Discussion

Oestriol given to neonates have been shown to increase plasma bilirubin levels (Lauritzen and Lehmann, 1967). When oestradiol was given to mothers 24 hours before delivery, the incidence and level of subsequent jaundice of the breast-fed neonate were found to be increased over the controls (Koivisto *et al.*, 1971). It is, however, difficult to understand that maternal consumption of oral contraceptive pills for a varying duration and after a varying interval since cessation could have any effect on the breast-fed infant's liability to jaundice. The figures, however, speak for themselves.

It should be noted that the oral contraceptive pill came into increasingly widespread use in the U.S.A. from 1958 and in the U.K. from 1960 onwards and that breast-milk jaundice was first recorded in 1963.

It would be interesting to know if these results could be confirmed in other centres.

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MEDICAL MEMORANDA

Nephrotic Syndrome: A Complication of Secondary Syphilis

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The association between secondary syphilis and the nephrotic syndrome is well recognized but very uncommon. Since Herrmann and Marr classified the renal complications of syphilis in 1935 about 30 cases have been recorded in the world literature. To our knowledge no case has been reported in the British literature during this time. As detailed histological appearances have been described on only three occasions (Brophy *et al.*, 1964; Falls *et al.*, 1965; Robins and Ladd, 1962) we feel it worth while reporting the following case.

Case Report

A 22-year-old woman was admitted to the Royal South Hants Hospital on 17 January 1969 for investigation of generalized oedema. Her initial complaint, two weeks previously, was of early-morning facial swelling. During the following two weeks her arms and legs also became oedematous and her weight increased by

25 kg. In association with these symptoms an irritant rash appeared on her body. She had been well before this episode and, in particular, there was no evidence of previous renal disease or of recent streptococcal infection. No medication of any kind had been given in the preceding few months. She was married with two children but was separated from her husband. Her two pregnancies, six and three years previously, had been uneventful and Wassermann reactions on both occasions were negative.

On admission she appeared pale and unwell, with a pyrexia of 100°F (37.8°C), pronounced periorbital oedema, and extensive pitting oedema from the waist downwards. There was no lymphadenopathy. The pulse was regular, 80/min, and the blood pressure was 105/70 mm Hg. The jugular venous pressure was not raised. Fine crepitations were heard at both lung bases. A red scaly macular rash covered the trunk but not the limbs. No abnormalities were found on neurological examination.

Laboratory investigations were: haemoglobin 10.5 g/100 ml; W.B.C. 5,100/mm³ (36% segmented neutrophils, 52% lymphocytes, 8% eosinophils); erythrocyte sedimentation rate 110 mm/hr (Westergren); total serum protein 3.9 g/100 ml (albumin 0.8 g/globulin 3.1 g); serum protein electrophoresis, diffuse increase in α_2 -globulin; serum cholesterol 325 mg/100 ml; serum creatinine 1.25 mg/100 ml; blood urea 54 mg/100 ml; serum electrolytes normal; antinuclear factor and L.E. cells not found. The urine deposit contained two red blood cells and four white cells per high-power field and some hyaline casts.

She was treated initially with frusemide but despite increasing doses continued to deteriorate. Three days after admission she developed bilateral pleural effusions with evidence of pneumonia. Treatment was supplemented with ampicillin and spironolactone. On 24 January positive serological results for syphilis were received and a course of procaine penicillin was started. Within three days she began to make a rapid recovery, and during the subsequent three weeks she lost 20 kg in weight and became oedema-free. The macular rash disappeared in a matter of days. Further serological examination confirmed syphilitic infection by showing a positive Venereal Disease Research Laboratory slide test, treponemal immobilization test, and fluorescent treponemal antibody test.

