheumatic endocarditis are outstanding from the frequency of associated inflammatory renal complications. Regarding the sex distribution of these 37 cases of secondary nephritis, 17 occurred in males and 20 in females, while according to age distribution 15 cases occurred in the 1st year of life, and 26 between birth and the end of the 6th year. About two-thirds of the cases, therefore, occurred in the first half of childhood.

SUMMARY.

Having completed the description of the 94 cases of primary and secondary nephritis on which this investigation is based, there remains the task of summarising shortly the salient characters of this disease in the child, in whom it appears in the vast majority of cases in pure form, without the underlying cardio-vascular component, which so frequently complicates the process in the adult. Broadly speaking, the chief feature which distinguishes juvenile from adult nephritis, is the acuity of the process in the former, the chronicity in the latter, acute forms predominating in paediatric clinics, and chronic forms in those attended by adults. The most characteristic type of nephritis in the child, and one which is almost exclusively confined to children and young adults, is the haemorrhagic form, considered by some investigators an embolic focal lesion, occurring generally at an interval of some days after an attack of angina, and characterised by abundant blood in the urine, by limitation of oedema to the face in most instances, and by mild constitutional disturbance. Such patients appear less severely ill than the majority of adults with nephritis. The immediate prognosis is excellent. Sufficient glomeruli would appear to remain intact in this type to maintain a fair degree of renal efficiency. That haemorrhagic nephritis can also be diffuse, and fatal/

fatal, however, is shown by the few examples in the present series.

The majority of the cases under discussion belong to the type of ordinary acute glomerulo-nephritis, where haemorrhage though sometimes present, is never so prominent as in the haemorrhagic variety. The former type is similar to that commonly occurring in adults, though capable in the young child, and particularly in the infant, of running a fulminating course, and leading to a fatal issue before the disease has progressed beyond a very early stage, though, on the other hand, the lesion in children can develop more quickly than in adults and a surprising degree of renal change is sometimes found histologically, after a very short clinical history. In infants resistance is relatively slight, not only to nephritis but to diseases in general. A large proportion of the patients forming the subject of this research, 66 or approximately 70 per cent., were under the age of 6 years, thus dying in the first half of childhood, while 35 died under the age of 1 year. Nephritis can occur in very early infancy, and may even date from intrauterine existence. The youngest infant with primary nephritis in this series was only 22 days old, and another 25 days, while in the cases of secondary nephritis, some of the infants lived only a very few days. It has been shown, both from the writer's own cases, and from a review of the literature, how little reliance can be placed on/

on naked-eye examination alone, in nephritis, since profound renal changes may be present microscopically though outward and visible manifestations of the disease are practically absent. While the macroscopic appearance gives no dependable information regarding the underlying histological condition, the latter in its turn, is no criterion of the severity of the lesion from the clinical point of view, while it is often unsafe to hazard a guess at the duration of the pathological process, since, while the disease may run an acute course in some cases, in others, probably of less initial severity, it may long remain latent, without progressing to the proliferative stage, though each patient is a law unto himself in this respect, different periods of time being required to reach the stage of contraction in individual cases.

This point is illustrated in the group of decapsulated kidneys, where in 3 cases all of the same relatively short duration, proliferative changes present in the kidneys were not of equal extent in each, other organs in this group with a much longer clinical history remaining enlarged and smooth, with little microscopic evidence of connective tissue overgrowth. Confirmation of this capacity to remain latent is found on reviewing the literature. Various authors record cases of several or even many years' duration, where proliferative changes were still slight.

On reviewing the 32 cases of haemorrhagic and exudative glomerulo-nephritis, it is seen that comparatively few of these children/

children died of renal insufficiency alone. Nephritic patients are peculiarly prone to develop secondary inflammatory lesions, and in the present autopsy series, over 80 per cent. had some acute inflammatory complication, the respiratory tract being involved in about 60 per cent. of all cases.

Cardiac hypertrophy was found in about one-third of these acute cases, where in the majority it was associated with a definite rise in the systolic blood pressure on clinical examination. Other investigators confirm the fact that even in young children the cardio-vascular system is readily affected in acute nephritis. Cerebral complications in children are not of true uraemic nature, but are due to a neuro-oedema rather than to a neuro-toxaemia. In 15 patients in the present series with acute nephritis, where the brain was examined, the organ was oedematous in 9 instances. A frequent finding in the acute exudative cases was oedema, occurring either in the subcutaneous tissues, the serous sacs, the internal organs, or any combination of these. In rather more than half these cases "swelling", appearing generally in the face, feet, or legs, was the first symptom to attract the relatives' attention. The appearance of oedema was frequently accompanied by abdominal pain, sometimes so severe as to suggest acute abdominal disease, or by sickness and vomiting, while occasionally symptoms referable to the respiratory tract predominated at the onset of the illness. In many

cases/

cases the onset of nephritis was fulminating, the child being seized with convulsions while apparently in good health, and dying in coma shortly thereafter.

With regard to the urine, the amount varied in the acute cases, the urinary output sometimes being diminished, though occasionally frequency of micturition was noted. Albumin and blood were frequent findings, the former being present in all but one of the patients, with an exudative lesion, while casts of various types were present in about half these children. Renal efficiency tests in a number of cases appeared to give rather contradictory results, and to yield little diagnostic information of value.

No instance is reported in the present series of true nephrosis, satisfying all the clinical and pathological requirements of the latter, on a rigid interpretation. A group of 4 cases with marked oedema, where the lesion was mainly tubular, and stigmata of disease in the glomeruli were slight, approach this type most closely, particularly in 3 instances. The 4th patient had abundant blood in the urine, and within the lumina of the tubules on histological examination. Since haemorrhage is intermittent, the haemorrhagic element in such cases might be readily missed, and the condition classified as a degenerative tubular lesion. Renal disease in this group corresponds to the tubular or parenchymatous type reported by various authors, and particularly in America. It has been

shown from a review of the literature that true nephrosis is at present considered a very rare, if not indeed an almost mythical lesion. According to modern interpretation, even minor glomerular lesions are considered inflammatory though, since the disease is of minimal intensity from the start it runs an extremely chronic course, thus allowing tubular degenerative changes to reach their full fruition, while proliferative changes remain in abeyance. Some inflammatory process may, however, cut short the life of the patient, since such individuals are very liable to pneumococcal and streptococcal infections.

