GLOMERULONEPHRITIS IN AFRICANS IN UGANDA

BY

H. M. LEATHER, M.D., M.R.C.P.

From the Departments of Medicine, Makerere College, Kampala, Uganda, and University of Bristol

Nephritis is a common disease in the African (Gelfand, 1957) and is a common cause of death from hypertensive heart failure. Becker (1946), from Johannesburg, found that out of a total of 3,000 necropsies hypertensive heart failure was present in 247 cases and that 85 of these were due to glomerulonephritis, the great majority being in the chronic phase of the disease. Uys (1954), again from necropsy studies, found glomerulonephritis to be the commonest cause of secondary hypertension. In Uganda, Davies (1949) found "some form of nephritis" to be present in 301 out of 2,994 necropsies, and, in these, congestive heart failure was the commonest single mode of death. Raper (1953), however, reporting on "nephritis and allied lesions in Central Africans," found only 23 cases of nephritis among 92 necropsies in which advanced renal disease had been present.

No comprehensive clinical studies of glomerulonephritis have been made on the African native in his home environment, the only recorded study being an analysis by Furman (1955) from Johannesburg of the case-records of European and Bantu patients suffering from nephritis. The present study was therefore made in order to learn more of the clinical features, the biochemical and histological findings, and, if possible, the course of glomerulonephritis in the Bantu.

Material and Method.—Between January, 1956, and February, 1957, all patients admitted to the wards of a medical unit, Mulago Hospital, in whom clinical evidence of renal disease was present, or who were otherwise hypertensive, were studied. An exception was made in the case of patients in whom transient albuminuria was present during the course of another illness—for example, pneumococcal pneumonia. Patients who were found on investigation to be suffering from renal disease other than glomerulonephritis—for example, pyelonephritis, amyloidosis, or essential hypertension—have been excluded from the present series and are reported elsewhere (Leather, 1959; and awaiting publication).

The details of the method used in this study are also recorded elsewhere (Leather, awaiting publication).

Findings.—Glomerulonephritis was found in 33 of the 67 patients in the entire study. It was the commonest cause of renal disease in each of the first four decades, and was present in 12 of the 13 children studied. It was not always possible to tell which stage in the natural history of the disease process a particular patient had reached. Classification, which was therefore difficult, has been made from a combination of clinical and histological findings and is as follows:

I. Glomerulonephritis in childhood	..	12 cases
II. Glomerulonephritis in adults	.. ..	21 ,,
"Acute" nephritis	.. ..	3 cases
Rapidly progressive "acute" nephritis	.. .. ..	3 ,,
Subacute nephritis	.. ..	1 case
Latent nephritis	.. ..	1 ,,
"Intermediate" nephritis	..	3 cases
Chronic nephritis	.. ..	10 ,,

Glomerulonephritis in Childhood

There were 12 children (6 boys and 6 girls) in whom a diagnosis of glomerulonephritis was made. The youngest was 4 years and the oldest 13. Nine of them were under 9. The youngest patients in the group were mostly girls. Various tribes were represented, and were in roughly the same proportion as for all Mulago Hospital admissions.

The dietary history revealed that about half the patients enjoyed a fairly good diet.

In seven patients there was a history of a recent infection, usually of the upper respiratory tract. In four, symptoms of nephritis followed within 11 days. The presenting symptom was always swelling of the body, and had usually been present for two to three weeks before admission to hospital. The swelling generally began in the face and neck, and over the course of several days spread to the rest of the body, the abdomen being particularly affected. The onset of abdominal swelling was often preceded by colicky abdominal pain.

Urinary symptoms were not striking and no patient gave a history of passing bloody urine. One child had complained of pain in the loin and several had passed less urine since the onset of the swelling.

Five of the patients gave a history of a similar previous illness, including one patient (Case 1) who had had Henoch's purpura. In two cases there was a family history of a similar illness in other siblings which had proved fatal.

The most striking clinical finding on examination in the children was oedema, which was nearly always generalized and often gross. Apart from the severity of the swelling, the feature of most interest was the somewhat unusual distribution in the tissues of the neck. Thus, while the face was somewhat rounded and the eyes were puffy, the neck was especially swollen and the hollow between the angle of the jaw and the upper chest was sometimes even obliterated. In two children the neck was actually extended by this swelling. Ascites was usually considerable. Bearing in mind the age of these patients, a diastolic pressure of more than 80 mm. Hg was regarded as abnormal, and by these standards most of the children were hypertensive. In four the diastolic pressure was over 100 mm. Hg, and in two of these it was 150 mm. Where diastolic pressures were high the pulse pressure was small, and in both patients in whom the diastolic pressure was 150 mm. Hg the pulse was often impalpable at the wrist. In one of these (Case 2) examination of the fundi revealed that all the arteries were uniformly narrowed and appeared to be in spasm. One recent haemorrhage was seen. In other children the fundi were normal.

Urinalysis revealed considerable albuminuria in all cases. Microscopical haematuria was invariably present, but in no case was the urine ever obviously blood-stained or even "smoky." A few pus cells were usually present, but were not regarded as significant. Casts were present in nearly all cases. Culture of the urine was sterile in most instances. In the remainder various organisms were grown, and were thought to be due to contamination of specimens, not obtained by catheterization, from female patients.

In two children clinical evidence of malnutrition was present. In one the skin on the front of the legs was

scaling and atrophic, and in the other the changes of early kwashiorkor were present in the hair.

Investigations revealed a mild degree of anaemia in most instances. One patient was severely anaemic. Malarial parasites were seen in small numbers in films of the peripheral blood in six cases. The parasites were usually of malignant tertian malaria, which is the commonest form of malaria occurring in the locality.

The blood-urea level on admission varied between 28 and 62 mg./100 ml.; in most cases it was under 40 mg. However, from the levels to which the blood urea sometimes subsequently fell, it was concluded that most of the levels on admission were, in fact, raised. The blood cholesterol was usually over 300 mg./100 ml. Serum protein levels were reduced, the average total on admission being 3.8 g./100 ml. (globulin 3.2 g., albumin 0.6 g.). Electrophoresis, except in one patient, revealed the "nephrotic" pattern with increase of the α_2- and β-globulin fractions, with reduction of albumin and sometimes of γ-globulin. Urinary protein, on electrophoresis, was generally found to contain approximately 60% of albumin. The remainder was globulin, of which the α_2 fraction was present in the smallest quantity.

A renal biopsy specimen was taken from the eight eldest patients in the series, and in all except one the clinical diagnosis of glomerulonephritis was confirmed, the exception being a patient from whom the specimen was taken six weeks after admission to hospital, when recovery from the nephritic episode was advanced. In some the degree of histological change was mild, but in three patients chronic nephritis was present.

