

reviewed. The diagnosis was made at necropsy in 8 out of the 9 children. On the basis of these families and a review of reported familial incidence in the literature, it is suggested that this condition may be a dominant autosomal trait rather than a recessive autosomal as previously suggested.

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The first child in Family III was under the care of Professor J. L. Henderson; the second child in Family III and the second child in Family IV were under the care of the late Professor R. W. B. Ellis. We are indebted to Dr. Douglas Bain for details of the necropsies which he carried out.

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## Glomerulonephritis associated with *Staphylococcus albus* in a Spitz Holter valve

The association of glomerulonephritis with infection of a ventriculoatrial shunt by *Staphylococcus albus* was first described by Black, Challacombe, and Ockenden (1965), and the presence of  $\gamma$ -globulin and complement in the glomeruli suggested that the glomerulonephritis was due to an immune response. The findings of immune deposits on the glomeruli in similar cases was also reported by Stickler *et al.* (1968) and Rames *et al.* (1970), who in addition described electron dense deposits in the glomeruli of their 3 patients. Staphylococcal antigen in the glomeruli of a further case of shunt nephritis was found by Kaufman and McIntosh (1971). 5 cases presented at clinical meetings were quoted by Rames *et al.* (1970) and 2 more cases were reported briefly by Leumann, Stauffer, and Wegmann (1971).

In this paper we report the findings in a 3-year-old boy who developed the nephrotic syndrome in association with *Staph. albus* infection of a ventriculoatrial shunt, and describe the light and electron microscopical changes in his kidney. He had a very high level of antibodies to *Staph. albus*, providing, for the first time, direct evidence of antibody response to this organism.

#### Case report

This boy had a Spitz Holter valve inserted at the age of 10 months for hydrocephalus due to aqueduct stenosis. He had hypospadias, undescended testes, slight webbing of the third and fourth fingers, incurved little fingers, and was mentally retarded. Chromosomal analysis showed an elongated short arm of chromosome 2.

At the age of 3½ years his spleen became palpable and soon afterwards he began to sweat excessively. Three months later he was admitted to hospital for surgical correction of a strabismus. He was febrile (temp. 37.8 °C), sweating, and had generalized oedema

TABLE  
Investigations

Urine	Protein 100 mg/100 ml Red blood cells 50/HPF Urea 59 mg/100 ml Bicarbonate 15 mEq/l. Plasma proteins: total 5.3 g/100 ml albumin 2.1 g/100 ml
Blood	
CSF	Creatinine clearance 61 ml/min per 1.73 m <sup>2</sup> Antistreptolysin —o titre 60 units $\beta_1$ C globulin 1/80 (normal) <i>Staph. albus</i> antibody titre 1 in 5120 Culture—sterile WBC 45 Culture: <i>Staph. albus</i>

and ascites. His blood pressure was 110 mmHg. Investigations (Table) showed that he had the nephrotic syndrome with microscopical haematuria, uraemia, and acidosis. Culture of CSF yielded *Staph. albus* though blood culture was sterile. His blood contained a very high level of antibody to *Staph. albus*, but serum  $\beta_1$ C globulin was normal. He was treated with cephaloridine and penicillin, and the valve, which yielded *Staph. albus* on culture, was removed. He remained very ill for the next 2 weeks with a rising blood urea level, heavy proteinuria, and an intermittent fever, but then began to improve. Percutaneous renal biopsy was performed under local anaesthesia and the findings are described below. He was discharged home a week later, taking cloxacillin and fusidic acid.

During the next few weeks proteinuria and haematuria resolved and his serum protein and blood urea levels returned to normal. The level of antibody to *Staph. albus* in his blood has declined steadily while the serum  $\beta_1$ C globulin concentration has remained normal. Antibiotic therapy was stopped after 3 months and his head has not increased in size since removal of the infected valve.

### Renal morphology

At percutaneous renal biopsy, material was prepared for light and electronmicroscopy; unfortunately the portion prepared for immunofluorescent studies contained no glomeruli. On light microscopy the glomeruli showed some lobulation with marked mesangial expansion due to increase of fibrillar material and proliferation of mesangial cells. Many capillary loops were occluded, but no polymorphonuclear cells were seen. There was localized reduplication of some capillary walls in all the glomeruli (Fig. 1) but there were also single unthickened walls surrounding open loops. On electron microscopy the thickened capillary walls were seen to be composed of variably dense material with occasional localized aggregations on the subendothelial aspect of the lamina densa of the basement membrane (Fig. 2). No sub-