It may be mentioned here that fat was scanty in practically all the cases, where frozen sections were available, and in no single instance was doubly refractile lipoid present, except in minimal amount, though the naked-eye appearance of one of the cases in the above group of 4, suggested the presence of myelin fat. Frozen sections, however, were not examined in this case.

Acute interstitial nephritis is represented in the present series by 4 cases, 2 of severe and 2 of slighter degree. Of the former, 1 case followed ulceration of the palate, with extensive sloughing of the pharyngeal tissues, and the other tuberculous ulceration of the bowel with extensive tabes mesenterica. The 2 milder cases occurred in congenital syphilitic infants, and in such patients a cellular infiltration/

infiltration of the interstitial tissue would appear to be the characteristic type of lesion. Various investigators have described acute interstitial nephritis following scarlet fever and diphtheria, either alone or associated with other exanthemata. This type of lesion sometimes occurs earlier in the course of scarlet fever than the more characteristic acute glomerulo-nephritis. Some writers believe that the severity of the interstitial renal lesion in the various exanthemata, depends on the degree of faucial involvement accompanying the former.

On reviewing the 10 operated cases reported in this study, as well as the whole series of 23 cases of which these 10 form part, the operation of decapsulation would appear to result in immediate benefit with amelioration of the clinical symptoms in many instances, though with permanent improvement in relatively few cases. On consulting the literature on this subject, the type of lesion where this operative procedure appears to yield the best results is acute glomerulo-nephritis with suppression of the urine, where it may be the means of saving life, though even in such cases, permanent cure results only in a proportion of patients.

Regarding the presence of etiological factors, a possible source of infection was found in rather more than 2/3rds of the entire series of primary nephritic cases. Such foci of infection as were found could be divided roughly into groups, including tonsillar/

tonsillar and respiratory lesions, septic conditions of the skin and mucous membranes, and various exanthemata, while in several cases illness or exhaustion of the mother during pregnancy might possibly have induced at least a predisposition to develop nephritis as a sequel to some slight infection. The hereditary factor in nephritis is stressed in the literature, many authors reporting the occurrence of acute or chronic nephritis in several generations of certain families, the disease being not only hereditary and familial - occurring in several members of these families - but sometimes congenital in addition, appearing soon after birth.

In the cases where an etiological factor was lacking both in the history and on clinical examination, absence, as has been suggested, may be more apparent than real, as a mild tonsillar infection might have been present a few days before the onset of nephritic symptoms, though this fact was not elicited, on questioning the patient's relatives. The whole trend of modern opinion is to regard nephritis, with few exceptions, as secondary to acute disease, or to a focus of infection, somewhere in the body, the lymphatic pharyngeal ring being of primary importance in this respect, while the superabundance of lymphoid tissue in the child is, in the opinion of some writers, correlated with the frequency of throat and respiratory lesions, as well as of nephritis, at an early age. It is frequently emphasized in the literature that/

that foci of infection are more readily demonstrable in the child than in the adult with nephritis. Any of the exanthemata can be followed by this disease, scarlet fever being the one most frequently complicated not only by glomerular but also by acute interstitial nephritis. Septic conditions of the skin and mucous membranes, of which impetigo contagiosa appears to be the chief, can also be regarded as of etiological importance in the causation of nephritis. The various chemical poisons sometimes responsible for the adult lesion hardly come into the picture of nephritis in the child, though in infants various external medicaments may prove extremely toxic to the kidneys, while such relatively slight diseases as mild catarrhal enteritis, or otitis media can determine in them a fatal nephritis.

Of the organisms responsible for the production of an inflammatory renal lesion streptococcus is by far the most important, while pneumococcus and staphylococcus play a subsidiary rôle, and very occasionally some other organism must be held responsible, e.g., B. coli, or B. tuberculosis. In the parenchymatous or tubular type of nephritis some authors find the focus of infection commonly located in the antra or nasal sinuses, staphylococcus of albus or aureus type being regarded as the source of renal damage. There is a growing tendency to regard nephritis in common with tuberculosis, pneumonia, and other diseases as an allergic manifestation/

manifestation, the result of previous immunisation, sufficient endotoxin being set free on lysis of streptococci in an immunised patient, to set up renal inflammation. Toxins which are produced in a distant focus of infection and which flood the circulation and not organisms themselves, are generally considered responsible for nephritis, though, according to some writers, scanty bacteria may actually reach the glomerular capillaries and be lysed, before they have a chance to multiply in situ.

The embolic non-suppurative focal nephritis of Löhlein, associated with bacterial endocarditis occupies a special place as the only hematogenous renal lesion of quite definite etiology, though by some writers the haemorrhagic type of nephritis common in childhood is also considered a focal lesion, due to the blocking of individual capillary loops by bacterial emboli. In septicaemic conditions also, bacteria are present in the kidneys, as well as in other organs.

In the whole series of juvenile cases under discussion, vascular changes except in a very small number of cases were entirely absent, though from a review of the literature, a rare form of renal disease occurs in the child, where vascular degeneration is of primary importance, the disease then running a clinical course comparable to that in the adult with a similar type of lesion, cardiac hypertrophy, albuminuric retinitis, and marked rise in the blood pressure all being found/

found, while at autopsy the kidneys are of primary granular contracted type, the predominating lesion on histological examination being vascular degeneration, to which the glomerular changes appear secondary. In adults this primary contracted kidney, or malignant nephrosclerosis predominates in male subjects, while in children, on the other hand, it is seen more frequently in girls than in boys. An interesting finding in juvenile cases of this type is the frequent presence of some renal developmental abnormality generally in the form of hypoplasia affecting sometimes one kidney or more rarely both organs. Various authors attribute this defective renal development to an associated defect in arteriogenesis. It would therefore appear that in children as in adults, a vascular lesion can determine the onset of chronic nephritis, but in the former, this arterial degeneration is not the result of the wear and tear of life, but of the initial poor quality of the "vital rubber."