Treatment

Treatment consisted of bed rest, fluid restriction, and a low-salt high-protein diet. In six cases chloroquine was given to clear the malarial parasitaemia. Penicillin was sometimes given for various infections which developed in hospital. In three patients who made no progress over the course of several weeks on this regime steroid therapy was instituted. One of these left hospital during the course of treatment before any improvement had taken place, and did not return. Another responded only moderately to a second course of corticotrophin, the first having been without effect. The third patient, a boy of 12, with massive oedema and ascites which had worsened during the first 10 weeks in hospital, responded dramatically to cortisone therapy (Case 3).

The duration of stay in hospital varied from three weeks to six months. Oedema and ascites usually improved slowly during this time, and in five patients had cleared, or almost cleared, by the time of discharge. Improvement in ascites was less marked than improvement in oedema. The degree of albuminuria fluctuated in most cases, but had lessened by the time of discharge in about half of them. In only one did it disappear completely, and, apart from this patient and the one who responded so well to cortisone therapy, it was not generally possible to correlate reduction of albuminuria with improvement in oedema and ascites, or with rise of the serum albumin level. Microscopical haematuria improved greatly and casts usually disappeared from the urinary sediment. In hospital the blood-urea level fell in seven patients, usually to between 16 and 20 mg./100 ml., but in two other patients it rose after discharge from hospital. The long-drawn-out course of acute nephritis in many of these children is illustrated by the case of a girl of 5 (Case 4) who was admitted to hospital with a 16-days history of massive oedema. Renal biopsy showed the picture of acute nephritis. After a protracted illness she was discharged from hospital still in the nephrotic stage. When seen 18 months later, however, she was apparently fully recovered.

Follow-up.—Of the nine children who attended for follow-up examination, three appeared to have recovered, two had improved, two had had recurrence of swelling (which in one case may have followed acute otitis media), and two had deteriorated. One of these was admitted in hypertensive left ventricular failure and died. The other, who had had Henoch's purpura, had developed severe hypertension and the blood urea had risen to 80 mg./100 ml.

Overall, the prognosis of the nephritis from which these children were suffering was thought to be poor.

Case 1

A Muganda boy aged 13 had been in hospital for two months, two years before the present admission, suffering from "nephritis." Generalized oedema with gross ascites had been present for a month prior to that admission and fever had occurred two days before the swelling began. The findings had included albuminuria, with casts in the centrifuged deposit. The B.P. had been 110/90. Oedema and ascites gradually subsided over the course of several weeks. Since discharge from hospital a rash had appeared from time to time, situated mainly on the arms and the trunk. It consisted of raised blotches which itched considerably, and dark spots were present in the centre of the blotches. It lasted from several hours to several days, and was often followed by colicky abdominal pain and black stools. Twelve days before the present admission the patient had developed coryza, cough, and fever, and three days later his face began to swell.

On examination there was moderate oedema of the face and neck, with slight oedema elsewhere. A moderate ascites was present and the liver and spleen were palpable; the B.P. was 130/90 and the fundi were normal. Urinalysis revealed heavy albuminuria, scanty microscopical haematuria, moderate pyuria, and a few cellular, hyaline, and granular casts. Urine culture was sterile.

Investigations.—Hb, 88%; R.B.C., 5,200,000/c.mm.; small malignant-tertian malarial parasitaemia; blood urea, 40 mg./100 ml.; blood cholesterol, 480 mg./100 ml.; serum proteins, 4.5 g./100 ml. (albumin 1.2 g., globulin 3.3 g.). Urine specific gravity range: 10 (1015–1005). The maximum urea concentration was 2.0 g./100 ml. and the urea clearance was 44% and 33% of normal. Renal biopsy revealed that some glomeruli were totally scarred and shrunken, while in others the capsular space was reduced because of adhesions. There was tubular atrophy, with dilatation and hyaline material in tubules. Some interstitial scarring was seen, and thickening of the wall of an interlobular artery was noted. There was also arteriolar thickening. Biopsy diagnosis: chronic glomerulonephritis. Biopsy culture was sterile. Chest *x*-ray film and E.C.G. were normal.

With bed rest, high-protein low-salt diet, and fluid restriction to 3 pints (1.7 litres) daily, oedema and ascites slowly improved. The malarial parasitaemia was treated with chloroquine, and ankylostomiasis with tetrachlorethylene.

The blood-pressure varied between 120/90 and 110/70 and the urinary findings remained unchanged. A rash appeared on several occasions, mainly on the trunk and the limbs, and lasted about two hours; it itched, was blotchy and urticarial, but no petechiae were seen. There were no attacks of abdominal pain while the patient was in hospital. Occult blood tests were intermittently positive and remained so after worming. Blood urea remained between 42 and 46 mg./100 ml. The serum albumin fell to 0.7 g./100 ml.

and electrophoresis of the serum proteins revealed the "nephrotic" pattern. At follow-up examination five weeks after discharge from hospital the blood-pressure had risen to 210/130 and the blood urea to 79 mg./100 ml.

Comment.—Henoch's purpura was associated with glomerulonephritis of two years' duration. Changes of chronic nephritis found on biopsy. Hypertension and renal insufficiency developed during the period of observation. Prognosis: poor.

Case 2

A Muganda girl aged 6 years was admitted to hospital with a history of generalized swelling of the body which had started in the face seven weeks previously. There was no history of any previous infection or of any similar illness. Intermittent vomiting and abdominal pain had been present since the onset. The patient had had to get up three times a night for micturition since the swelling began, and shortly before admission this nocturia had increased up to 10 times nightly.

Examination showed considerable generalized oedema and ascites, the face and the neck being particularly swollen. The pulse was very weak and was sometimes impalpable at the wrist. The B.P. was 170/150 and the heart normal. Examination of the fundi revealed that all the arteries were uniformly narrow and appeared to be in spasm. One recent haemorrhage was present. Urinalysis revealed a heavy albuminuria with slight microscopical haematuria and a few granular casts in the centrifuged deposit. Urine culture was sterile.

Investigations on Admission.—Hb, 105%; R.B.C., 6,200,000/c.mm.; blood film, normal; blood urea, 28 mg./100 ml.; blood cholesterol, 450 mg./100 ml.; serum proteins, 4.7 g./100 ml. (albumin 0.6 g., globulin 4.1 g.). The maximum urea concentration was 1.4 g./100 ml. and urea clearance 24% and 40% of normal. Renal biopsy (Fig. 1) showed severe renal damage, 8 of the 29 glomeruli present in biopsy being reduced to hyaline scars and the remainder being partially scarred. Digitation of the glomerular tuft was observed and all the glomeruli were ischaemic to a greater or lesser extent. There was considerable ischaemic atrophy of the tubules, some of which contained hyaline casts.