Despite the satisfactory clinical response gross proteinuria and hypoalbuminaemia persisted. In view of this a renal biopsy was performed early in April. A detailed report of the light and electron microscopical findings is given below. She was seen regularly as an outpatient after her discharge from hospital. Her clinical improvement continued and diuretics were stopped by the end of May. Since this time there has been no recurrence of oedema. On 29 July proteinuria persisted, with a serum albumin of 1.9 g/100 ml. By October the serum albumin had returned to normal at

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3.5 g/100 ml and a 24-hour urine sample contained about 1 g of protein. In May 1970 the urine was protein-free and the serological tests for syphilis had all become negative, apart from the fluorescent treponemal antibody test. When last seen in November 1970 she was well, with a normal serum creatinine and no proteinuria.

LIGHT MICROSCOPY

At least 40 glomeruli were present in the sections examined. All of them showed diffuse endothelial cell hyperplasia of moderate degree (Fig. 1), and many completely filled Bowman's capsule. There was variable slight thickening of the mesangium but leucocytic infiltration was not seen and there was no proliferation of epithelial cells. Glomerular basement membrane was normal.

FIG. 1—Glomerulus showing hypercellularity and proliferation. (H. and E. $\times 267$)

FIG. 2—Electron photomicrograph of part of glomerulus showing occlusion of capillary loop by hyperplastic endothelium (END). There is a tendency to fusion of the epithelial cell foot processes (FP) and irregularity and some thickening of the basement membrane (BM). The epithelial cells (EP) show some swelling and the presence of a few vacuoles. N = Nucleus of endothelial cell.

Whereas most of the proximal and distal convoluted tubules were normal there were small foci of tubular atrophy with associated basement membrane thickening and interstitial fibrosis. More

striking was the presence of homogenous casts and associated proliferation of tubular epithelium in a few proximal tubules. Small foci of round cell infiltration were present in the interstitium. No appreciable abnormality was seen in the vasculature.

The histological appearances were those of endothelial cell proliferative glomerulonephritis.

ELECTRON MICROSCOPY

Several glomeruli were present in the biopsy specimen, all of which showed similar changes (Fig. 2). An occasional capsular adhesion was seen. The epithelial cells exhibited fairly extensive fusion of their foot processes and some cytoplasmic swelling. In several places there was a tendency to vacuole formation, and moderate numbers of fat droplets were also present within the cytoplasm.

The basement membranes were irregular with some thickening and contained ill-defined deposits which were not confined to any particular aspect of the membrane. In some capillaries the endothelial cells showed little change. In others, however, there was a swelling of the cytoplasm and moderate proliferation. There was a slight tendency for basement membrane-like material to accumulate in the mesangial areas and also in the interstices between the proliferated endothelial cells.

The tubules contained cellular casts, and some cellular debris had also refluxed into the urinary space within Bowman's capsule. The proximal tubular epithelium focally showed increased numbers of small spherical electron-dense bodies, some probably being lysosomes. In both the proximal and distal tubules there were occasional degenerating epithelial cells. The basement membranes surrounding the proximal and distal convoluted tubules were irregularly thickened and there was slight interstitial fibrosis.

The changes were those of a proliferative type of glomerulonephritis predominantly involving the endothelial cells but with changes in the epithelial and mesangial cells as well as the basement membranes.

Comment

Though we have no definite evidence that the nephrotic syndrome in this patient was secondary to a syphilitic infection simultaneous development of these two conditions independently would seem a remarkable coincidence. Moreover, the spontaneous cure within 18 months of an adult onset nephrosis associated with proliferative glomerulonephritis is unusual (Black *et al.*, 1970).

Evidence from previous cases suggests that nephrosis occurring in association with secondary syphilis has a very good prognosis. In reported cases treated with penicillin the interval between the start of treatment and the disappearance of proteinuria varied from two to six weeks. It would therefore seem wise to screen all cases of proteinuria for evidence of syphilitic infection. Herrmann and Marr's figures suggest that this would make a useful contribution to the detection and control of syphilis. A curable though evidently rare cause of nephrosis would also be identified.

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