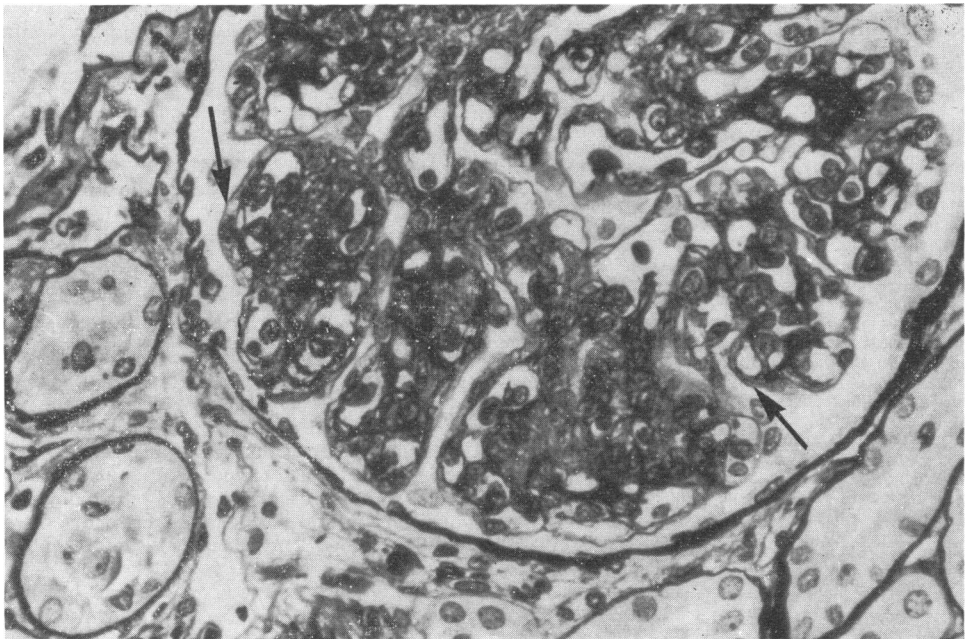


FIG. 1.—Part of a glomerulus illustrating lobulation of the tuft with moderate mesangial proliferation. Thickening and reduplication of capillary walls is clearly shown (arrows) and some capillaries are occluded. (PASM.  $\times$  512.)

