Discussion

Two 10-year-old monozygotic twins with a preleukaemic syndrome ended in a rapidly fatal myelomonocytic leukaemia. Leukaemia in twins generally begins during the first 5 years of life (MacMahon and Levy, 1964). In our patients the disease reached full development at the age of 10. They also differ from the earlier reported cases by having had a rather long preleukaemic phase. The similarity of the clinical picture of both twins suggests the important role of genetic factors.

The presence of a Ph^1 chromosome in the final phase of the disease in twin 2 is interesting. In most reported cases of Ph^1 positive acute myeloblastic leukaemia (Cannellos and Whang-Peng, 1972; Baccarani *et al.*, 1973) a myeloblastic crisis of an unapparent chronic myeloid leukaemia (CML) had been suggested. In our patients signs or symptoms of CML were never detected. Nevertheless, the possibility that these patients might have presented a CML that evolved from a preleukaemic phase into the blastic crisis, skipping the classical CML phase, cannot be ruled out.

Summary

A case of monozygotic twins with a preleukaemic phase of 3½ years is reported. The final haematological picture was that of myelomonocytic leukaemia. The karyotype investigated in one twin during the final period of the disease showed a Ph^1 chromosome.

We thank Drs. D. Catovsky and Susan Hollan for helpful suggestions.

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Use of a simple duodenal capsule to study upper intestinal microflora

Microbial contamination of the upper gut has recently been shown in malnourished children from Central America (Mata *et al.*, 1972), Australia (Gracey and Stone, 1972), South-East Asia (Gracey *et al.*, 1973), and Africa (Heyworth and Brown, 1975). In many places where malnutrition is still common radiological facilities for intestinal intubation are absent or inadequate, thus preventing studies on the real prevalence of this microbiological abnormality. We report the use of a simple and safe device which can be used to obtain samples of upper intestinal secretions without radiology.

Materials and methods

Patients. Indonisian children were studied, 7 boys and 3 girls. Their ages ranged from 18 months to 10 years; the mean age was 6 years. All patients were undernourished. Using the Wellcome method of nutritional classification (*Lancet*, 1970), 7 were marasmic, 1 had kwashiorkor, and 2 were underweight. 7 had diarrhoeal disorders including 4 who were known to have parasitic infestations by stool microscopy.

Duodenal capsule. The paediatric Enterotest Capsule* (Fig.) consists of a no. 1 size gelatin capsule (20 mm × 6 mm) containing a silicone rubber bag. Attached to the bag and packed into the capsule is

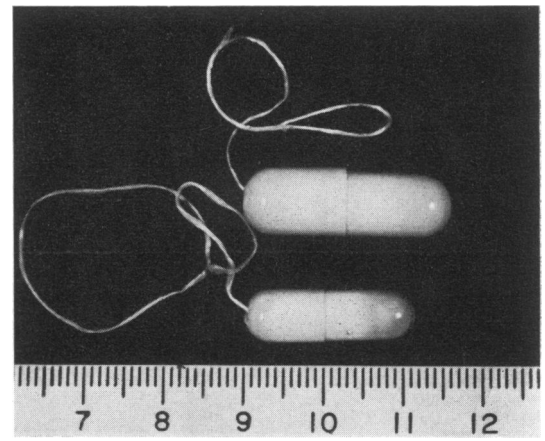

Fig. *Adult (above) and paediatric (below) Enterotest capsules. The scale is in cm and mm.*

*Enterotest (TM) Health Development Corporation, Palo Alto, California.

a fine yarn line 90 cm long. The patient is asked to swallow a little water, then the capsule is introduced into the mouth while holding the free end of the line. He is then asked to swallow a little more water. After the capsule has been swallowed the free end is taped to the cheek and the patient allowed to walk about with his parents. The gelatin dissolves and the weighted bag passes into the duodenum. Our practice is to leave the capsule for 2 hours before withdrawal; in all instances the end of the line had reached the upper intestine by that time. One patient pulled the line out after 30 minutes but even then the upper intestinal lumen had been reached. The line is withdrawn gently and usually about 50 cm of the distal end is bile stained; the *p*H can be checked with a *p*H stick which is provided and which leaves a colour which can be read off against a chart. The intestinal secretions can be scraped off with a sterile glove and examined immediately under the microscope. Specimens can also be collected for microbiological investigations.

Microbiological methods. A throat swab was taken from each patient before the tube was swallowed. After the line was withdrawn a small sample of intestinal secretion was scraped off with a sterile rubber glove and examined microscopically for parasites. A specimen of approximately 0·2 ml was then collected into 2 ml of transport medium (1·8 ml glucose broth and 0·2 ml glycerol) and immediately deep-frozen. Specimens were transported personally by air on 'dry-ice' to Australia where the microbiological studies were done. Specimens were plated aerobically and anaerobically on selective media and growth measured quantitatively as described previously (Gracey *et al.*, 1973). Results of throat swabs were used to exclude artefactual contamination of intestinal specimens from above during collection. Results refer only to specimens where such contamination was excluded.