Chronic nephritis in the child also, is sometimes found in a solitary kidney, as in 2 of the 9 patients with a proliferative nephritis in the present series, while another instance occurred in an infant who lived for 25 days with a minimal amount of renal tissue, both kidneys being only the size of haricot beans, and showing on histological examination thickened arteries, and a developmental "lag", many glomeruli being still at an embryonic stage, and the seat/

of acute and more chronic inflammatory change. That such maldeveloped kidneys are prone to degenerative lesions is illustrated by various cases reported in the literature, where even in young adults, in whom defective arteriogenesis has caused renal hypoplasia, unripe glomeruli are present in association with chronic inflammatory change. In the kidneys of young infants embryonic glomeruli are also seen not infrequently, and these structures are a ready prey to degenerative processes.

Another form of chronic nephritis which occurs in children and often dates from birth, or even from intrauterine existence, according to some investigators, is the chronic interstitial nephritis of obscure etiology, associated with bone changes, "renal rickets", no case of which is represented in the present series.

Various investigators have followed for months or years series of cases of acute nephritis occurring in children, to determine the incidence of chronic disease developing from the original acute attack. On comparing statistics, relatively fewer juvenile than adult cases progress to a chronic stage, and a young patient who has recovered completely from acute nephritis appears to be no more susceptible to renal damage following acute exanthemata, or other infective conditions than a normal child.

Secondary Nephritis. (37 cases)

On examining the kidneys of 163 patients with various acute inflammatory lesions, 37 cases of secondary nephritis were discovered - approximately 22.70 per cent. of the whole series. The great majority of these cases of nephritis were clinically silent, the manifestations of the primary disease overshadowing the renal lesion. Various writers have found nephritis of diffuse or focal type at autopsy in cases with widespread septic lesions or septicaemia. Streptococcal sepsis is considered particularly apt to damage the kidneys, and this would appear to hold good in the present investigation, where in the septic group, half the cases with streptococcal infection showed a severe renal lesion. Pneumococcal and staphylococcal infections were next in importance etiologically, while the infecting organism in one patient with nephritis was B. coli. As the kidneys in this case were the seat of developmental abnormality, both being hydronephrotic, they may have been susceptible to the toxins of an organism not often affecting normal kidneys. Rheumatic endocarditis appears to be frequently complicated by nephritis, the lesion being diffuse in all cases affected in the present series. As some writers have pointed out, more than one type of renal lesion is possible in this condition, since in addition to actual bacteraemia the circulation is flooded by toxins.

In the small group of congenital syphilitics, renal involvement/

involvement was frequent, 2 cases showing an ordinary acute nephritis, while in other 2 an early acute interstitial lesion was present, One of these infants showing, in addition, slight delay in renal development, with traces of a neogenic zone. This is a frequent finding, according to some authors, in infants dying of congenital syphilis.

The pneumonia and gastro-enteritis groups in the present series showed only a small percentage of nephritic complications, though many of these patients were infants and young children. In diphtheria, meningitis, jaundice, and tuberculosis, nephritic complications occurred, though in the majority of cases, the disease was of relatively mild type. One of the tuberculous patients had a well-marked acute interstitial nephritis. Small series of patients with marasmus, malignant tumours, and various blood diseases were free from any evidence of an acute renal inflammation.

In conclusion, nephritis in the child possesses special characteristics, and although some phases of the disease, particularly in older children, closely resemble the adult type of lesion, and all adult varieties including even the primary granular contracted kidney, would appear capable of reproduction in exceptional circumstances in juvenile kidneys, nephritic manifestations as a whole in the child, differ sufficiently from those in the adult, to merit a separate description.

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THE PATHOLOGY OF NON-SUPPURATIVE NEPHRITIS IN CHILDREN

- PHOTO-MICROGRAPHS -

By

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Royal Hospital for Sick Children, Glasgow.

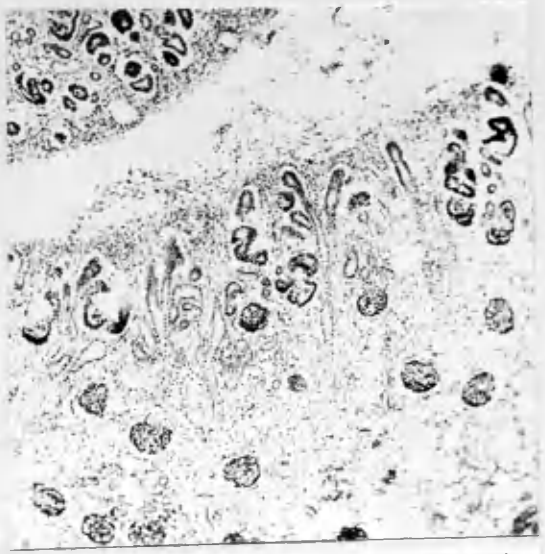

Fig.1. Foetal Kidney about 4th month. x 75. H.& E. Neogenic zone under capsule with glomerular anlage.

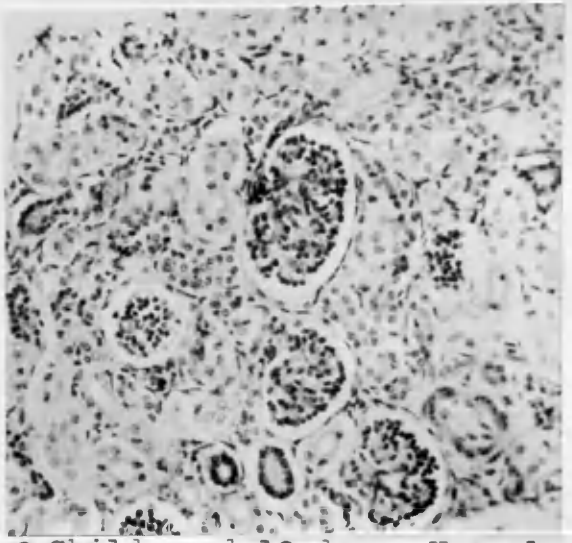

Fig.2. Child aged 10 days. Normal Infantile Kidney. x 150. H.& E. Closely-packed glomeruli with prominent tuft epithelium. Immature forms seen. Tubules small.