Treatment with bed rest and a low-salt high-protein diet was instituted. Shortly after admission status epilepticus, attributed to hypertensive encephalopathy, developed and lasted for several days. It eventually responded to treatment with paraldehyde and phenobarbitone intramuscularly, and magnesium sulphate enemata. During seven weeks in hospital the oedema subsided but the hypertension persisted. The child returned to hospital twice during the next four months, once with a sore throat (from which no pathogenic organisms were isolated) and once with coryza. The clinical findings were unchanged though the blood urea at the second visit was 42 mg./100 ml. At the end of four months she was admitted in acute left ventricular failure. The blood-pressure was 150/140, the radial pulse was impalpable at the wrist, and a gallop rhythm was heard over the praecordium. The urinary findings were unchanged. The blood urea had risen to 118 mg./100 ml. Treatment with mersalyl and digitalis was of no avail and she died two days after admission.

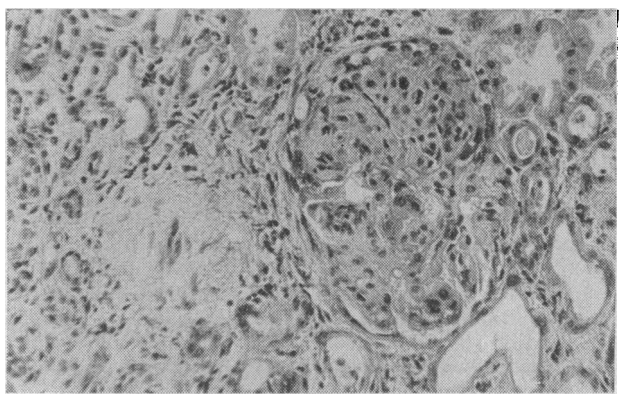

FIG. 1.—Case 2. Renal biopsy (H. and E. ×114), showing two glomeruli, one hyalinized and one with marked capsular adhesions and developing ischaemia. Illness was of nine weeks' duration when the biopsy was taken. Death from hypertensive heart failure occurred five months later.

At necropsy both lungs were oedematous and small pleural effusions were found; the left ventricle was enlarged. The kidneys weighed 150 g. each; the capsules were stripped with difficulty, leaving a finely granular surface. On the cut surface the cortex was slightly reduced. The renal pelves, renal vessels, ureters, and bladder were normal. Histology of the kidney revealed changes similar to those seen on biopsy.

Comment.—Rapidly progressive glomerulonephritis with gross hypertension; death within six months of the onset. Advanced changes of "chronic" nephritis were present on renal biopsy nine weeks after symptoms began.

Case 3

A Muganda boy aged 12 years was admitted to hospital with a history of illness of three months' duration which began with colicky abdominal pain and was followed a day later by swelling of the face and neck. The swelling gradually spread to the rest of the body. Nocturia had occurred three times nightly since the onset. (He had been admitted to hospital with a similar illness nine months previously. Cough and fever had preceded that episode, in which gross oedema and gross albuminuria, with microscopical haematuria and casts in the urinary deposit, had been present. The blood-pressure was 146/98 at that time. Oedema had disappeared by the time of discharge.)

On admission there was considerable oedema and ascites, the blood-pressure was 110/85 and the fundi were normal. Urinalysis revealed heavy albuminuria with moderate microscopical haematuria and hyaline casts in the centrifuged deposit. Urine culture was sterile.

Investigations.—Hb, 58%; R.B.C., 3,500,000/c.mm.; blood film normal; blood urea, 62 mg./100 ml.; blood cholesterol, 447 mg./100 ml.; serum proteins, 3.6 g./100 ml. (albumin 0.4 g., globulin 3.2 g.); electrophoresis revealed the "nephrotic pattern" (Fig. 2). The maximum urine concentration was 1016 and the maximum urea concentration 1.15 g./100 ml. with urea clearance values of 21% and 22%

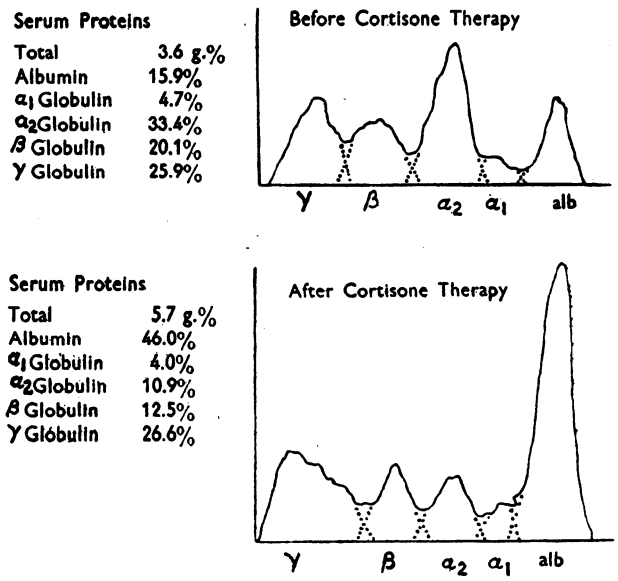

FIG. 2.—Case 3. Electrophoretic pattern of serum proteins before and after steroid therapy.

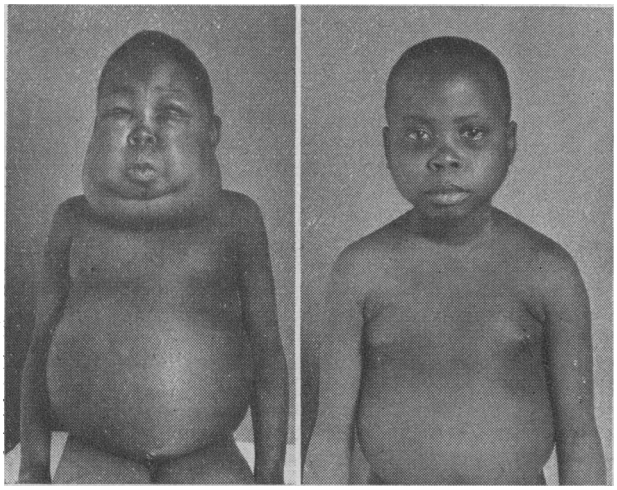

FIG. 3.—Case 3. Before and after steroid therapy.

of normal. Renal biopsy revealed the changes of glomerulonephritis, with advanced scarring of a few of the glomeruli present.

