

We believe that this was accomplished: two random strains of *E coli* would probably not show the degree of identity found in our tests. *E coli* adheres to uroepithelium by pili, which are protein filaments on its surface. They are of two types, depending on whether adhesion is inhibited by mannose (mannose-sensitive) or not (mannose-resistant). The *E coli* strains produced only mannose-resistant pili, and such strains are found in only 26% of unselected cases of significant *E coli* bacteriuria (Abraham *et al*, in preparation). Symptomatic urinary tract infection correlates highly with isolation of such strains.<sup>2</sup>

We assumed that our patient had unwittingly ingested *E coli* SP88, that her intestinal tract had thus become colonised, and that her urinary tract infection had come about by the accepted ascending route.<sup>3</sup> We were unable to find *E coli* with the required characteristics in her faecal flora. We cannot exclude that she had transferred the infecting strain to the introitus from her fingers. Nevertheless our observations suggest that *E coli* SP88 is highly virulent for the urinary tract and that mannose-resistant pili may be a long-sought colonisation and virulence factor of *E coli* in the urinary tract.

We thank Peter Yeoman for invaluable technical work and Dr B Rowe, of the Enteric Reference Laboratory, and his staff for help with the serological analysis.

<sup>1</sup> Wilson CR, Totten PA, Baldwin JN. Rapid procedure for the detection of plasmids in *Staphylococcus epidermidis*. *Appl Environ Microbiol* 1978;**36**:368-74.

<sup>2</sup> Svanberg-Eden C. Clinical relevance of adhesion in urinary tract infections. In: Taylor-Robinson D, O'Connor M, eds. *Adhesion and micro-organism pathogenicity*. Tunbridge Wells: Pitman (in press). *Ciba Foundation Symposium*, No 80.)

<sup>3</sup> Sussman M, Asscher AW. Urinary tract infection. In: Black D, Jones NF, eds. *Renal disease*. 4th ed. Oxford: Blackwell Scientific, 1979:400-36.

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## Crohn's disease in Turner's syndrome

Attention has recently been drawn to the growing number of cases of inflammatory bowel disease reported in patients with Turner's syndrome.<sup>1</sup> We describe two further patients with cytogenetically proved Turner's syndrome, both of whom developed Crohn's disease.

### Case reports

*Case 1*—This girl had presented at the age of 14 years with short stature. She had the typical facial appearance of Turner's syndrome, together with multiple pigmented naevi, an increased carrying angle, and widely spaced nipples. Her karyotype was 46Xi(Xq). One year later she developed bilateral effusions in her knees and pain and swelling of two metacarpophalangeal joints. No autoantibodies were found. The arthritis progressed, affecting the cervical spine, and erosive changes were seen radiologically. Her HLA type was A2A11:B7B27. Alternate-day steroid treatment was required to control her symptoms. At 18 years she developed bilateral uveitis, which was treated with topical steroids and mydriatics. From the age of 15 she had had intermittent diarrhoea, but results of barium-meal and follow-through studies at that time were considered to be normal. Colonoscopy at the age of 18, however, showed mild inflammation throughout the colon. Biopsy specimens from various sites showed histiocytic granulomata with multinucleate giant cells, the appearances being those of Crohn's disease. She is currently being treated with sulphasalazine.

*Case 2*—A 15-year-old girl presented with painless effusion of the left knee. She was small and prepubertal and, though there were no obvious clinical features of Turner's syndrome, chromosome analysis showed a 45X/46XX karyotype. Over the next six months she lost weight and developed abdominal pain and diarrhoea. Barium studies showed ulceration of the

terminal ileum with a fistula to the sigmoid colon. A clinical diagnosis of Crohn's disease was made. She subsequently developed an abdominal mass and a discharge from the umbilicus. A sinogram confirmed a fistulous connection to the distal ileum and to the bladder. Right hemicolectomy was performed, and histological examination of the resected terminal ileum confirmed the diagnosis of Crohn's disease. Nine days after operation she developed tetanus, and she eventually died despite intensive care.

### Comment

Turner's syndrome comprises several well-known external signs with ovarian dysgenesis and failure of secondary sexual development. Certain internal abnormalities such as horseshoe kidney and coarctation of the aorta are also recognised as occurring with increased frequency. An association with autoimmune thyroiditis is well described, and the number of recent case reports of inflammatory bowel disease in Turner's syndrome strongly suggest that this also represents a true association.<sup>1 2</sup>

It has been suggested<sup>2</sup> that inflammatory bowel disease is triggered by an environmental factor in a genetically susceptible individual, and that an abnormality of the X chromosome may influence the genetic predisposition, thus rendering patients with Turner's syndrome more susceptible to the disease. Interestingly there is an unusually high prevalence of karyotypes featuring a structurally abnormal X chromosome, as in our first patient.