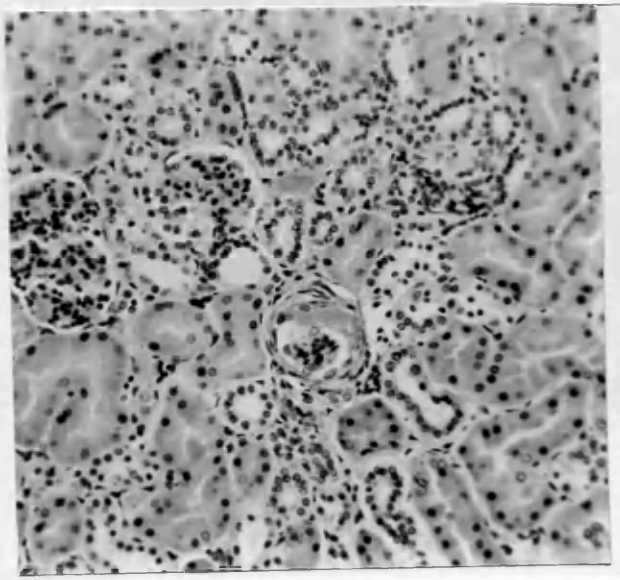

Fig.3. Child aged 27 weeks. Immature Glomerulus undergoing degeneration. Capsule thickened and adherent to shrunken tuft.

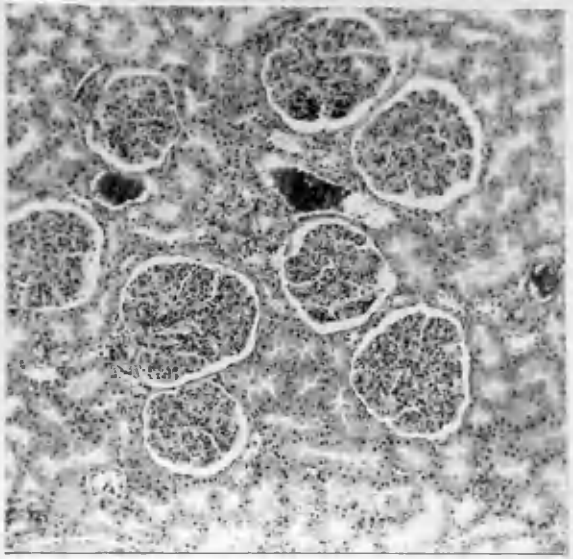

Fig.4. Child aged 10 years. Acute Glomerulo-nephritis. x 75. H.& E. Large swollen digitate cellular glomeruli.

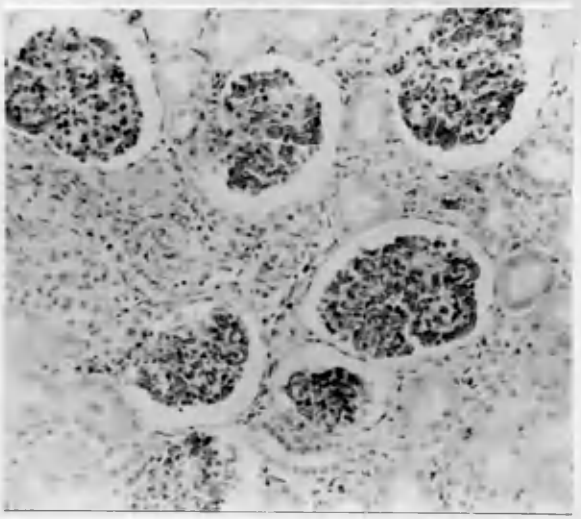

Fig.5. Child aged 14 weeks. x 220. H.& E. Acute Glomerulo-nephritis. Intense glomerular congestion only lesion. Illness 3 weeks.

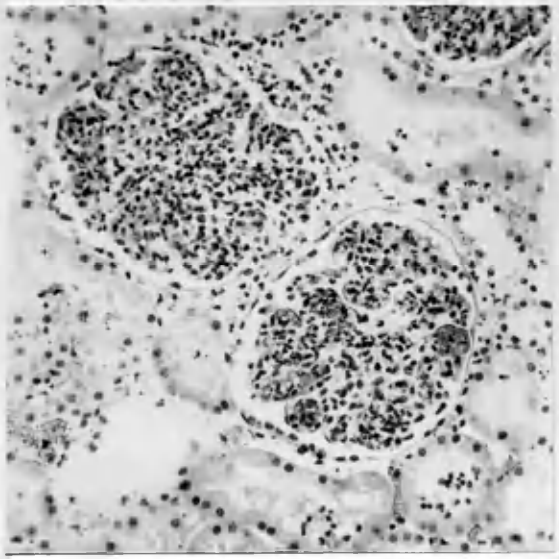

Fig.6 Child aged 8 years. Streptococcal Septicaemia. Acute Glomerulo-nephritis. x 200.H.& E. Many polymorphs in enlarged cellular tufts.

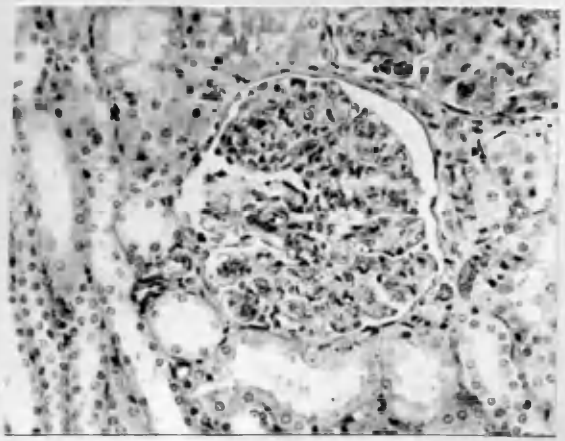

Fig.7.Child aged 6 years. Acute Glomerulo-nephritis. x 200. H. & E. Proliferation of capillary endothelium in tuft, with occlusion of lumina. Illness less than 24 hours.

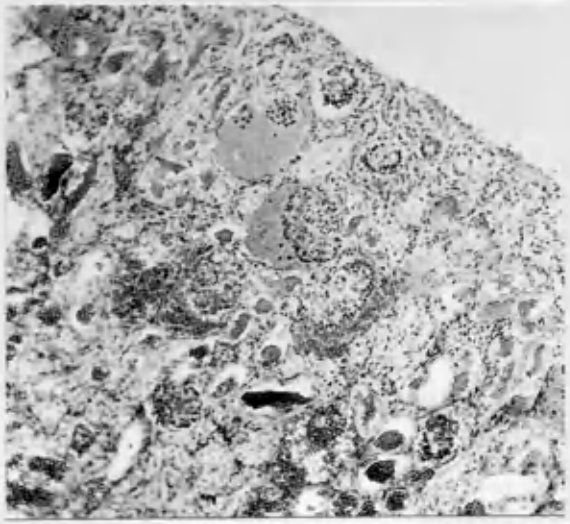

Fig.8.Same case. x 100. H.& E. Haemorrhage into capsules and tubules. Immature glomeruli immediately under capsule.