Treatment with bed rest and a high-protein low-salt diet with fluid restriction was instituted. The patient's general condition deteriorated over the first 10 weeks in hospital and gross oedema caused extension of the neck, with difficulty in breathing at times. Tapping of the ascites was necessary. The blood urea rose to 76 mg./100 ml. As the clinical condition continued to deteriorate cortisone, 100 mg. daily, was given for 14 days, and then "tailed off" over the next three weeks. There was a dramatic response to this treatment. Diuresis began 13 days after steroid therapy was begun, and over the period of a week the weight fell from 72 to 48 lb. (32.7 to 21.8 kg.). Two months later, at the time of discharge from hospital, all oedema had disappeared. The blood urea was 19 mg./100 ml.; blood cholesterol, 105 mg./100 ml.; serum proteins, 5.7 g./100 ml. (albumin 2.5 g., globulin 3.2 g.); and the electrophoretic pattern normal. Maximum urine concentration was 1022 and dilution 1002. Maximum urea concentration was 3.46 g./100 ml. with urea clearance 97% and 113% of normal. A second renal biopsy revealed similar changes to the first: 17 of the 24 glomeruli present were normal, four were partially fibrosed, and in three there was considerable scarring.

At follow-up examination three months later the boy had grown, looked well, and was symptom-free (Fig. 3). The blood-pressure was 95/65. Urinalysis revealed slight albuminuria, and slight microscopical haematuria persisted. Laboratory findings were as on discharge from hospital.

Comment.—Glomerulonephritis in a nephrotic phase with excellent response to cortisone therapy.

Case 4

A Munyaruanda girl aged 5 years was admitted to hospital with a history of swelling of the body of 16 days' duration, which began in the face and became generalized within a week of the onset. Fever and sore throat had occurred several days before the swelling appeared. Nocturia had been present since the onset of the illness. The only other sibling had died at the age of 7 years of swelling "similar to this." The diet was poor.

On examination there was considerable generalized oedema, with gross ascites. The B.P. was 100/70 and the fundi were normal. Scattered crepitations were heard throughout both lungs. Urinalysis revealed heavy albuminuria, considerable haematuria, but no casts.

Investigations.—Hb, 80%; R.B.C., 3,800,000/c.mm.; small malignant-tertian malarial parasitaemia, throat swab culture; no beta-haemolytic streptococci; blood urea, 50 mg./100 ml.; blood cholesterol, 500 mg./100 ml.; serum proteins, 4.6 g./100 ml. (albumin 0.7 g., globulin 3.9 g.); electrophoresis of serum proteins (Fig. 4) revealed the "nephrotic pattern." Electrophoresis of urinary proteins revealed albumin together with a small amount of γ-, β-, and α_1-globulin, and a trace of α_2-globulin. Proteinuria, estimated by Esbach's reagent, was 13.5 g./l. Renal biopsy (Fig. 5) revealed changes of acute glomerulonephritis. Appreciable renal damage was present, 8 of the 23 glomeruli in the biopsy being badly affected. There was much haemorrhage in some glomeruli, and one was infarcted.

The child was treated with bed rest and a low-salt high-protein diet. Chloroquine therapy was given to clear the malarial parasitaemia, and two courses of corticotrophin resulted in slight temporary improvement but did not substantially alter the patient's general condition. Albuminuria varied between 3 and 22 g./l. and microscopical haematuria persisted. Small numbers of casts were seen in the centrifuged deposit from time to time. The blood-pressure remained normal during the six months the patient was in hospital and the blood urea rose to 100 mg./100 ml. The blood cholesterol fell to 210 mg./100 ml. Some general improvement occurred in the patient's condition at the end of six months and she was discharged. Since then she has been seen at follow-up on several occasions, the last being 18 months after discharge, when she was reported to have fully recovered.

Comment.—Acute glomerulonephritis; prolonged nephrotic phase.

Glomerulonephritis in Adults

Early or "Acute" Nephritis

These three patients were all young men whose presenting complaint was of swelling of the body. No previous history of similar illness was given, though

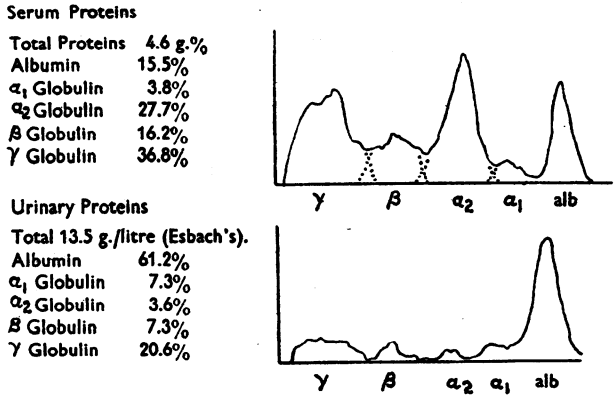

FIG. 4.—Case 4. Electrophoretic pattern of serum and urinary protein.

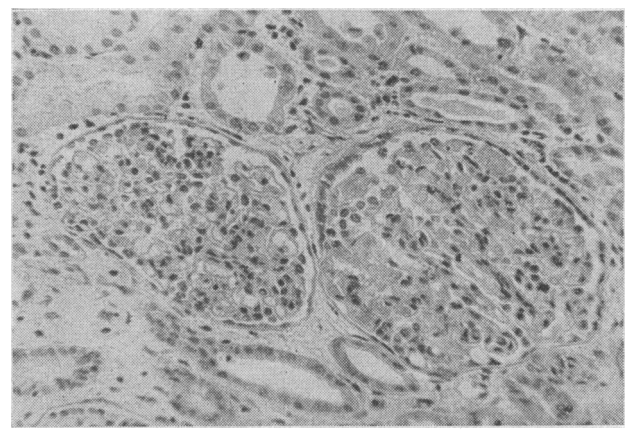

FIG. 5.—Case 4. Renal biopsy (H. and E. ×87), showing acute glomerulonephritis. Note the swelling and cellularity of the glomerular tuft.

there was evidence in one to suggest that renal damage may have dated from an attack of pneumonia a year previously. One patient had had a sore throat and fever a week before the onset of the swelling, but neither of the others gave a history of recent infection. No symptoms of urinary disorder were present, and, in particular, no patient gave a history of passing bloody urine.

Clinical findings on admission included moderate, usually generalized, oedema associated with considerable albuminuria. In two patients the urine was "smoky" on admission and casts were present in the urinary sediment; the blood-pressure was raised in these two cases and linear haemorrhages were present in the fundi of one. In both, the blood urea was raised. Renal biopsy revealed changes of acute glomerulonephritis, and a second biopsy, taken six to eight weeks after the first, revealed in both cases some regression in the histological changes, though in one case digitation of the glomerular tufts suggested that ischaemic change was occurring. Clinically, a moderate improvement took place with bed rest and a low-salt high-protein diet. Oedema, albuminuria, and haematuria lessened and the fundi returned to normal in the patient in whom they had been affected. Hypertension persisted, however, and, though the blood-urea level had fallen, it had not returned to normal by the time of discharge from hospital. The prognosis was therefore guarded. In the third patient (Case 5), who was only mildly, if at all, hypertensive on admission, and in whom microscopical haematuria was slight, the features of the nephrotic syndrome were present. Considerable improvement took place during the three weeks of hospital treatment.