Though arthritis occurs in up to 10% of patients with Crohn's disease, its severity usually parallels the activity of the intestinal disease, large joints are usually affected, and radiological changes are rare. Our first patient had the clinical picture of severe juvenile rheumatoid arthritis, which, together with her uveitis, may represent a separate association between autoimmune disease and an X chromosome abnormality.

It is clearly important to regard non-specific symptoms such as malaise, intermittent diarrhoea, and weight loss with suspicion in any patient with Turner's syndrome, as these symptoms call for further investigation of the gastrointestinal tract.

We thank Dr C B Williams for performing the colonoscopy in case 1.

<sup>1</sup> Price WH. A high incidence of chronic inflammatory bowel disease in patients with Turner's syndrome. *J Med Genet* 1979;**16**:263-6.

<sup>2</sup> Arulantham K, Kramer MS, Gryboski JD. The association of inflammatory bowel disease and X chromosomal abnormality. *Pediatrics* 1980;**66**:63-7.

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## Acute nephrotic syndrome with reversible renal failure after phenylbutazone

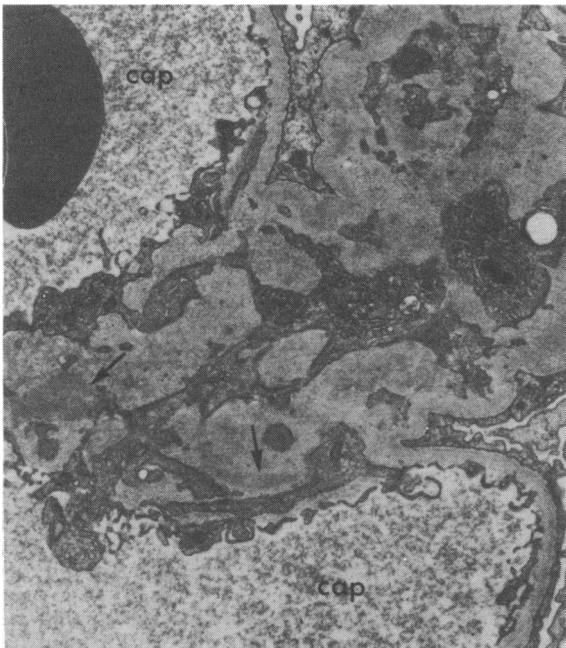
The side effects of phenylbutazone chiefly affect the stomach and bone marrow. Adverse renal effects include sodium retention, acute tubular necrosis, haematuria, and interstitial nephritis.<sup>1</sup> The nephrotic syndrome complicating phenylbutazone treatment is uncommon. We report a patient in whom acute nephrotic syndrome occurred during phenylbutazone treatment.

### Case report

An 81-year-old Caucasian man took phenylbutazone 100 mg four times a day for 10 days for a painful right ankle. Three weeks later a 30-day course of the drug in the same dose was started. He stopped taking the drug on the 25th day, when he developed peripheral oedema. He continued throughout with salbutamol and beclomethasone by aerosol, which he had been taking for four years. He had had a brief course of phenylbutazone for backache about one year previously. On admission his blood pressure was 180/80 mm Hg and he had anasarca. The urine contained 35 g of protein daily. The blood urea concentration was 9 mmol/l (54 mg/100 ml) and rapidly rose to 47 mmol/l (282 mg/100 ml). The creatinine clearance fell from 38 to 8 ml/

min and oliguria developed over one week. Prednisolone 60 mg daily was given for nine days at this stage.

A renal biopsy was performed 20 days after the nephrotic state began, the creatinine clearance then being 15 ml/min and urine protein excretion 8.2 g/day. Examination by light microscopy showed that 10% of the glomeruli were obsolete but the others appeared normal. There was focal tubular damage with regenerating epithelium and mitoses. Immunoperoxidase staining showed that the glomerular capillary walls and mesangium contained tiny amounts of granular IgA and IgM with no IgG, C3, C1q, or C4. Ultrastructurally there were occasional tiny intramembranous and sub-endothelial electron-dense deposits in the glomerular capillary walls and in the mesangium (figure). There was widespread loss of epithelial cell foot processes. Immune complexes were not present in the serum, the complement profile was normal, the DNA binding was in the normal range, and autoantibodies were absent. The patient's lymphocytes did not transform in vitro when cultured with phenylbutazone. Two months later the proteinuria was 4.4 g/day and the creatinine clearance 36 ml/min; by four months the proteinuria had ceased and the clearance risen to 58 ml/min.



Electron micrograph of part of a glomerulus in renal biopsy taken 20 days after onset of nephrotic syndrome. The mesangium is slightly increased in amount and contains small electron-dense deposits (arrows). cap = Capillary lumen (original magnification  $\times 11\,400$ ).

### Comment

A similar event was recorded in a 69-year-old Caucasian woman who had taken phenylbutazone 100 mg three times daily for four years because of osteoarthritis. She was taking no other drugs. A nephrotic syndrome with oliguria developed. Phenylbutazone was stopped. A renal biopsy was performed when the blood urea concentration was 17.5 mmol/l (105 mg/100 ml). The glomeruli were normal on light microscopy but electron microscopy showed electron-dense deposits in the glomerular capillary basement membranes. The condition resolved, and 17 months later there was no proteinuria and renal function was normal (Committee on Safety of Medicines, personal communication).