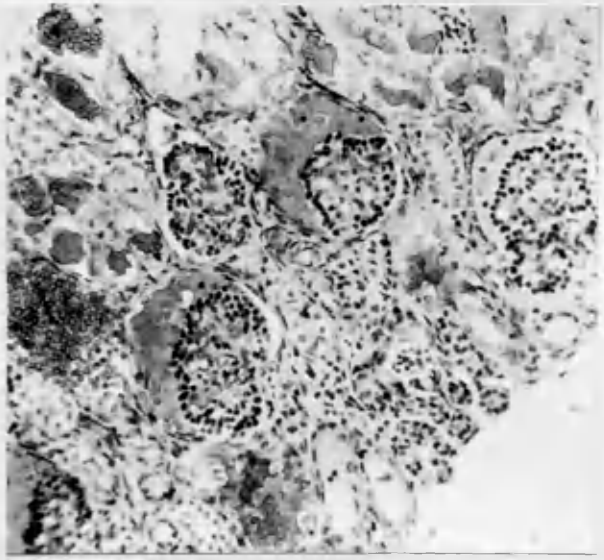

Fig.9.Child aged 22 days. Haemorrhagic Nephritis. Abundant capsular haemorrhage. Infantile type of glomeruli. Some tubular haemorrhage. x 200. H.& E.

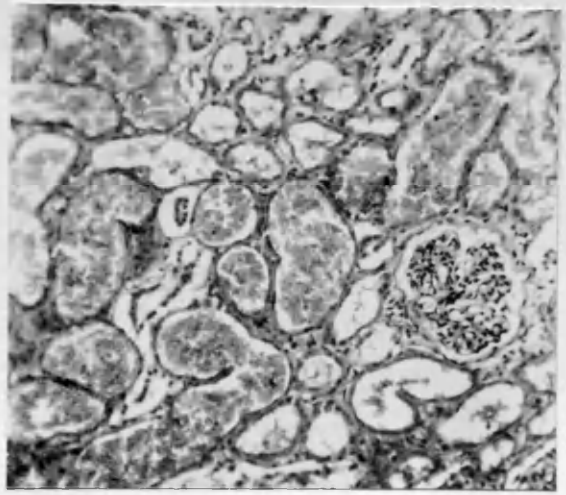

Fig10.Child aged 11 years. Haemorrhagic Nephritis. x 150. H.& E. Tubules distended by haemorrhage. Flat epithelium.

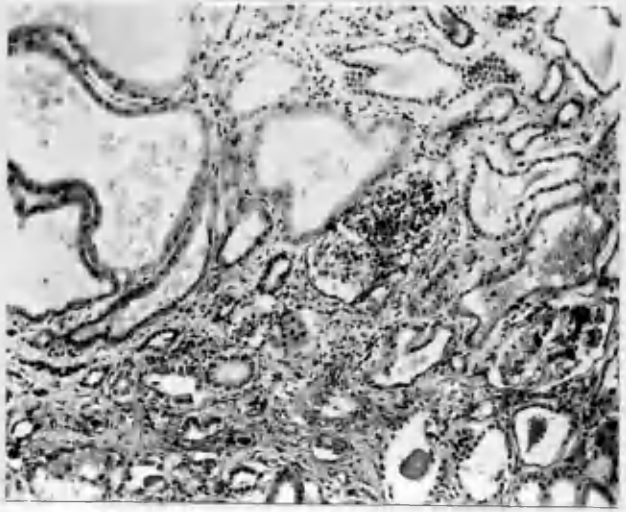

Fig.11. Child aged 18 months. Single Hydronephrotic Kidney with Chronic Nephritis and Tubular Hyperplasia. x 100.H.& E. Fibrosed glomerulus with capsular adhesions. Marked tubular dilatation. Interstitial fibrosis.

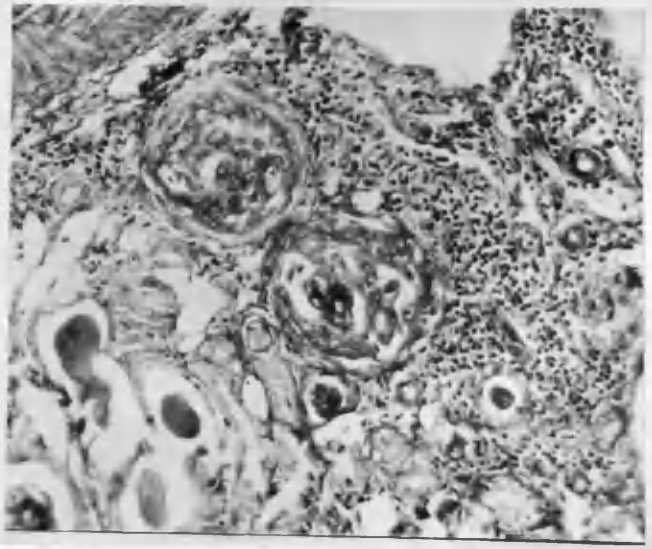

Fig.12. Child aged 6 months. Chronic Nephritis. x 200.H.& E. Capsular proliferation. Adhesions to fibrosed tufts. Interstitial cell infiltration. Tubules dilated with casts.

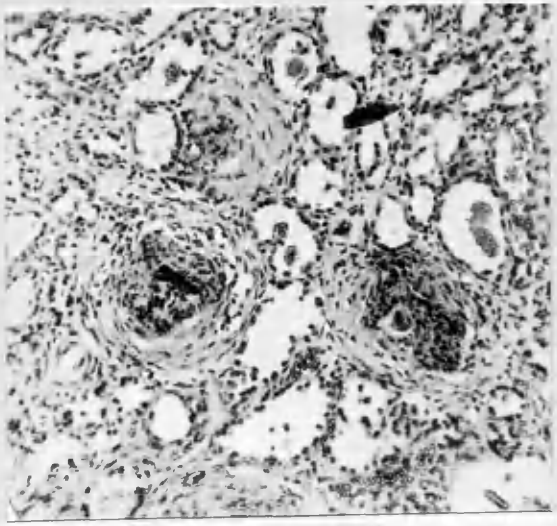

Fig.13. Child aged 7 years. Early Chronic Nephritis. x 150.H.& E. Epithelial crescents with adhesions to tufts, the seat of fibrosis.

