ment of pneumonia in this condition. (1) Spasms and convulsions, the main signs of tetanus, both cause contraction of the stomach, resulting in aspiration pneumonia. (2) Apnoea, the direct effect of tetanus toxin upon respiratory centres. Though most drugs used for sedation in tetanus cause respiratory depression, so that shallow respirations might contribute to pulmonary collapse and secondary infection, we see bronchopneumonia predominantly among convulsing infants.

To detect this severe and common complication, any clue would be valuable. Cough is rarely seen in the heavily sedated infant, and lung signs are hard to detect as tetanic manifestations tend to obscure them. Feeble respiratory movements, cyanosis, hypothermia, sudden loss of tetanic signs, and/or a drop in the amount of sedation required, have proved to be the best indications of developing bronchopneumonia. It is uncertain whether hypoxia, caused by chest infection, or the toxic effects of secondary infection increases the central nervous system's sensitivity to drugs, or suppresses drug metabolism in the liver and so causes drug accumulation and increased sedation of the infant.

Since infants were nursed flat in bed, the pathological distribution of pulmonary lesions could be an indication of a mechanical factor. Furthermore, the heavy sedation could be an important cause of respiratory depression leading to anoxia and eventually to pulmonary haemorrhage (mechanical ventilation was not used).

Most of these infants were under-fed to avoid aspiration of intragastric content. This state of dehydration could have contributed to development of 3 cases of renal vein thrombosis.

This study confirms the importance of pulmonary complications, in particular pneumonia and pulmonary haemorrhage, as causes of death in neonatal tetanus and emphasizes the need for adequate pulmonary ventilation and frequent change of position of the infant, and the hazard of oversedation. In addition, there are problems related to feeding which include aspiration of vomit and dehydration from too vigorous restriction of fluid intake.

Summary

Of 125 newborn infants with tetanus studied clinically, 75 died. Hypothermia and bronchopneumonia were the commonest events leading to death. A sudden drop in the amount of sedation required, loss of or diminished tetanic signs, and hypothermia usually indicated the onset of bronchopneumonia.

A later series of 108 cases with 75 deaths (54

necropsies) formed the basis of a pathological study. Pulmonary pathology was found in 46 out of the 54 necropsies: mainly pulmonary haemorrhage, aspiration pneumonia, and bronchopneumonia, particularly of the right upper lobe. Adrenal haemorrhage and renal vein thrombosis also occurred.

I am indebted to Professor R. G. Hendrickse and Dr. P. Barns for criticism; to Mrs. N. Shiva and Dr. A. Najafian for their encouragement; and to Dr. F. Rafat who performed the necropsies. The study was supported by a grant from the Ministry of Science and Higher Education of Iran.

References

- Adams, E. B., Laurence, D. R., and Smith, J. W. G. (1969). *Tetanus*, p. 89. Blackwell, Oxford.
- Creech, O., Glover, A., and Ochsner, A. (1957). Tetanus: evaluation of treatment at Charity Hospital, New Orleans, Louisiana. *Annals of Surgery*, **146**, 369-383.
- Patel, J. C., Goodluck, P. L., Sheshia, S. A., and Deshpande, D. H. (1965). Morbid anatomical lesions in tetanus. *Proceedings of the First International Conference on Tetanus*, p. 303. Ed. by J. C. Patel. Study Group of Tetanus, King Edward Memorial Hospital, Bombay.
- Salimpour, R. (1971). Amobarbital chlorpromazine in the treatment of tetanus neonatorum. *Tropical and Geographical Medicine*, **23**, 131-134.
- Veronesi, R. (1967). Epidemiology of tetanus. *Principles on Tetanus*, p. 43. Ed. by L. Eckmann. Huber, Bern.
- Wright, R. (1960). The treatment of tetanus. MD thesis, University of Cape Town.

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Intestinal damage in rotavirus and adenovirus gastroenteritis assessed by D-xylose malabsorption

There is increasing evidence that rotavirus (Flewett *et al.*, 1974) is an important aetiological agent in acute infantile gastroenteritis (Davidson *et al.*, 1975). These viruses have been recovered from the proximal small intestine of infected infants in association with mucosal damage (Bishop *et al.*, 1973). Adenovirus has been implicated as a cause of gastroenteritis in sporadic cases (Ramos-Alvarez and Olarte, 1964), and in South African infants

(Schoub *et al.*, 1975), but has also been recovered as frequently from control subjects (Yow *et al.*, 1970). However, studies of epidemic diarrhoea in a closed community (Flewett *et al.*, 1975) showed adenovirus only in the faeces of patients with diarrhoea, but not in those with normal stools. The presence of this virus in the small intestine in association with symptoms and histological change has not yet been reported.

The 1-hour blood-xylose test (Rolles *et al.*, 1973) is in common use as a screening test for coeliac disease because xylose malabsorption can indicate mucosal damage. We have assessed the absorption of xylose in infants with acute gastroenteritis who were excreting rotavirus or adenovirus. We hoped to confirm that both viruses could be found in the small intestine in infants with acute gastroenteritis, and to find indirect evidence of mucosal damage.

Patients and methods

Fifteen infants aged 2–16 months with acute gastroenteritis were investigated; bacterial pathogens, including enteropathogenic *E. coli* serotypes, were not detected in duodenal juices or stools. Intestinal intubation was performed, without recourse to radiology, in all infants while they were symptomatic. 3 patients had repeat convalescent intubation 6 days after the first. To overcome any delay in gastric emptying 5 g D-xylose in 50 ml water was then infused via the tube into the small intestine over a 3- to 4-minute period (after fasting for 4 hours) and a 1-hour blood-xylose level determined.

