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Significance of vesicoureteric reflux

Sir,

I was a little disturbed at the unsubstantiated conclusion made by Moncrieff and Whitelaw (*Archives*, 1976, **51**, 893) that vesicoureteric reflux (VUR) in the absence of a complicating urinary tract infection (UTI) does not cause renal damage. Although the majority of patients with VUR come to clinical attention because of a UTI, there is now compelling evidence from radiological studies in infants and children (Rolleston *et al.*, 1975), renal function studies in children (Aperia *et al.*, 1976), and morphological studies in pigs (Hodson *et al.*, 1975) that progressive renal damage may occur in the context of gross VUR. This damage may develop and progress in the continued absence of complicating UTIs. In addition, early surgery to correct gross VUR may lead to a resumption of normal renal growth despite the fact that successful antireflux surgery does not influence the incidence of subsequent UTIs (McRae *et al.*, 1974).

Moreover if intrarenal reflux can be shown, focal renal scarring may develop in the areas of affected renal parenchyma (Rolleston *et al.*, 1974; Uldall *et al.*, 1976; Bourne *et al.*, 1976). The significance of intrarenal reflux has been confirmed in studies of the pathogenesis of reflux nephropathy in the pig experimental model (Hodson *et al.*, 1975). Infection was not an essential factor in scar formation but it did intensify the scarring process. The main conclusion from these human and animal studies is that gross VUR, and not UTI, is essential for the development of renal damage. The observation that the severity of the VUR is the single most important determining factor as to whether renal damage will occur has been the major breakthrough in the understanding of this subject in recent years (Bailey, 1973).

The recent letter in your journal by Cowen (*Archives*, 1977, **52**, 254) should be regarded with caution. Cowen concluded that a micturating cystourethrogram was not worthwhile in the investigation of an infant with a UTI if the intravenous urogram was normal. This statement was based on a study of only 20 neonates and cannot be supported in the light of a substantial number of published reports (including, in this journal, Drew and Acton, 1976) which have shown that 50-60% of infants under

the age of one year with a UTI have VUR, and more importantly that in 8-13% of these the VUR is gross in degree. In the latter patients the intravenous urogram may appear normal. I agree, however, that a micturating cystourethrogram is not indicated if a good quality intravenous urogram has been shown to be completely normal in a child over the age of 4 years.

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Dr. M. Moncrieff comments:

We thank Dr. Bailey for drawing our attention to this point. In the discussion of our results we quoted Smellie and Normand (1975) who state that new renal scars 'almost invariably develop' in association with infection. We should have repeated this phrase in the summary. However, the point of our paper was that with a normal intravenous urogram (IVU) 'gross VUR' which 'is essential for the development of renal damage' is very unlikely to be present, being found in only 2 of 70 ureters in our series. Cystography is undoubtedly unpleasant and sometimes hazardous (McAlister *et al.*, 1974), and we feel that our suggestion of deferring cystography until a second infection occurs in those with a normal IVU is the lesser of two evils.

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Effect of ascorbic acid on urinary hydroxyproline in children receiving corticosteroids

Sir,

Saphyakhajon *et al.* (1977), studying children receiving adrenal steroids for the treatment of juvenile rheumatoid arthritis (JRA), criticize our observations (Liakakos *et al.*, 1974a), stating that they did not find an increase in the amount of urinary hydroxyproline (HOP) with the simultaneous administration of large doses of ascorbic acid. Our study material, however, did not include children with JRA. It consisted of 6 children with rheumatic fever and 2 with the nephrotic syndrome. The observed discrepancy between their results and ours may well be attributed to differences in the study material, as in JRA the amount of HOP in the urine is found to be diminished (Smith *et al.*, 1968).

The same authors do not state the amount of steroids administered to their children. Our children received prednisolone 2 mg/kg body weight per day. If, by any chance, the dose of corticosteroids administered was too small it could not cause a further reduction in the amount of already low values of HOP found in JRA. The authors also do not mention in their letter whether their children were receiving salicylates simultaneously with steroids on a standard therapeutic basis. As we have previously shown (Liakakos *et al.*, 1974b), administration of therapeutic doses of aspirin to children causes a decreased urinary HOP which cannot be restored with administration of large doses of ascorbic acid.

Our recent observations in guinea pigs receiving corticosteroids have shown that prednisolone causes a narrowing in the epiphyseal plate of the tibia bones of these animals, whereas this effect is entirely inhibited with the simultaneous administration of ascorbic acid (unpublished data).

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Congenital abnormalities associated with extrahepatic portal hypertension

Sir,

In the May issue of the *Archives* (1977, **52**, 383), Odièvre and co-workers draw attention to the association of congenital abnormalities in children with extrahepatic portal hypertension of unknown cause. None of the children described by them nor those recorded in published reports had affected sibs.

We reviewed 8 patients with extrahepatic portal hypertension seen by us in the last 7 years. Of these, 1 had had omphalitis and 7 had extrahepatic portal hypertension of unknown cause. Of those 7 children, 3 had associated congenital abnormalities and 2 of these were in sibs. 1 patient had pyloric stenosis and congenital stricture of the sphincter of Oddi. The other 2 cases with extrahepatic portal hypertension were in brothers, 1 of whom had pulmonary stenosis and atrial septal defect, and the other pulmonary stenosis and pyloric stenosis. Atrial septal defect, pulmonary stenosis, and pyloric stenosis have all been described previously in association with extrahepatic portal hypertension.

This is the first report to our knowledge of the association of extrahepatic portal hypertension and congenital stricture of the sphincter of Oddi, and of the occurrence of extrahepatic portal hypertension and congenital abnormalities in sibs. These findings suggest that some cases of extrahepatic portal hypertension are not only congenital in origin, but might be genetically determined.

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