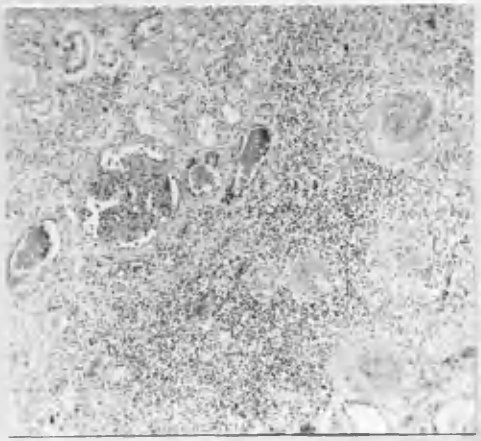

Fig.14. Child aged 13½ years. Chronic Nephritis in Single Kidney. x 50.H.& E. Glomerulus with adhesions and peri-glomerular fibrosis, also hyalinised glomeruli. Interstitial increase and cell infiltration.

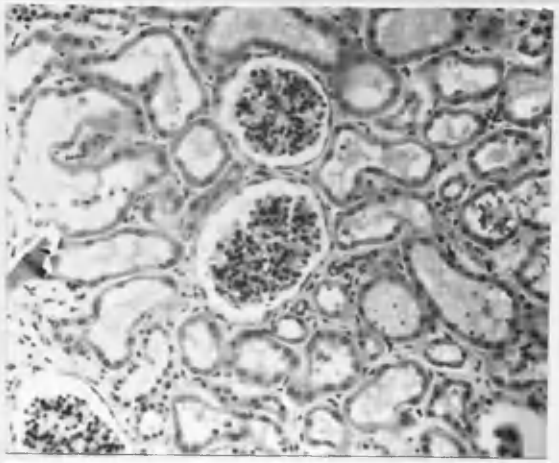

Fig.15. Child aged 23 months. x 150.H.& E. Mild Glomerulitis. Tubular Degeneration. Glomeruli show little change but haemorrhage seen in one tubule. Flat epithelium. Oedema of stroma.

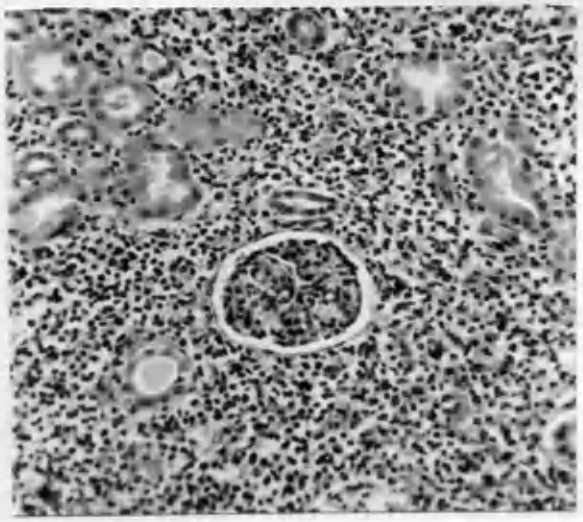

Fig16. Child aged 5½ months. Ulceration of palate. Acute Interstitial Nephritis. x 200 H.& E. Dense round cell infiltration of interstitial tissue.

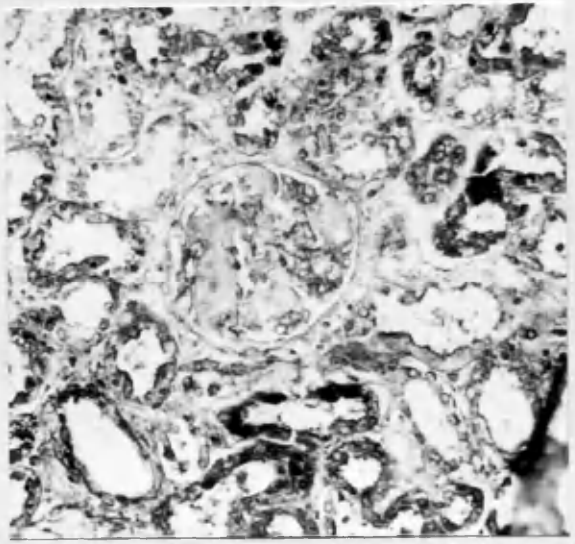

Fig.17. Child aged 10 years. Pott's Disease. Sub-acute Nephritis and Amyloid Degeneration. x 200.H.&E. Glomerulus showing amyloid.

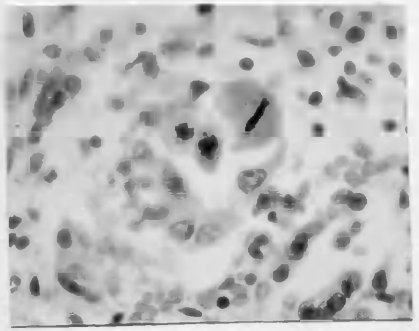

Fig.18. Child aged 11 months. Tabes Mesenterica. Acute Interstitial Nephritis. x 400. H.& E. Tubular regeneration. Mitotic figures present in epithelium.

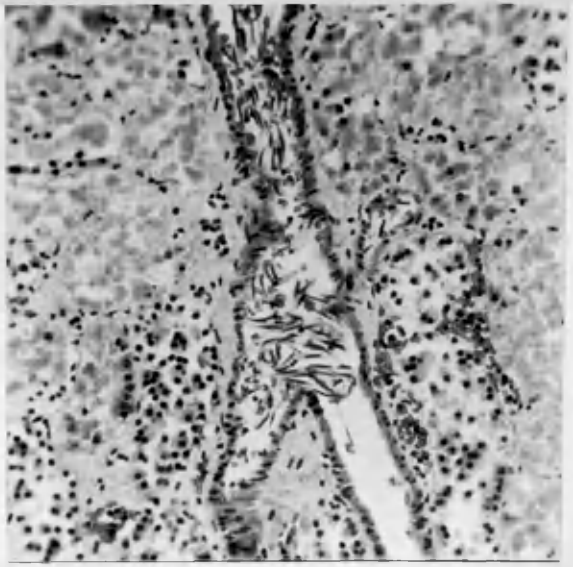

Fig.19. Child aged 9 years. No clinical evidence of Nephritis. x 200.H.& E. Small vessel with masses of endothelial cells lying free. Necrosis of secreting epithelium.

