

prostaglandin assay. We are indebted to Mr. D. G. Taylor for details of the operative procedure and samples of tumour.

REFERENCES

- Bloom, S. R., Polak, J. M., and Pearce, A. G. E. (1973). Vasoactive intestinal peptide and watery-diarrhoea syndrome. *Lancet*, **2**, 14.
- Hamilton, J. R., Radde, I. C., and Johnson, G. (1968). Diarrhoea associated with adrenal ganglioneuroma. New findings related to the pathogenesis of diarrhoea. *American Journal of Medicine*, **44**, 453.
- Hawfield, H. H., and Daisley, G. W. (1952). A report of a case of a functional adrenal ganglioneuroma. *Clinical Proceedings of the Children's Hospital (Washington)*, **8**, 98.
- Rosenstein, B. J., and Engelman, K. (1963). Diarrhea in a child with a catecholamine-secreting ganglioneuroma. *Journal of Pediatrics*, **63**, 217.
- Sandler, M., Karim, S. M. M., and Williams, E. D. (1968). Prostaglandins in amine-peptide-secreting tumours. *Lancet*, **2**, 1053.
- Smellie, J. M., and Sandler, M. (1961). Secreting intrathoracic ganglioneuroma. *Proceedings of the Royal Society of Medicine*, **54**, 327.
- Stickler, G. B., Hallenbeck, G. A., Flock, E. V., and Rosevear, J. W. (1962). Catecholamines and diarrhea in ganglioneuroblastoma. *American Journal of Diseases of Children*, **104**, 598.
- Verner, J. V., and Morrison, A. B. (1958). Islet cell tumor and a syndrome of refractory watery diarrhea and hypokalemia. *American Journal of Medicine*, **25**, 374.

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Sex-related incidence in proteus infection of the urinary tract in childhood

In childhood, as in adult life, males enjoy relative freedom from urinary tract infection (UTI). Two exceptions are well recognized. One is in the first months of life, when UTI is commoner in males than in females, and the other when UTI is associated with obstructive malformation, which also shows a male preponderance (Smellie *et al.*, 1964; Stansfeld, 1966; Smallpeice, 1968). With these exceptions, most cases of UTI in childhood occur in females and are due to *Esch. coli*. This has largely overshadowed the very different sex distribution of UTI due to *Proteus* species.

In the group of 44 boys with primary UTI studied by Bergström (1972) *Esch. coli* accounted for less than half the infections, while *Proteus* was

the most frequent of the other organisms found. In age-matched female controls few organisms other than *Esch. coli* were found and *Proteus* did not occur. *Proteus* occurs more frequently in children with repeated UTI: Mann (1972) found *P. mirabilis* in 75% of all cases of UTI in boys under the age of 14, compared with 15% in girls, and isolated the organism from the prepuccial sac in 20 of 51 healthy boys under the age of 10.

We report our observations on *Proteus* organisms as urinary pathogens and contaminants, and also on *Proteus* in balanitis and on prepuccial swabs from normal children.

Materials and methods

The Oxoid Dipslide with both MacConkey's medium and cysteine lactose electrolyte-deficient medium (CLED) is routinely employed in the wards and out-patient and casualty departments of the hospital. For the past two years the laboratory has operated an alphabetically-filed punched-card system for its records of routine clinical specimens. This has made it possible to retrieve information on *Proteus* bacteriuria of definite or suspected significance. Infections in surgical patients were excluded from the study.

Because *Proteus* isolates from the urinary tract are *P. mirabilis* in nearly all cases biochemical tests have not been carried out routinely to distinguish the various species, but a series of 55 consecutive isolates was examined to confirm the predominant role of *P. mirabilis*.

Records of the isolation of *Proteus* from patients with balanitis were retrieved from the laboratory's files. For comparison, prepuccial swabs were obtained from a number of healthy boys attending the developmental clinics and a small number of meatal swabs were taken from healthy circumcised boys. The age distributions of the two groups were similar, with medians of between 2 and 3 years.

