

The differences between the two groups in all respects are insignificant. The differences between the two groups in respect of numbers of exchange transfusions per infant were analysed by means of the Wilcoxon rank-sum test. There was a difference of 24% in favour of the treated group in respect of the number of late exchange transfusions per infant, but this gives a  $\chi^2$  value of 1.95 ( $P > 0.01$ ) by this test.

One very severely affected infant in the control group (cord blood Hb 7.5 g/dl, serum bilirubin 88  $\mu\text{mol/l}$  (5.5 mg/100 ml)) died during exchange transfusion. Hydrops fetalis was found at necropsy.

### Discussion

The dose of sodium amytal given in this trial was small, equivalent to about 1.5 mg/kg body weight per day. Ramboer *et al.* (1969) gave phenobarbitone 60 mg/day from the 31st to 33rd week of pregnancy. Trolle (1968) gave phenobarbitone 50–200 mg/day for at least 8 days before delivery. There are, however, theoretical grounds for questioning the safety of larger doses of antenatal barbiturates (Wilson, 1969). We chose the smallest dose we thought likely to be effective. Possibly in a larger series the difference between the two groups in respect of late exchange transfusions might have reached statistical significance. But we ended the trial when Moller and Ebbesen (1975) reported a controlled trial of phototherapy in rhesus-haemolytic disease, since withholding phototherapy no longer seemed ethically justified. It remains probable, on the basis of the work of Trolle (1968) and of Ramboer *et al.* (1969), that larger doses of barbiturates given antenatally for longer periods would reduce the need for exchange transfusions in rhesus haemolytic disease.

### Summary

In a double-blind controlled trial sodium amytal 100 mg was given antenatally to infants with rhesus incompatibility. The drug was given nightly for 7 days before delivery to mothers in a treated group. Placebo tablets were given to mothers in a control group. There was no significant difference between the two groups in their cord blood bilirubin levels or the number of exchange transfusions required by defined criteria. We conclude that antenatal sodium amytal, as used in this trial, is of no value in the management of rhesus haemolytic disease of the newborn.

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## The stomach in malnutrition

Protein-energy malnutrition is one of the major health problems facing mankind. Recent reports 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) indicate that the contents of the upper small intestine of malnourished infants and children are contaminated with bacteria. This may contribute to the production of diarrhoea and malnutrition in these children and thus worsen their state (Gracey *et al.*, 1975). Bacterial proliferation in the upper intestine in malnutrition may result from repeated contamination from polluted living conditions, impaired immune defence mechanisms, and a breakdown in normal intrinsic defence mechanisms in the gastrointestinal tract. Gastric acid secretion is one of these normal defences and is important in controlling the intestinal microflora (Drasar *et al.*, 1969), but there are no reports of the adequacy of this function in malnourished infants and children. This was investigated in a group of patients in Jakarta, Indonesia.

**Patients and methods**

Fourteen patients were included in the study—11 girls and 3 boys whose ages ranged from 7 to 54 months. By the Wellcome Classification (*Lancet*, 1970), 7 of the 14 were undernourished, 4 had kwashiorkor, and 3 were marasmic. Specimens for serum gastrin and gastric acid secretion were obtained from 21 age- and sex-matched controls in the same hospital who had no clinical evidence of malnutrition or gastrointestinal disease. These 21 children were being intubated and having blood taken as part of a wider community health study to establish the patterns and prevalence of clinical and subclinical gastrointestinal diseases, including parasitic infestations of the upper intestine, in children in metropolitan Jakarta where nutritional problems and diarrhoeal diseases are endemic. Gastric biopsy was not performed in the control group.

After an overnight fast blood samples were taken and the stomach intubated perorally with a radio-opaque, red rubber Levin's gastric tube. Patients were swaddled and laid on their left side and their gastric contents were aspirated manually at frequent, regular intervals. Gastric juice was collected for four 15-minute periods (basal secretion) and then 6  $\mu\text{g}/\text{kg}$  pentagastrin (Peptavlon, ICI, England) was given subcutaneously. Aspiration was continued for a further hour in four 15-minute periods. Volumes of individual specimens were separately measured and the HCl content estimated by titration to pH 7.4.

Specimens for biopsy were taken with a Quinton multipurpose suction paediatric tube (Quinton Instruments, Seattle, USA).

Serum gastrin levels were estimated by radio-immunoassay (Hansky *et al.*, 1971).

**Results**

In the control group unstimulated and stimulated gastric acid secretion did not differ from previously quoted figures (Dodge, 1975). Basal gastric acid output was below normal in 4 of the 7 infants and in 5 of the 7 children over one year of age.

In all the patients maximal acid output (that is, in the 60 minutes after pentagastrin stimulation) was reduced as was peak acid output, which is the highest rate of secretion in two consecutive 15-minute periods after pentagastrin stimulation (Table).