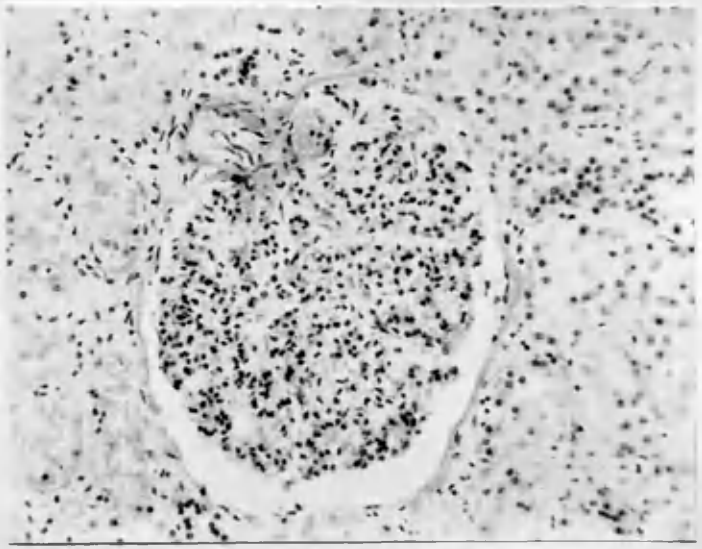

Fig.20. Same case. Enlarged cellular glomerulus. x 200. H.& E. Endothelial cells in afferent arteriole and similar cells in tuft capillaries.

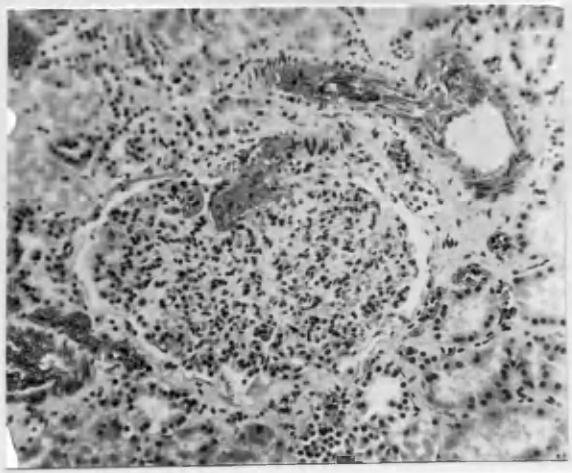

Fig.21.Same case. x 150. H.& E. Another glomerulus with endothelial cells in lumen of afferent arteriole.

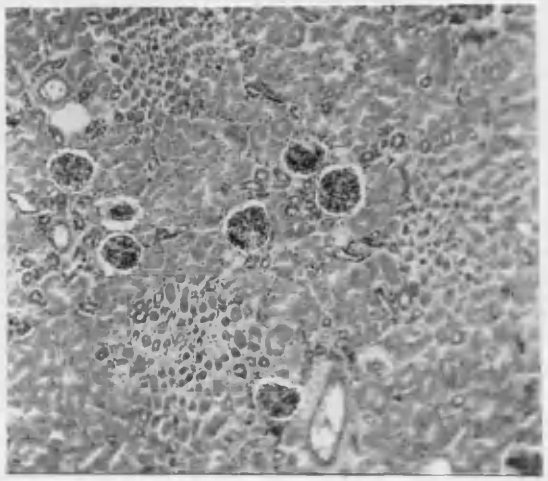

Fig.22.Child aged 15 months.
Acute Gastro-enteritis. x 75.H.& E.
Extensive necrosis of secreting epithelium. No glomerular lesion.

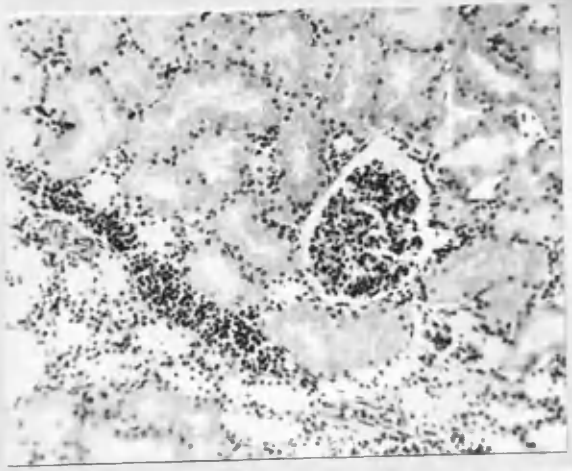

Fig. 23. Child aged 6 years. Lymphatic Leukaemia. x 200. H. & E. Vessel packed with lymphocytes. Similar cells in tuft capillaries.

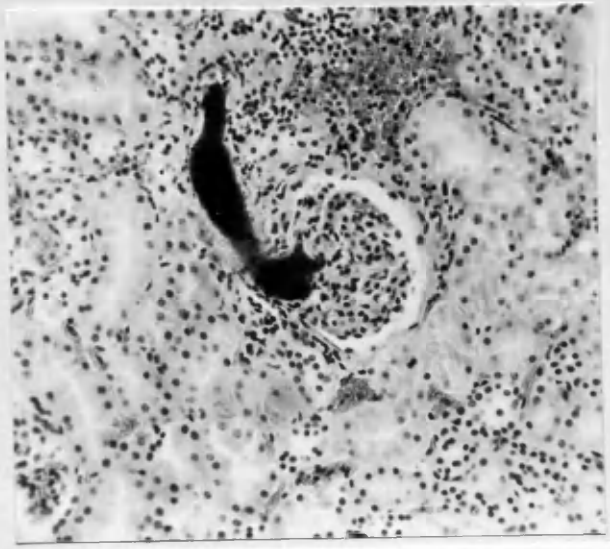

Fig.24. Child aged 10½ years. Streptococcal Septicaemia. x 200. H.& E.
Afferent arteriole plugged with streptococcal embolus.