Case 5

A Muganda man aged 27 was well until a month before admission to hospital. He then developed fever and pain on swallowing, which lasted for a few days. A week later the feet and hands began to swell, and later this swelling spread to the abdomen and the face. During this time he felt unwell, and dull aching pain developed in the abdomen and loins. The patient had passed urine twice nightly all his life, and since the onset of the present illness three or four times nightly. There had been no other urinary symptoms and no past history of illness. The diet was fair only, and included, in addition to matoke (banana) and lumonde (sweet potato), meat once weekly and fish once a fortnight. No milk or butter was eaten.

On examination oedema was slight over the face, moderate over the legs, and considerable over the back. A soft apical systolic murmur was heard. The blood-pressure was 155/80 and the fundi were normal. A moderate ascites was present. The bladder, urethra, and prostate were normal, the urine stream was good, and a soft rubber catheter passed easily. There was no residual urine. Urinalysis revealed a heavy cloud of albumin, and in the centrifuged deposit a few red cells, pus cells, and granular casts were seen. Urine culture was sterile.

Investigations.—Hb, 100%; R.B.C., 4,700,000/c.mm.; reticulocytes, 1.0%. Blood film: red cells normal; very occasional malignant-tertian malarial parasites present; platelet count normal; white blood count 16,800, including 9,900 eosinophils; blood urea, 21 mg./100 ml.; serum cholesterol, 410 mg./100 ml. Total plasma protein, 4.3 g. (albumin 0.7 g., globulin 3.6 g.); electrophoresis of serum protein revealed some increase in α_2-globulin while electrophoresis of urinary protein revealed albumin with slight amounts of γ-, β-, and α_1-globulin; only the faintest trace of α_2-globulin developed. Urinary protein, estimated with Esbach's reagent, was 4 g./l. Maximum urine concentration, 1013, dilution 1008. Maximum urea concentration was 0.94 g./100 ml. and urea clearance 71% and 81% of average normal function. Renal biopsy revealed changes of acute glomerulonephritis. The glomerular tufts were cellular and contained moderate numbers of polymorphonuclear leucocytes; recent capsular adhesions were present and a little epithelial proliferation was seen. There was no scarring or arteriolar change. Biopsy culture was sterile. Intravenous pyelography showed nothing abnormal. The chest *x*-ray film, heart-screening, and electrocardiograms were all within normal limits.

Treatment with bed rest and a high-protein low-salt diet was instituted. Two weeks after admission pyrexia of 103° F. (39.4° C.) developed, lasting for eight days. Blood culture was sterile, and white blood count and blood film, throat swab culture, and chest *x*-ray film revealed no abnormality that would account for the pyrexia, which settled after a course of systemic penicillin. While in hospital oedema subsided and only slight swelling of the ankles remained on discharge from hospital. Albuminuria had decreased considerably, slight microscopical haematuria and a few granular casts were still present. The blood-pressure had remained normal throughout.

Comment.—Recent onset of oedema, with features of the "nephrotic syndrome," followed a sore throat. Renal biopsy revealed acute glomerulonephritis. Clinical improvement occurred during three weeks in hospital.

Rapidly Progressive Glomerulonephritis

Three patients fell into this category. Two died in hospital and the third was discharged home eight weeks after admission. His condition on leaving hospital was poor and he did not return for follow-up examination. All three were between 20 and 30 years of age. Symptoms were of short duration and none gave a significant history of previous illness. In two patients extensive oedema had appeared over the course of a few weeks, while the third patient presented in left ventricular failure (Case 6). All were in uraemia and all had a raised blood-pressure. In two cases hypertension was severe and both these patients died from heart failure associated with renal insufficiency. In both cases severe changes in the fundi were present and included papilloedema in one, and a severe retinitis, with many fresh haemorrhages, in the other. In both cases early arteriolar necrosis was seen on renal microscopy. In all three cases some changes of acute nephritis were present in renal biopsy sections.

Case 6

A Munyaruanda man aged 25 had been well until eight weeks before admission to hospital, when he developed breathlessness on exertion. Since then he had woken nearly every night with "something choking him." He had to sit up and wait for the breathlessness, which was associated with a dry cough and palpitations, to subside. These attacks generally lasted half an hour. There were no other symptoms, and, apart from an attack of gonorrhoea in 1951, there was no past history of illness. The diet, which included meat twice weekly, was fairly good.

On examination the patient was orthopnoeic. The pulse was regular, 120 a minute, and rather "hard" in character. The artery wall was normal. The heart was enlarged and a presystolic gallop rhythm, heard best at the apex, was present over most of the praecordium. Some basal rales were heard. There was no jugular congestion and ankle oedema was minimal. The blood-pressure was 170/130. In the fundi, marked arterial change and nipping at the venous crossings were seen and many fresh linear haemorrhages and soft exudates were present. The optic disks were normal. The liver was somewhat enlarged, the urethra and prostate were normal, the urine stream was good. A catheter was passed easily and there was no residual urine. Urinalysis revealed slight albuminuria, and in the centrifuged deposit a few white blood cells, red blood cells, and very

occasional granular casts were seen. Urine culture was sterile.

Investigations.—Hb, 85%; R.B.C., 4,000,000/c.mm.; reticulocytes, 2.9%; white blood count and platelet counts normal; blood urea, 108 mg./100 ml.; blood cholesterol, 223 mg./100 ml.; plasma proteins, 6.5 g./100 ml. (albumin 2.7 g., globulin 3.8 g.); electrophoresis of serum proteins revealed a normal pattern. Renal biopsy revealed very severe renal damage; all the glomeruli were affected and the vast majority showed complete capsular adhesion. All were very ischaemic, but in many a little blood was still passing through the glomeruli and none were totally fibrosed. The glomerular lesions all appeared to be of the same duration. The tubules were dilated and the arteries present showed interstitial thickening. Arteriolar necrosis had occurred. The appearances were those of advanced glomerulonephritis, probably of recent origin. Chest *x*-ray examination revealed a moderate-sized left pleural effusion, and heart-screening showed marked left ventricular enlargement.

Treatment with bed rest, a low-salt diet, liberal fluid intake, digitalis, and mersalyl was instituted. There was no significant response. The blood urea continued to rise and the patient died six weeks after admission to hospital. Six days before death the blood-urea level was 240 mg./100 ml.

Necropsy revealed cardiac enlargement (heart weight 440 g.) with left ventricular hypertrophy. The kidneys were of normal size (157 g. each) and of normal consistency; the capsules stripped with ease, leaving a smooth surface. A very small indentation over the lower pole of the right kidney indicated the position of the renal biopsy. On the cut surface the cortex was a little narrowed; the corticomedullary junction was fairly clear. Histological findings were as described above.