Mean serum gastrin in the control group ( $n=21$ ) was 47 pg/ml and in the malnourished group ( $n=14$ ) was 38 pg/ml. Using the Wilcoxon rank sum test the difference between the two groups was significant ( $P<0.005$ ).

**Table Gastric acid secretion ( $\mu\text{mol}/\text{kg}$  per h) in 14 malnourished children**

Case no.	Age (m)	Basal acid output	Maximal acid output	Peak acid output
1	54	24	50	73
2	10	7	40	60
3	42	41	100	158
4	11	84	120	165
5	24	22	131	185
6	11	15	27	42
7	7	68	89	101
8	23	43	76	101
9	24	19	125	183
10	7	48	160	184
11	23	24	80	119
12	7	29	43	53
13	11	12	42	69
14	10	7	—	—
Normal range (Dodge, 1975)	0-12 12-60	34-69 37-94	221-293 244-258	280 411

Satisfactory specimens for biopsy were obtained from 9 patients. Paraffin sections showed all to be derived from fundal-type mucosa. One showed moderately severe chronic gastritis with some atrophy (Rao *et al.*, 1975) (Fig.), 5 had mild chronic gastritis, 2 had mild superficial gastritis, and one was normal apart from mild superficial leucocytic exudates. There were no complications.

**Discussion**

This study has shown that gastric acid secretion was reduced in a group of infants and young children with protein-energy malnutrition. In most patients the basal gastric acid output was low in the resting state and in all there were impaired responses to stimulation by pentagastrin.

This finding, along with the reduced gastrin levels and the presence of gastritis in most patients, suggests that impaired gastric function is an important complication of childhood malnutrition. The reduced rate of production of gastric acid probably contributes to bacterial overgrowth in the upper gut (Mata *et al.*, 1972; Gracey and Stone, 1972; Gracey *et al.*, 1973; Heyworth and Brown, 1975) by allowing large numbers of micro-organisms to escape the controlling influence of gastric acid (Drasar *et al.*, 1969) and thereby colonize the upper small bowel. Infants and children with malnutrition and diarrhoeal diseases have high bacterial counts in gastric contents (Gracey *et al.*, 1973; Maffei and Nóbrega, 1975) and probably this contributed to the histological abnormalities found in the present study.

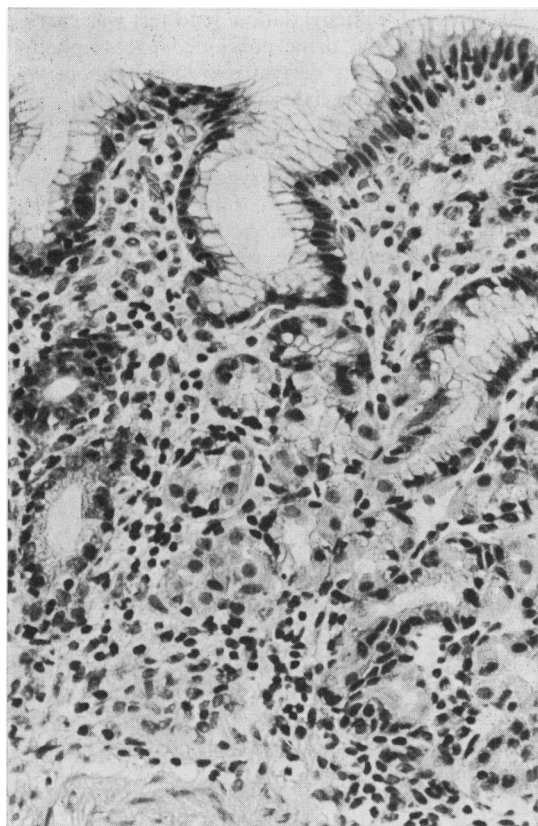


Fig. Gastric biopsy of a malnourished Indonesian child showing moderately severe chronic gastritis with a mild degree of atrophy. Leucocytic exudates, predominantly lymphocytes and plasma cells with some eosinophils, extend the full thickness of the gastric mucosa. Note intestinal metaplasia in gland left of centre of field. (H. and E.  $\times 330$ ).

These disturbances are probably yet another manifestation of the complex synergism of infection and nutrition so characteristic of childhood malnutrition (Scrimshaw *et al.*, 1969).

### Summary

Basal gastric acid output was reduced in 9 out of 14 infants and young children with malnutrition compared with 21 age-matched controls. In all the patients the response of the gastric mucosa to stimulation by pentagastrin was impaired, and gastritis of variable severity was present in 8 out of the 9 patients in whom biopsies were performed. Impaired gastric acid secretion probably contributes

towards bacterial overgrowth and diarrhoeal diseases in malnourished children.

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