Results

Trophozoites of *Giardia lamblia* were found by microscopy in the fresh smears from 2 patients, in 1 patient ascaris worms and eggs were found, and in 3 patients profuse fungal mycelia were observed. Large numbers ($>10^5$/ml) of organisms were isolated from intestinal samples of 6 patients; in 3 others $>10^4$ bacteria/ml were grown. Heavy growth of anaerobes occurred in 9 specimens while faecal bacteria were isolated in excessive numbers in 5 and enterobacteria in 3 instances (Table).

Discussion

This preliminary study has shown that the paediatric Enterotest duodenal capsule can be used to study the upper intestinal microflora in children. The adult-sized capsule has previously been shown to be of use in diagnosis of parasitic infestations (Beal *et al.*, 1970) and in the present study using a paediatric capsule parasites were found in 3 of the 10 patients. Cultures of intestinal samples showed that all except one of these patients had microbial contamination of the upper gut similar to the results found in a similar group of patients in the same institution some years ago (Gracey *et al.*, 1973).

The safety and simplicity of the method make it attractive. It has the added advantages over standard methods of intestinal intubation that it can be performed by relatively inexperienced operators and does not require radiological facilities. It should be useful in studying the human intestinal microflora in places where radiology is not available, and could easily be used in field studies.

Two disadvantages should be considered. Firstly it is rather unpleasant for the subjects but a skilful and patient nurse or doctor should be able to get even small children to swallow the device; small sips of water are very helpful. Once the capsule is swallowed it causes very little discomfort. The other potential problem is the assessment of microbiological results. It is essential to take throat swabs for culture before withdrawing the line since the distal part of the line will become contaminated with oropharyngeal secretions when it is withdrawn. Care should be taken to cross-check the results of the throat swabs against the intestinal swabs to remove artificial contamination before the intestinal results are reported.

Table *Small intestinal microflora in 10 malnourished Indonesian children*

	Gram-positive bacteria	*Candida*	*Entero-bacteria*	*Faecal bacteria*	*Anaerobes*	*Total organisms*
No. of isolations $>10^3$/ml	2	3	3	5	9	9
Range of isolations in all patients	$0–1·4\times10^4$	$0–5·6\times10^4$	$0–2·1\times10^5$	$0–2·1\times10^5$	$0–9·0\times10^6$	$0–9·2\times10^6$

Summary

The upper intestinal microflora was studied in 10 malnourished Indonesian children using the paediatric Enterotest Capsules. Trophozoites of *Giardia lamblia* were found in 2 specimens, profuse fungal mycelia in 3, and ascaris worms and eggs in 1. In 9 patients an abnormally profuse small intestinal bacterial flora was found. Provided precautions are taken to exclude artefactual contamination of the line on its withdrawal, this is a safe and simple method for studying the upper gut flora which could be applied to field conditions since it does not require radiological facilities.

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Hepatic dysfunction in association with pancreatic insufficiency and cyclical neutropenia

Shwachman-Diamond syndrome

The syndrome of pancreatic achylia and cyclical neutropenia (Shwachman-Diamond syndrome), has been recognized for 13 years, though it now encompasses a far wider range of clinical abnormalities than was initially realized. In 1964 Shwachman *et al.* first distinguished these patients from those suffering from cystic fibrosis, and commented on an association of pancreatic insufficiency with growth retardation, bone marrow dysfunction, raised Hb-F levels, and galactosuria. Skeletal abnormalities were next noted, and in 1967 Burke *et al.* observed metaphyseal dysostosis in 3 cases; subsequent reports by others have recently been reviewed by McLennan and Steinbach (1974). In addition to metaphyseal disturbances, abnormal tubulations of long bones, clinodactyly, phalangeal hypoplasia, and narrowing of the sacrosciatic notches have been noted. Dys-γ-globulinaemia was next noted by Goldstein (1968) and has been described in 5 further patients (Doe, 1973), in each case involving a reduction in the serum concentrations of one or more of the immunoglobulins. As far as we can determine only one living patient with histological but not clinical evidence of liver dysfunction has previously been described (Bodian *et al.*, 1964). In a retrospective review of 18 children whose necropsies had shown exocrine hypoplasia and lipomatosis of the pancreas they noted that 11 had shown a fatty liver or cirrhosis. Cyclical neutropenia had not been shown in life in any of them. Higashi *et al.* (1967) observed inflammatory cell infiltration in the periportal tissue of the liver obtained at necropsy in a 2-year-old child with pancreatic insufficiency and cyclical neutropenia.

We presently have 4 children with this syndrome under our care as detailed in the Table. One of them (Case 1) has clinical evidence of hepatic dysfunction and is the subject of the case report.

Case report

A male, weighing 2·9 kg at birth, is the son of healthy unrelated parents. Frequent, loose, offensive stools were noted from birth, but appetite was good and there was no unusual frequency of respiratory or other infections. Height and weight remained below the 3rd centile, and he was referred (with his sister, Case 2) for investigation at the age of 9 months. On examination there were no abnormalities apart