Comment.—Fulminating glomerulonephritis. Death from renal and hypertensive cardiac failure in 14 weeks from the onset of illness.

Subacute Nephritis

One patient admitted with the nephrotic syndrome ran a subacute course. Over a period of several months the blood-pressure rose to hypertensive levels and the blood urea likewise steadily increased.

Latent Nephritis

One patient, a 32-year-old woman, was thought to have glomerulonephritis in a latent phase. Her symptoms of palpitations were thought to be due to extrasystoles. Moderately severe hypertension was associated with cardiac enlargement. Slight changes in the fundi were present. Urinalysis revealed no albuminuria, and virtually no abnormality was seen in the centrifuged deposit. The renal-function tests, blood urea, and serum cholesterol were all likewise normal. Renal biopsy, however, revealed slight but definite changes of glomerulonephritis.

"Intermediate" Nephritis

The first of these three patients had glomerulonephritis, a urethral stricture with secondary infection of the urine, and severe anaemia. A general improvement took place over the course of two months' treatment in hospital. The second patient also had a severe anaemia, thought to have been partly associated with nephritis. In the third, a woman of 40, swelling of the limbs and face had been present intermittently for several years. Albuminuria and microscopical haematuria were present, and a renal biopsy revealed evidence of mild active nephritis.

Chronic Glomerulonephritis

In 10 patients (nine males, one female) a diagnosis of chronic glomerulonephritis was reached. Their ages ranged from 20 to 41 years. Histological material was obtained from needle biopsy of the kidney in eight cases (in two of which post-mortem material was subsequently available), and in the other two cases from necropsy. These patients had been too ill to warrant biopsy.

The diagnosis of chronic nephritis was confirmed histologically in all but one case. In this patient the histological findings were most probably those of chronic nephritis, though chronic pyelonephritis remained a possibility. On the clinical features a diagnosis of chronic nephritis was made.

Congestive heart failure was the commonest mode of presentation in this group and was the reason for admission to hospital in six cases. Two others came to hospital because of generalized swelling, which in one was severe. In one patient recurrent abdominal swelling of three years' duration, due to ascites, was the only complaint. The remaining patient complained of severe headache and deterioration of vision.

The history revealed that two patients had been in Mulago Hospital with a similar illness 5 and 18 months previously, while another had attended the out-patient department with oedema and albuminuria two years before the present admission. The only female patient had been oedematous with both the second and third pregnancies, and in both cases the baby had been stillborn. In this last pregnancy an illness had occurred which from the patient's description was probably heart failure. The first pregnancy had been uneventful. Four male patients gave a history of gonorrhoea between 7 and 15 years previously, but no late effects of this disease were found and none of the patients had urethral strictures. The dietary history generally revealed that a fairly good diet was taken.

Oedema was usually slight to moderate in degree and, with congestive heart failure, dependent in distribution. In two cases oedema was virtually absent, while in one it was severe and generalized. Swelling of the face was present intermittently in several patients. Swelling of the abdomen, due to ascites, occurred when oedema was severe. In one patient it was the only complaint and was present in the absence of oedema. In this patient the blood-pressure was within normal limits, but in all the others it was raised, and in four the diastolic pressure was 150 mm. Hg. A severe retinitis was present in patients whose diastolic pressure was 130 mm. Hg or over. In those patients whose diastolic pressure was below 130 mm. Hg retinitis was absent, though narrowing and tortuosity of the arteries with increase of the light reflex was often seen. Two patients had papilloedema, and the diastolic blood-pressure in both cases was 150 mm. Hg or over.

There was clinical and radiological evidence of left ventricular enlargement, and electrocardiographic evidence of left ventricular strain in all except the patient in whom the blood-pressure was normal. A moderate degree of albuminuria was a constant occurrence. Microscopical haematuria was also always present, though in most cases it was slight. Pus cells were usually less than 5 per c.mm. A few granular and hyaline casts were generally seen in the centrifuged deposit. From each patient several urine cultures were performed, and were repeatedly sterile, except in two from whom organisms thought to be contaminants were grown. In both these cases few pus cells were present in the centrifuged deposit and subsequent urine cultures were sterile. Cultures taken from the renal-biopsy needle were sterile in all cases.

Anaemia was a common finding, the haemoglobin varying between 22% and 83%. Some degree of

azotaemia was present in all patients; in four the blood urea was over 150 mg./100 ml. Urine concentration and dilution tests nearly always revealed gross impairment of renal function, and urea concentration and clearance tests showed similar results.

Histological studies of the kidney revealed considerable damage in all. In most cases many glomeruli were totally scarred while others showed varying degrees of ischaemic change. Capsular adhesions were common and arteriosclerosis was often seen. Secondary tubular degeneration was usually present.

Total serum protein levels ranged from 5 to 6.2 g./100 ml.; the average was 5.5 g. Serum albumin levels varied between 0.6 and 2.3 g. (average 1.7 g.), and serum globulin from 2.8 to 5.2 g. (average 3.8 g.). The electrophoretic pattern of the serum proteins was studied in seven cases. Apart from hypoalbuminaemia, two were normal, in four there was some increase in γ-globulin, and in the remaining case the "nephrotic" pattern was present.

The length of time patients were under observation varied from three days to a year, but with previous admissions to Mulago Hospital this period of observation was up to three years in duration. Four patients died during the study period, and all came to necropsy. In three who had been under observation for several months the illnesses had been clinically similar, and death was in all cases due to hypertensive heart failure associated with uraemia (see Case 7). The fourth patient, who was suffering from malignant hypertension, died shortly after admission from an intracerebral haemorrhage.

Of the six remaining patients, one, the only female patient with chronic nephritis, suffered from heart failure and renal insufficiency, and the blood urea rose from 153 to 204 mg./100 ml. during three weeks in hospital. Two others made a good recovery from hypertensive heart failure, but, in one, failure had already recurred at a follow-up examination three weeks after discharge. A fourth, who complained of severe headache and failing vision, suffered from malignant hypertension (B.P. 240/160). The blood-urea level rose from 59 to 157 mg./100 ml. during six weeks' observation.

In the remaining two cases the disease progressed more slowly. In one the only complaint was a recurrent ascites, which had been present for three years. The blood-urea level remained between 150 and 160 mg./100 ml. during the nine weeks of hospital treatment. The blood-pressure was within normal limits and no deterioration occurred in his general condition while under observation. The remaining patient, aged 22, was discharged from hospital with a high blood-pressure, albuminuria, and raised blood urea. Three years later his condition was unchanged.