Results

Over a two-year period 125 children were found to have *Proteus* bacteriuria of definite or suspected significance: 80% of those with repeated counts exceeding 10^5 organisms/ml were males (Table I). The first column of Table I shows the number of children with viable counts in the range conventionally regarded as 'doubtful'—that is, 10^4 to 10^5 *Proteus*/ml—or with counts of 10^5 or more which were not confirmed on further investigation. The second column shows the number of children with counts of more than 10^5 *Proteus*/ml on at least two consecutive occasions. Suprapubic aspiration was carried out on 15 children below the age of 3 years. The results in only 14 are shown in the third column because in one case the aspirated urine was sterile.

The identity of the original infecting organism

TABLE I
Proteus isolation from urine

	Doubtful counts (10^{4-5} or $>10^5$ /ml unconfirmed)		Significant counts ($>10^5$ /ml repeated)		Infection proved by suprapubic aspiration	
	No. of children	%	No. of children	%	No. of children	%
Males	66	73	28	80	11	79
Females	24	27	7	20	3	21
Total	90	100	35	100	14	100

TABLE II
Distribution of initial infecting organism according to sex in 169 children attending renal clinic

Infecting organism	Males		Females		Both sexes	
	No.	%	No.	%	No.	%
<i>Esch. coli</i>	29	52	84	74	113	67
<i>Proteus</i> spp.	21	38	9	8	30	18
Other enterobacteria	6	11	16	14	22	13
Other organisms	0	0	4	4	4	2
Total	56	100	113	100	169	100

was known in 169 out of 193 children attending the hospital clinic for UTI. The causative organisms were unknown in the remainder because treatment had started before they were referred. Only the *Proteus* infections showed a male preponderance (Table II).

Proteus was isolated from the prepuce of 30% of 89 (30%) normal boys and from 10 out of 31 boys (32%) with balanitis. Only 1 out of 8 circumcised boys yielded *Proteus* from a meatal swab. Indole-negative *P. mirabilis* strains constituted 50 out of 55 (91%) of the series of isolates examined.

Discussion

The excess of male children that we have found with UTI due to *Proteus* accords with previous reports (Bergström, 1972; Mann, 1972). In boys *Proteus* is the causative organism in 75% of all cases of UTI, as Mann (1972) has reported, but if first infections only are considered *Proteus* still ranks second to *Esch. coli*; Bergström's (1972) figure of 35% due to *Proteus* compares with our own figure of 38%.

Whether the sex distribution demonstrated is true of *Proteus mirabilis* only is not clear, and the predominance of *P. mirabilis* over other *Proteus* species

in UTI is such that only a very large series of cases could provide evidence on this point. Most of the children had the usual symptoms associated with UTI. There were no asymptomatic children among the confirmed cases due to *Proteus*. No case of urolithiasis occurred in this series.

Proteus was isolated from the prepuce of 30% of our boys compared with 39% in Mann's (1972) series. Because of the possibility of repeated contamination of boys' urines with *Proteus*, careful confirmation of suspected UTI is essential. Suprapubic aspiration of the bladder in 12 boys disproved 1 suspected infection and confirmed the remainder. Once *Proteus* infection is proved the association of this organism with stone formation (Myers, 1957; Ghazali, Barratt, and Williams, 1973) and with a greater likelihood of renal abnormality (Fairley *et al.*, 1971) and recurrent infection (Kunin, Deutscher, and Paquin, 1964) provides sufficient reason for radiological investigation after the first episode of infection.

Our evidence does not indicate that *Proteus* plays any significant part in the causation of balanitis. Whether circumcision would reduce the likelihood of UTI due to *Proteus* remains to be established. There were too few circumcised boys in this study to allow a definite opinion.

Summary

Over a 2-year period 80% of children found to have significant *Proteus* bacteriuria were boys. The organism was isolated from the prepuce in 30% of normal boys and 32% of those with balanitis. *Proteus* urinary tract infection should be carefully confirmed and proved cases thoroughly investigated.