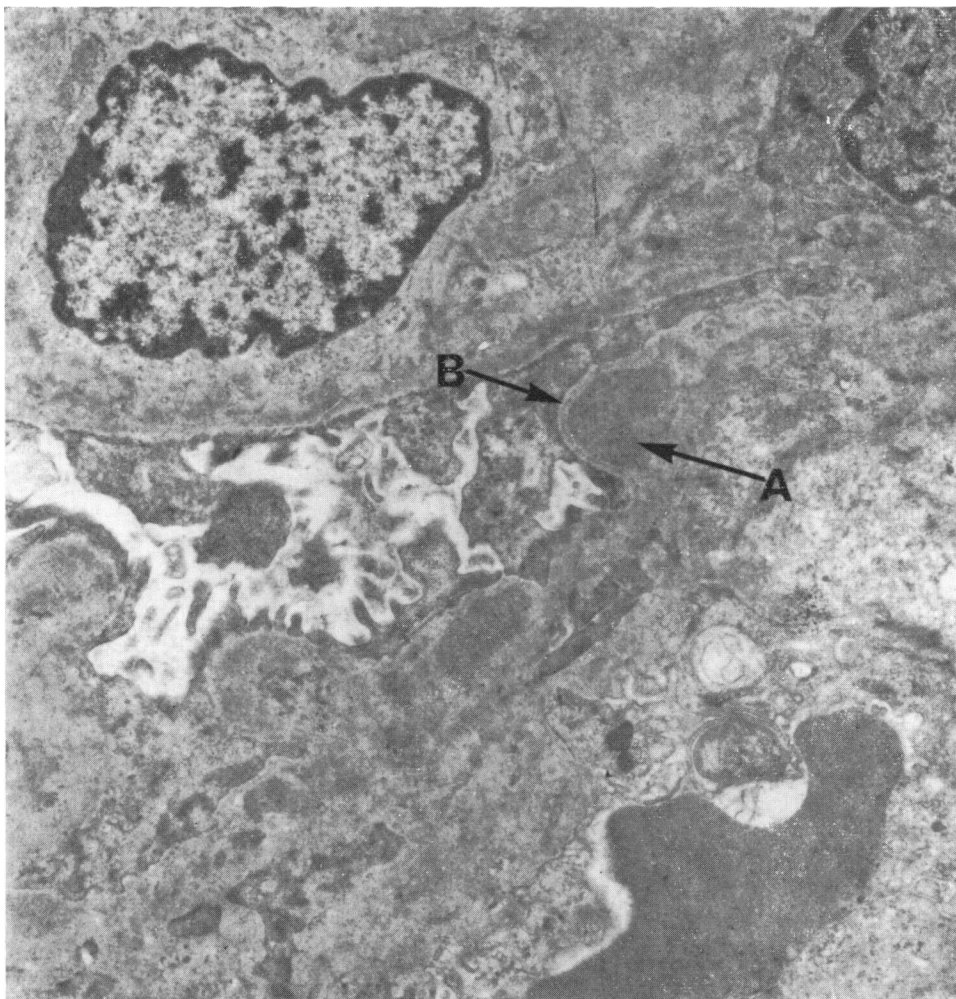


FIG. 2.—Electron micrograph in which thickening of the basement membrane is apparent and two electron-dense aggregations are shown, one of which 'A' projects from the basement membrane into the urinary space, but is separated from podocytic cytoplasm by lamina densa 'B'. ( $\times 6666$ .)

epithelial humps were seen on light or electron-microscopy.

#### Comment

A review of reported cases, mentioned in the introduction, shows that the disease is characterized by chronic septicaemia, with fever, sweating, and splenomegaly, followed by the development of the nephrotic syndrome with haematuria, uraemia, and acidosis. Serum complement may be reduced and *Staph. albus* can be cultured from the blood and CSF. Histological examination of renal tissues usually shows endothelial cell proliferation and

thickening of the capillary basement membrane. Dense aggregations in the subendothelial region of the basement membrane are demonstrable by electronmicroscopy, and immunofluorescent studies reveal deposits of fibrinogen, complement, and  $\gamma$ -globulin in the glomeruli. In one case (Kaufman and McIntosh, 1971) *Staph. albus* antigen was found in the glomeruli. Despite removal of the infected valve, the majority of cases have died.

Our case resembles those previously described. In addition, the patient initially had a high titre of antibodies to *Staph. albus*, which provides evidence of antibody response to this organism

that has not previously been shown. It is surprising that the serum complement level has remained normal.

The thickening of capillary walls is seen on electronmicroscopy to be due to subendothelial aggregations and increase in cytoplasm, but there is not the marked 'layering' present, which is seen in membranoproliferative glomerulonephritis (Cameron *et al.*, 1970). Though one of the two isolated electron dense aggregations, illustrated in Fig. 2, appears to project from the epithelial surface it is not typical of a 'hump' as seen in poststreptococcal glomerulonephritis (Herdson, Jennings, and Earle, 1966). It is separated from the podocytic cytoplasm by a fine layer of lamina densa, unlike a hump which rests on the epithelial side of the basement membrane totally surrounded by fused foot processes.

The finding of staphylococcal antibodies in the blood and nodular deposits of staphylococcal antigen together with complement, fibrinogen, and IgG in the glomeruli, supports the concept of an immunological cause of the glomerulonephritis. The electron dense aggregations in the basement membrane most resemble the nonspecific aggregations found in acute poststreptococcal glomerulonephritis and are considered to be antigen-antibody complexes (Herdson *et al.*, 1966). The glomerulonephritis associated with *Staph. albus* infection of an atrioventricular shunt appears to be a further example of immune complex disease in man similar to that found in experimental glomerulonephritis in animals (Dixon, Feldman, and Vazquez, 1961).

### Summary

A 3½-year-old mentally retarded boy who had had a Spitz Holter valve inserted at 10 months for hydrocephalus developed the nephrotic syndrome with haematuria, acidosis, and uraemia. *Staphylococcus albus* was cultured from CSF obtained from the valve. Antibody to *Staph. albus* was present in the blood at a titre of 1/5120, but serum  $\beta_1$ C globulin was normal. The infected valve was removed, and he was treated with antibiotics for 3 months. The nephrotic syndrome has remitted and renal function has returned to normal. Renal biopsy showed proliferative glomerulonephritis with variable thickening of the capillary walls, and electronmicroscopy showed marked thickening of the basement membrane due to subendothelial deposits.

We thank Drs. J. Emery and W. Barton for measuring the *Staph. albus* antibody titre, and Dr. Insley for performing the chromosome analysis.

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## Muscular performance in cystic fibrosis patients and its relation to vitamin E

It is generally felt that children suffering from cystic fibrosis (CF) should be encouraged to lead as normal lives as possible and this in particular includes full physical activity. It was our clinical impression that many CF children performed extremely well at various sports and we therefore wished to measure their muscle performance in carefully controlled tests as compared with normal subjects.

In addition, there is current interest as to whether vitamin E may play a role in athletic performance (*British Medical Journal*, 1971), and since cystic fibrosis sufferers have consistently low vitamin E blood levels (Bennett and Medwadowski, 1967; Muller and Harries, 1969; Harries and Muller,