Case 7

A Munyaruanda man aged 20 was admitted to hospital with congestive heart failure. He had been in hospital three months previously with a similar illness, and findings at that time had included: B.P. 150/125, pulsus alternans, cardiac enlargement, gallop rhythm, jugular venous congestion, oedema, ascites, albuminuria, and a few casts in the urinary deposit. A moderate response to bed rest, digitalis, and mersalyl therapy had occurred. On discharge the B.P. was 160/110.

The findings at the present admission were similar to the previous ones; the blood-pressure, however, had fallen to 120/95. The fundi were normal.

Investigations.—Hb, 70%; R.B.C., 4,200,000/c.mm.; small malignant-tertian malarial parasitaemia; blood urea, 44 mg./100 ml.; blood cholesterol, 166 mg./100 ml.; serum proteins, 5.9 g./100 ml. (albumin 1.2 g., globulin 4.7 g.). The maximum urine concentration was 1010. No renal biopsy was taken, as the patient was uncooperative. Chest *x*-ray examination revealed an increase in the transverse diameter of the heart, and on fluoroscopy left ventricular enlargement was noted. The electrocardiogram revealed left ventricular strain.

A slight initial response to treatment with bed rest, digitalis, and mercurial diuretics was followed by a gradual deterioration over the course of several weeks, during which time the blood urea rose steadily to 210 mg./100 ml.; pericardial friction developed. The patient died seven weeks after admission.

At necropsy the heart weighed 460 g. and there was left ventricular enlargement. The kidneys weighed 110 g. each, the capsules were lightly adherent, and the surface of the kidneys was finely granular. Microscopy revealed a large number of totally scarred glomeruli uniformly distributed throughout the kidney substance. The appearances were those of chronic glomerulonephritis (Fig. 6).

Comment.—Chronic glomerulonephritis with hypertensive heart failure; terminal renal insufficiency.

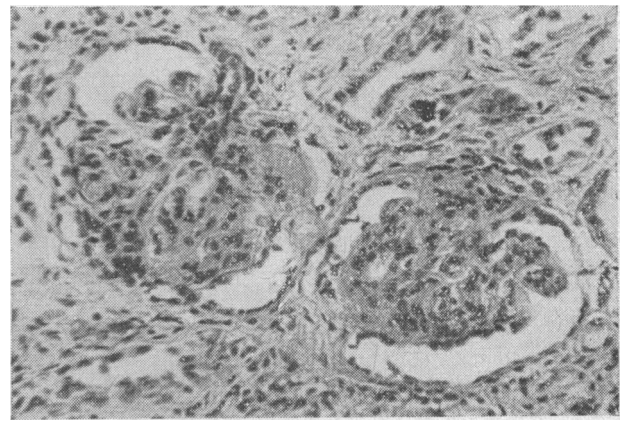

FIG. 6.—Case 7. Necropsy specimen (H. and E. ×114), showing chronic glomerulonephritis. Two ischaemic adherent cellular glomeruli are present. The patient, a youth aged 20, died from hypertensive heart failure with renal insufficiency.

Discussion

Gelfand (1957) stated that "the acute form of glomerulonephritis [in the Bantu] is not altogether rare, though possibly less frequent than in the European," and that in most cases there was haematuria visible to the naked eye. He suggested, however, that haematuria was so often due to bilharzia that its value as a sign of acute nephritis was diminished. Gelfand also found subacute or nephrotic nephritis to be an "extraordinarily common and serious form of nephritis." Furman (1955) analysed the records of 220 cases of nephritis in Bantu subjects and, "using the criteria of Ellis (1942)," classified the cases into Types I and II. He found 68% were Type I and 32% were Type II. Type I cases, however, were characterized by absence of macroscopic haematuria and by a prolonged oedematous phase lasting up to three to four months. Under these circumstances the division of cases into the two types must have been difficult, particularly as it was stated that, "the clinical picture of these patients [with Type I nephritis], often several weeks after the onset of

the illness, is superficially similar to that of a patient with Type II nephritis." Type I nephritis was a disease of childhood and adult life, while Type II was a disease predominantly of young adults.

In Uganda it would appear that glomerulonephritis in the Bantu is also a disease of the younger age-groups. Of the 33 patients described the eldest was 41 years old. This youthful distribution was not entirely due to the tendency for young people to be admitted to hospital in Uganda. In Fig. 7 is shown the age distribution of the whole group of 67 patients with various forms of renal disease or hypertension from which the present series was drawn. It is seen that glomerulonephritis occupies most of the younger half of the series, and in fact was present in 32 out of 48 patients up to the age of 40 years. Above this age only one out of 19 patients was shown to have glomerulonephritis.

No sex distribution was evident that could not be accounted for by the different proportion of males and females admitted to medical wards in Kampala, and no particular tribal distribution was noted.

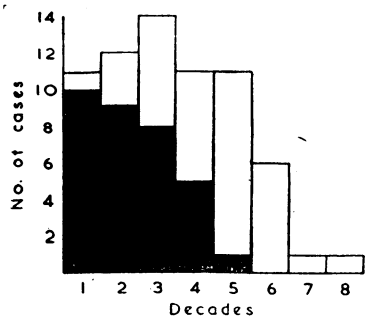

FIG. 7.—Incidence of glomerulonephritis in 67 patients with various forms of renal disease and hypertension.

In the 12 children with glomerulonephritis a characteristic pattern emerged. The dominant clinical features were oedema and albuminuria which, together with the finding of hypercholesterolaemia and hypoalbuminaemia, constituted the features of the nephrotic syndrome. The electrophoretic pattern of the serum proteins, moreover, with increase in α_2 and β-globulin fractions, with a decrease in albumin and sometimes of γ-globulin, was that described as occurring in the nephrotic syndrome in children (Stickler, Burke, and McKenzie, 1954). (That the proportion of albumin in the urinary protein was relatively low was attributable to the very low levels of serum albumin (MacInnes and Longsworth, 1939; Luetscher, 1940).)

On the other hand, hypertension was usually present, and in some cases (generally those in which advanced histological changes were present in the kidney) was sometimes severe. Microscopical haematuria was invariable and the blood urea was generally slightly raised. Moreover, the histological features were, in varying degrees, those associated with Type I nephritis (Ellis, 1942), though in some cases chronic changes were present. The overall pattern of the disease in these children was therefore fairly uniform and contained features of both Ellis types of nephritis. In our present state of imperfect knowledge it would perhaps be wise to refer to the illness simply as "oedematous glomerulonephritis." The prognosis, however, appeared to be more closely akin to that of Ellis Type II nephritis than to Ellis Type I, as in the short time of study one of these children died, several relapsed, while in others the degree of histological change as seen from renal biopsy left little doubt about the ultimate fatal outcome of the disease.