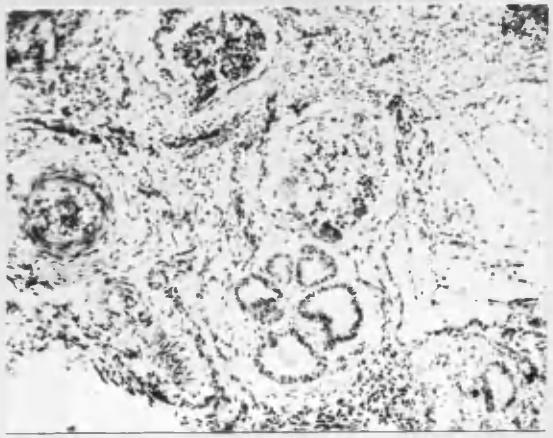

Fig.25.Child aged 25 days. Bilateral Renal Hypoplasia. Group of tubules with embryonic epithelium surrounded by foetal connective tissue. Enlarged cellular glomerulus. Interstitial increase. Tubular dilatation. Small thick-walled arteriole seen. x 100. H.& E.

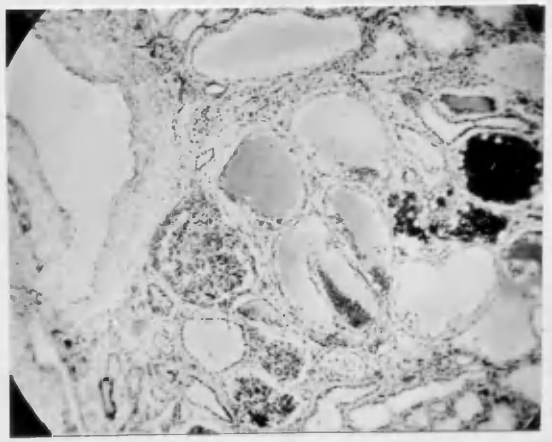

Fig.26. Same case. x 60. H.& E. Enlarged cellular glomerulus. Tubular dilatation with exudate in lumina. Scanty red cells in some. Interstitial increase.

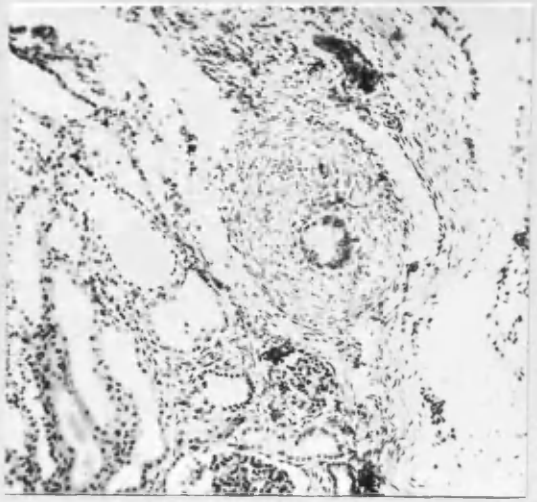

Fig.27. Same case. x 100. H.& E. Primitive tubule seen surrounded by concentric layer of foetal connective tissue. Glomerulus seen with capsular haemorrhage. Wide tubules with flat epithelium.

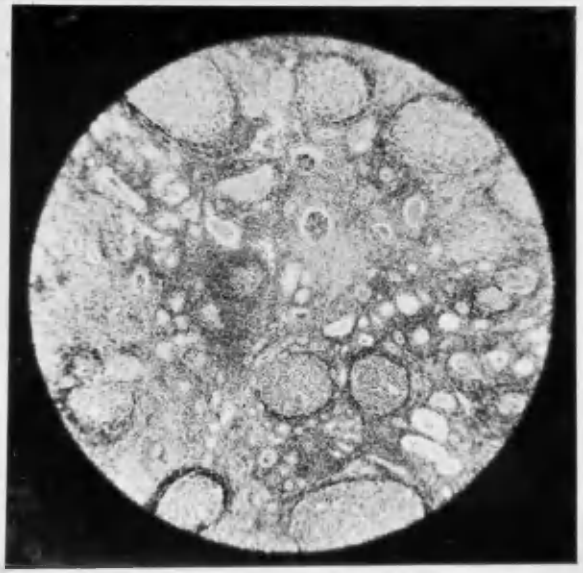

Fig.28. Child aged 18 months. Chronic abscesses in Kidney. x 60. H.& E. Numerous lymphoid follicles in sub-capsular cortex with cellular infiltration.

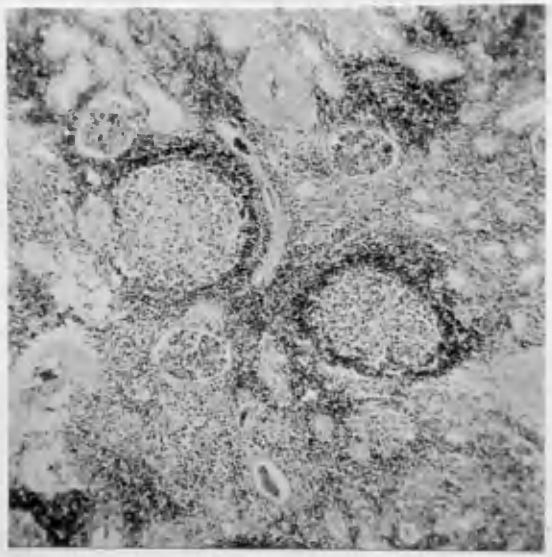

Fig. 29. Same case as Fig. 28. x 90. H and E. Well formed lymph follicles seen with cellular infiltration in kidney.

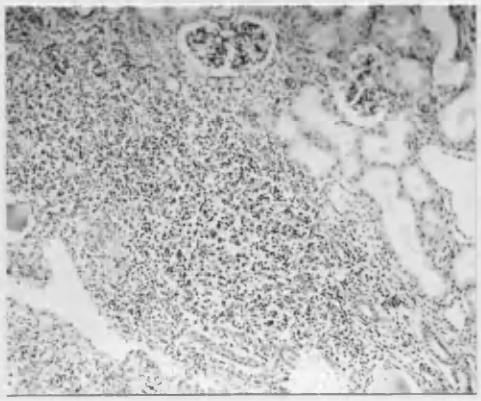

Fig. 30. Child aged 43 weeks. Von Jaksch's anaemia. X 75.H and E. Foci of lymphocytic infiltration with imperfect follicle formation.