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REFERENCES

- Bergström, T. (1972). Sex differences in childhood urinary tract infection. *Archives of Disease in Childhood*, **47**, 227.
- Fairley, K. F., Carson, N. E., Gutch, R. C., Leighton, P., Grounds, A. D., Laird, E. C., McCallum, P. H. G., Sleeman, R. L., and O'Keefe, C. M. (1971). Site of infection in acute urinary-tract infection in general practice. *Lancet*, **2**, 615.
- Ghazali, S., Barratt, T. M., and Williams, D. I. (1973). Childhood urolithiasis in Britain. *Archives of Disease in Childhood*, **48**, 291.
- Kunin, C. M., Deutscher, R., and Paquin, A. (1964). Urinary tract infection in school children: an epidemiological, clinical and laboratory study. *Medicine*, **43**, 91.
- Mann, P. G. (1972). *Proteus* urinary infections in childhood. *Journal of Clinical Pathology*, **25**, 551.
- Myers, N. A. A. (1957). Urolithiasis in childhood. *Archives of Disease in Childhood*, **32**, 48.
- Smallpeice, V. (1968). *Urinary Tract Infection in Childhood and Its Reference to Disease in Adult Life*, p. 30. Heinemann, London.
- Smellie, J. M., Hodson, C. J., Edwards, D., and Normand, I. C. S. (1964). Clinical and radiological features of urinary infections in childhood. *British Medical Journal*, **2**, 1222.
- Stansfeld, J. M. (1966). Clinical observations relating to incidence and aetiology of urinary-tract infections in children. *British Medical Journal*, **1**, 631.

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Exchange transfusion in severe neonatal infection with sclerema

Although improvement in obstetric practices, careful handling of the newborn, rational use of antibiotics, and general supportive treatment have improved the prognosis of neonatal septicaemia, it is still an important cause of death in the neonatal period (Nicolopoulos, Anagnostakis, and Xanthou, 1973). Exchange transfusion has been used successfully in adults for the treatment of postabortion sepsis (Verkhovskü and Drach, 1965) and other

severe infections (McLean and Luke, 1969), but in only a few cases of neonatal septicaemia (Prod'hom *et al.*, 1974). This paper describes the cases of two newborn babies with severe neonatal infection who were treated successfully with repeated exchange transfusions.

Case reports

Case 1. A male weighing 1950 g was born prematurely at 33 weeks. Pregnancy and delivery were normal; no cause was apparent for the premature labour. His weight was normal for gestational age. When 30 hours old he started having spells of apnoea and cyanosis. Serum Ca, Mg, Na, Cl, K, and total CO₂ and blood pH and glucose were all normal. A peripheral blood white cell count showed pronounced neutrophilia with a shift to the left. Throat, nose, and umbilical swabs and blood and cerebrospinal fluid were cultured. Treatment with ampicillin and gentamicin was started because the baby was thought to have septicaemia. During the next two days his condition deteriorated. He became lethargic and developed mild jaundice (bilirubin 12 mg/100 ml), which was treated with phototherapy. Meanwhile the CSF proved normal but the blood culture grew *Klebsiella* which was sensitive to gentamicin and cephalothin. Therefore ampicillin was substituted for cephalothin. In spite of adequate specific antibiotic therapy the baby's condition progressively deteriorated and sclerema developed in his legs. After five days of therapy with gentamicin and cephalothin the sclerema was steadily progressing up the trunk. The white blood cell count now showed a pronounced neutropenia. At this point it was decided that the baby might benefit from exchange transfusion. Fresh blood with citrate glucose as anticoagulant was used after warming and adding sodium bicarbonate to correct the pH. An exchange of 180 ml of blood/kg over two hours was well tolerated and it was repeated 18 hours later. The baby's condition improved dramatically after the second exchange transfusion. The sclerema disappeared within 48 hours, and subsequent progress was uneventful. Antibiotics were discontinued when the patient was 15 days old and he was discharged one month later in good condition.

Case 2. A male aged 2 days was admitted because of jaundice. He had been delivered normally at term after an apparently uneventful pregnancy but he was small for dates (birthweight 2100 g). On admission he was lethargic and deeply jaundiced. Blood glucose was 18 mg/100 ml, serum unconjugated bilirubin 30 mg/100 ml, Hb 11.2 g/100 ml, and Coombs's test negative. The hypoglycaemia was treated with intravenous glucose while blood was being prepared for exchange transfusion. The latter went smoothly until 340 ml of blood had been exchanged, when the baby had a cardiac arrest. He was resuscitated and placed in an incubator. Shortly afterwards he had a convulsion. The CSF contained 72 polymorphs/mm³ and a peripheral blood white cell count suggested infection. With a diagnosis