The aetiology of the disease is not clear. Nephritis in the tropics has been attributed by several workers to malarial infection (Manson-Bahr and Maybury, 1927; Goldie, 1930; Giglioli, 1932; Carothers, 1934; James 1939), the quartan malarial parasite being usually held responsible. Carothers (1934) found 10 out of 15 children with nephritis to have a quartan-malaria parasitaemia, whereas in only 18 out of 217 children without nephritis was quartan parasitaemia demonstrated. Carothers felt that, "in so far as one could judge from the limited number of cases, it would appear probable that quartan malaria might be a factor in the causation of nephritis." The cases described by these various authors do not form a very homogeneous pattern, and it is not surprising, after all, that malaria and nephritis should co-exist in tropical countries. Raper (1953) has pointed out that the pathological findings in the five cases described by Giglioli (1932) as being characteristic of malarial nephritis were, in three of the cases, those of chronic (probably pyelo-) nephritis, and Raper felt that the photomicrographs in two of these cases confirmed this opinion.

In the present series, malarial parasitaemia was present in 6 of the 12 children with glomerulonephritis. This would not be an unusual finding in a similar group of children in hospital in Kampala without nephritis, in whom the blood was searched periodically over a period of many weeks. The majority, moreover, were of malignant tertian malaria, which is the usual malarial infection in the district. Treatment of the parasitaemia with chloroquine did not result in improvement in the state of the nephritis. James (1939), however, stated that malarial nephritis responded well to treatment with antimalarial agents. It therefore seemed that, apart from its general effect as a chronic infective state, malaria was not aetiologically connected with the nephritis from which these children suffered.

In seven of the children there was a history of recent infection, usually of the upper respiratory tract, and in four this had occurred within 11 days of the onset of oedema. Haemolytic streptococci were not isolated from the throat swab in these patients, though attempts were made to do so in some cases. Haemolytic streptococcal infections are said to be very uncommon among Africans in tropical Africa. Davies (1947), from post-mortem studies in Uganda, found that most pyogenic infections were due to the pneumococcus or staphylococcus. The rarity of acute rheumatism, chorea, and rheumatic nodules has been mentioned by Donnison (1928) and Williams (1939) from East Africa, and by Jelliffe and Reed (1953) from Nigeria. The latter authors isolated beta-haemolytic streptococci from the throats of only 0.9% of schoolchildren between the ages of 4 and 18 years, a carrier rate which appeared to the authors to be significantly lower than that found in most temperate regions. However, though it is possible that haemolytic streptococcal infections are relatively uncommon among Africans in Uganda they are certainly seen, from time to time, in hospital practice, and chronic rheumatic heart disease is by no means uncommon (Shaper and Shaper, 1958). It seems possible, therefore, that the infection which these children developed before the onset of nephritis may have been, in fact, streptococcal, and that nephritis in Uganda may be aetiologically connected with the streptococcus as it is in Europe.

The extreme degrees of oedema seen in some of the patients (especially the children with glomerulonephritis) were thought to be associated with gross hypoalbuminaemia. The cause of this was partly albuminuria, which was usually heavy (in one child, loss of urinary protein reached a level of 22 g./litre at a time when the serum albumin level was 0.49%). In some patients the serum albumin level continued to fall after admission to hospital, presumably because the patients were admitted early in the course of their illness before the drain of albumin in their urine had fully depleted the serum protein level. Another factor in the development of gross oedema may have been that the serum protein levels of even apparently healthy Africans in Uganda are different from European normals (Holmes, Stanier, Semambo, and Jones, 1951), the albumin levels being lower and the globulin levels higher than in Europeans. The serum albumin levels in these patients, especially in the children, were therefore probably low before the urinary loss began.

Summary

Thirty-three African patients suffering from glomerulonephritis were studied. In all but the youngest cases the diagnosis was confirmed by renal biopsy.

The 12 children in the series presented with massive oedema and ascites associated with heavy albuminuria. Haematuria was only microscopical. A rise in blood-pressure was common. The serum albumin level was constantly low and the serum cholesterol usually raised. Electrophoresis of serum protein characteristically revealed a "nephrotic" pattern. Some rise in the blood-urea level was common in the early stages of the illness. Changes of acute nephritis were generally seen on renal biopsy, though in three out of eight cases in which this was done chronic nephritis was present. The illness ran a protracted course, abruptly curtailed in one case by steroid therapy. The overall prognosis appeared to be poor.

Renal biopsy revealed acute nephritis in 6 of the 21 adult patients. One presented with the nephrotic syndrome and made an apparently good recovery. In two others with a raised blood-pressure, macroscopic haematuria, and a raised blood urea, some improvement took place in hospital. In the remaining three the disease was rapidly progressive, two dying in hospital. Severe hypertension, retinopathy, renal insufficiency, and heart failure were characteristic of these cases in which severe changes of recent origin were present on renal biopsy.

Chronic nephritis was present in 10 cases, and in these hypertensive heart failure was the commonest mode of presentation. Advanced retinopathy was usual in the presence of severe hypertension. The blood urea was raised in all cases, and in four patients who died while under observation death was due to heart failure associated with insufficiency.

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ACUTE APPENDICITIS IN PREGNANCY

BY

WILLIAM P. BLACK, M.B., F.R.C.S.Ed., M.R.C.O.G.

Lecturer, Department of Obstetrics and Gynaecology, University of Leeds

Acute appendicitis in pregnancy is a subject about which much has been written in American journals but which has had little attention in British literature. The incidence is between 0.5 and 1 per 1,000 pregnancies, and mismanagement of this condition carries a significant maternal mortality.

The diagnosis of appendicitis is frequently difficult in the pregnant, as in the very young, the very old, and the obese. Particularly in pregnancy is the early diagnosis most important, because the mortality of appendicitis complicating pregnancy and the puerperium is the mortality of delay.

Of the 25 cases of acute appendicitis in pregnancy here presented, 10 occurred in Glasgow Royal Maternity and Women's Hospital between 1942 and 1953 (an incidence of 0.26 per 1,000 births), 3 occurred in Eastern District Hospital, Glasgow (an incidence of 1.4 per 1,000 births), and 8 were treated in the Maternity Hospital at Leeds between 1948 and 1959 (an incidence of 0.36 per 1,000 births). Four were treated in the general surgical wards of Glasgow Royal Infirmary.

From the literature 348 cases of appendicitis in pregnancy were collected, giving a total of 373 cases, including the present series.

Incidence of Acute Appendicitis

In acute appendicitis in general, two-thirds of cases occur between 11 and 30 years of age, and two-thirds are male (Tashiro and Zinninger, 1946). One-third of the male patients have perforative appendicitis, compared with one-fifth of the females. Three-quarters of all cases of so-called chronic appendicitis occur between 11 and 30 years of age, and two-thirds of these are females (Shelley, 1938). Appendicitis, therefore, is