The evidence that phenylbutazone caused the nephrotic state in these two patients is threefold. Firstly, there was a clear relation between drug ingestion and the onset of proteinuria and renal failure. Secondly, the renal condition improved after the drug was stopped. Thirdly, the nephrotic syndrome is uncommon in the elderly: it is seen most frequently in the 3-30 age group.<sup>2</sup> The severity of the renal failure in both patients may be a feature of the phenylbutazone-related lesion. Glomerular morphology was similar in both patients. The nephrotic syndrome was reported in three patients taking phenylbutazone in 1959,<sup>3</sup> but the reported glomerular changes are difficult to evaluate.

Acute interstitial nephritis and papillary necrosis are well-recognised complications of nonsteroidal anti-inflammatory agents. Reversible renal failure and heavy proteinuria may complicate the use of nap-

roxen, fenoprofen, or indomethacin.<sup>4,5</sup> The two patients cited above, together with the four reported by Brezin *et al*<sup>4</sup> and Gary *et al*,<sup>5</sup> had severe renal failure, heavy proteinuria, and glomeruli which were normal on light microscopy. The clinical course of these six patients was sufficiently uniform to produce a characteristic clinicopathological picture.

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<sup>1</sup> Wade A, Reynolds JEF, eds. *The Extra Pharmacopoeia*. 27th ed. London: The Pharmaceutical Press, 1977:208.

<sup>2</sup> Cameron JS. Nephrotic syndrome. *Br Med J* 1970;iv:350-3.

<sup>3</sup> Miatello VR, Carbajal BF, Gottlieb D, Sadler TN. Síndrome nefrótico consecutivo a la ingestión de fenilbutazona. *Prensa Médica Argentina* 1959;46:2552-8.

<sup>4</sup> Brezin JH, Katz SM, Schwartz AB, Chinitz JL. Reversible renal failure and nephrotic syndrome associated with non steroidal anti-inflammatory drugs. *N Engl J Med* 1979;301:1271-3.

<sup>5</sup> Gary NE, Dodelson R, Eisinger, RP. Indomethacin-associated acute renal failure. *Am J Med* 1980;69:135-6.

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## Intravenous amiodarone in ventricular fibrillation

Amiodarone is a class III antiarrhythmic agent available in Britain for named patients only. Most clinical experience has been gained on the Continent and in South America. There is little experience in the use of the intravenous formulation.<sup>1</sup> We report its use in two patients with ventricular fibrillation.

### Case reports

**Case 1**—A 45-year-old man sustained an inferior myocardial infarct, complicated in the first six hours by a short episode of complete heart block. Ten days later he had a cardiac arrest and was found to have ventricular fibrillation. He responded to 300 J cardioversion after 100 mg disopyramide had been given. Despite a lignocaine infusion (4 mg/min) and continued disopyramide infusion (0.5 mg/min) he developed ventricular fibrillation eight times, each requiring cardioversion. Bretylium (100 mg) followed by an infusion (3 mg/min) also failed to prevent frequent ventricular fibrillation. After 18 hours and a total of 35 cardioversions a temporary transvenous pacing wire was inserted. Over the next 36 hours he remained stable while paced at 130/min but when the pacing rate was reduced R-on-T ventricular ectopic beats heralded the return of ventricular fibrillation. Procainamide (serum concentration 7.2 mg/l) and then mexiletine (100 mg immediately followed by 0.5 mg/min) failed to control this phenomenon. Ventricular fibrillation occurred twice while the pacing rate was 130/min. Fifty-four hours after the initial cardiac arrest and after 41 cardioversions 200 mg amiodarone was given intravenously over 30 seconds. Systolic blood pressure fell abruptly to 55 mm Hg, the pacemaker was turned off, and sinus rhythm at 80/min returned with no ventricular ectopic beats. Blood pressure rose over the next 10 minutes to 95 mm Hg. A total of 800 mg amiodarone was infused over 24 hours, after which he continued with oral amiodarone 600 mg daily. At follow-up two months later he was well with no cardiac symptoms, taking amiodarone alone.

**Case 2**—A 65-year-old man underwent aortic valve replacement, repair of an aneurysmal ascending aorta with woven Teflon, and two coronary artery vein grafts. Eight weeks later a leak from the lower end of the Teflon aortic repair was resutured. After the second operation he had various arrhythmias, including multifocal ventricular ectopic beats, which were treated with lignocaine and procainamide durules (500 mg thrice daily). Nine days later he had a cardiac arrest and was found to be in ventricular fibrillation, unresponsive to an initial 400 J cardioversion. Cardiopulmonary resuscitation was started; the lignocaine infusion was increased and supplemented by a 50 mg bolus. The serum potassium concentration was corrected from 3.2 mmol