Specimens of small intestinal juice (recognized by pH) and stool were examined by electron microscope and routine virus isolation from the stools was attempted in HEp2 cells, primary or secondary rhesus monkey kidney, and human embryonic kidney cultures.

Results

No viral pathogen. In 3 patients no viral pathogen was found and a 1-hour blood-xylose was >1.30 mmol/l (Fig. 1).

Rotavirus. 8 patients were excreting rotavirus in their stools and in 6 of them virus particles were also found in the intestinal aspirate. In these 6 the blood-xylose level was low (range 0.15–0.78 mmol/l). In the 2 infants in whom rotavirus was found in the stool alone, the blood-xylose was >1.26 mmol/l (Fig. 1).

Adenovirus. 4 patients were excreting adenovirus in their stools and in 3 of them adenovirus was also

Fig. 1 1-hour blood xylose levels (admission studies), related to virological findings.

Fig. 2 Acute and convalescent 1-hour blood xylose levels in 3 infants.

found in the intestinal juice. These 3 patients showed low blood-xylose levels (0.4–0.85 mmol/l) in contrast to the fourth patient whose blood-xylose level was normal (2 mmol/l).

Repeat intubations were performed in the convalescent period on 3 patients who had had a virus in their intestinal juice; and blood-xylose levels detectable were now normal in 2 (Fig. 2).

In the third patient there was an improvement, though the xylose level remained low (0.60 mmol/l).

Discussion

The association between the presence of rotavirus and adenovirus in the lumen of the small intestine and a low blood-xylose suggests strongly that both these viruses can cause small intestinal dysfunction. Utilization of xylose by micro-organisms in the small intestine is not a real possibility; bacterial counts were low and these viruses do not metabolize xylose.

It is tempting to speculate that xylose malabsorption is the result of mucosal damage by the virus (Bishop *et al.*, 1973), but we have no proof of this because jejunal biopsy was not performed. The data indicate the importance of seeking pathogens in the intestinal fluid as well as in stools. We do not know the explanation of the symptoms in those infants where virus was found in the faeces only, but it is possible that the demonstrated viruses were not true pathogens.

This evidence strongly supports the earlier epidemiological studies implicating adenovirus as a causative agent in acute infantile gastroenteritis. The technique of intraduodenal xylose absorption may provide a valuable indicator of intestinal dysfunction in gastroenteritis caused by other agents when intestinal biopsies are considered unethical.

Summary

The absorption of D-xylose infused into the duodenum was assessed in infants with acute gastroenteritis. 1-hour blood-xylose levels were low in 6 patients found to harbour rotavirus in the small intestinal aspirate. Normal levels (>1.26 mmol/l) were obtained in the absence of virus particles in the small intestine in a further 6 patients: in 3 of these adenovirus or rotavirus was recovered from the stools.

Three patients with adenovirus in the small intestinal juice and ill with acute gastroenteritis also had low xylose levels. This finding supports earlier epidemiological studies that adenovirus may be a causative agent of acute infantile gastroenteritis. The association between virus in the small intestine and xylose malabsorption may indicate mucosal damage. Formal proof of this is awaited.

We thank Dr. M. M. Tarlow, under whose care patients were admitted; Dr. H. G. Sammons and staff, Clinical Chemistry Department, East Birmingham Hospital, for xylose measurements; and

Professor C. M. Anderson for her continuing support. N.E. was in receipt of a grant from the Children's Research Fund, Liverpool.

References

- Bishop, R. F., Davidson, G. P., Holmes, I. H., and Ruck, B. J. (1973). Virus particles in epithelial cells of duodenal mucosa from children with acute non-bacterial gastroenteritis. *Lancet*, **2**, 1281-1283.
- Davidson, G. P., Bishop, R. F., Townley, R. R. W., Holmes, I. H., and Ruck, B. J. (1975). Importance of a new virus in acute sporadic enteritis in children. *Lancet*, **1**, 242-246.
- Flewett, T. H., Bryden, A. S., Davies, H. A., Woode, G. N., Bridger, J. C., and Derrick, J. M. (1974). Relation between viruses from acute gastroenteritis of children and newborn calves. *Lancet*, **2**, 61-63.
- Flewett, T. H., Bryden, A. S., Davies, H. A., and Morris, C. A. (1975). Epidemic viral enteritis in a long-stay children's ward. *Lancet*, **1**, 4-5.
- Ramos-Alvarez, M., and Olarte, J. (1964). Diarrheal diseases of children: the occurrence of enteropathogenic viruses and bacteria. *American Journal of Diseases of Children*, **107**, 218-231.
- Rolls, C. J., Kendall, M. J., Nutter, S., and Anderson, C. M. (1973). One-hour blood-xylose screening-test for coeliac disease in infants and young children. *Lancet*, **2**, 1043-1045.
- Schoub, B. D., Koornhof, H. J., Lecatsas, G., Prozesky, O. W., Freiman, I., Hartman, E., and Kassel, H. (1975). Viruses in acute summer gastroenteritis in black infants. *Lancet*, **1**, 1093-1094.
- Yow, M. D., Melnick, J. L., Blattner, R. J., Stephenson, W. B., Robinson, N. M., and Burkhardt, M. A. (1970). The association of viruses and bacteria with infantile diarrhea. *American Journal of Epidemiology*, **92**, 33-39.
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Hypoglycaemia in congenital adrenal hyperplasia

It is well known that salt-wasting occurs in many children with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency and paediatricians are familiar with the salt-losing crises which can arise in such patients. Though hypoglycaemia has only occasionally been reported in the disorder (White and Sutton, 1951; Wilkins, 1965) we suspect that this complication is more common than is generally recognized and give the case histories of 2 young children with CAH who became acutely ill as a result of hypoglycaemia.