Protracted diarrhoea in infancy

Analysis of 82 cases with particular reference to diagnosis and management

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SUMMARY Eighty-two cases of protracted diarrhoea in infancy presenting over a 6-year period have been analysed, with particular reference to diagnosis and management. The patients fell into 1 of 2 categories according to whether a specific diagnosis was established or not. A diagnosis (category 1) was established in 59 (72%), the commonest diagnoses being coeliac disease (33·2%), secondary disaccharide intolerance (12·2%), and cows’ milk protein intolerance (11·3%). Other diagnoses included primary sucrase-isomaltase deficiency, Shwachman’s syndrome, ulcerative colitis, ganglioneuroma, defective opsonization, staphylococcal pneumonia, and Hirschsprung’s disease.

Despite intensive investigation a diagnosis could not be established in 23 (28%) infants (category 2). Age of onset of symptoms in this group tended to be earlier than in category 1 patients, and 6 (7%) presented with diarrhoea dating from birth. Of particular interest in these 6 patients was the high incidence of associated extraintestinal anomalies, and of sibs who had died after protracted diarrhoea dating from birth. 4 of these 6 infants died, accounting for a mortality of 5% for the whole series. The remaining 17 (21%) patients in category 2 presented at a mean age of 4·9 weeks with a range of 1–18 weeks. All these 17 patients made an excellent response after institution of a chicken-based dietary formula, the details of which are presented. The pathophysiological mechanisms which may be operating in infants with protracted diarrhoea are discussed.

An infant presenting with protracted diarrhoea and failure to thrive often presents major problems in diagnosis and management, particularly if the patient’s general condition precludes intensive investigation. There have been very few reported series of protracted diarrhoea in infancy, and in each report the numbers of patients have been small, varying from 10 to 20 cases (Avery et al., 1968; Hyman et al., 1971; Lloyd-Still et al., 1973). Mortality rates of 45% (Avery et al., 1968) and 70% (Hyman et al., 1971) reflect the difficulties in management which these infants pose, and the nonresponsiveness to dietary treatment in patients in whom a specific diagnosis cannot be established has been emphasized.

We report 82 infants with protracted diarrhoea, paying particular attention to the differential diagnoses, and to the management of those patients in whom a specific diagnosis could not be established.

Patients and methods

An infant (less than 1 year old) is defined as having protracted diarrhoea in infancy if he has four or more loose stools per day for longer than 2 weeks, and either loses or fails to gain body weight during this period. The patients presented to The Hospital for Sick Children during the 6-year period 1970–1975, and detailed analysis was confined to those infants in whom a specific diagnosis could not be established. Patients whose symptoms occurred after surgery of the gastrointestinal tract, and those with cystic fibrosis, were excluded from the study. Clinical and laboratory methods used for assessment and diagnosis are outlined in Appendix A.

A diagnosis of coeliac disease was made on the basis of a clinical response to a gluten-free diet (and a jejunal biopsy which had the appearance of subtotal villous atrophy when the patient’s condition permitted the investigation), and a subsequent gluten challenge (Packer et al., 1974). The criteria for a diagnosis of cows’ milk protein intolerance were as previously described (Harries, 1975).
Results

The patients fell into one of two categories according to whether a specific diagnosis was established or not. Category 1 consisted of 59 (70%) patients in whom a diagnosis was established, and category 2 the remaining 23 (28%) infants in whom no cause for the diarrhoea could be established.

Category 1 patients. The age of referral to us and the diagnoses in category 1 patients are shown in Table 1. The commonest diagnoses were coeliac disease (33%), secondary disaccharide intolerance (12%), and cows’ milk protein intolerance (11%). Other causes of protracted diarrhoea included conditions such as primary sucrase-isomaltase deficiency, Shwachman’s syndrome, ulcerative colitis, ganglioneuroma, defective opsonization, and staphylococcal pneumonia. Of particular importance was the finding of a surgical cause for the protracted diarrhoea in 3 patients.

Category 2 patients. In the 23 patients in whom a firm diagnosis could not be established, the age of onset of symptoms tended to be earlier than in category 1 patients, and 6 presented with diarrhoea dating from birth (see Table 2). These 6 infants present a particularly interesting group and despite exhaustive investigations no known cause for their severe diarrhoea could be found. 2 sibs had agensis of the corpus callosum and both died, as did one infant with recurrent acidosis and hyperammonaemia of undetermined cause. One patient had protracted diarrhoea in association with glycogen deposition in mitochondria of skeletal muscle cells, and recovered. The remaining 2 patients had sibs who had died after protracted diarrhoea. In one of these patients profuse watery diarrhoea was associated with hypoplastic villous atrophy of the small intestinal mucosa possibly due to an as yet unrecognized genetically determined abnormality of vitamin B12 metabolism; this patient also died and will be reported in detail elsewhere.

Category 2 patients presenting after birth. The majority of infants in category 2 (17 cases) presented at varying intervals after birth having previously been in good health.

Clinical features. All 17 were referred from other hospitals where a variety of therapeutic dietary manipulations had been unsuccessful, and most had required intravenous fluids before referral. The mean age of onset of the diarrhoea was 4-9 weeks, range 1–18 weeks, and the mode of onset was usually acute diarrhoea with or without vomiting. In 2 cases enteropathogenic serotype strains of E. coli were cultured from the stools during the initial illness. None of the patients had been breast fed and only 3 had received gluten-containing foods before their presenting symptoms. The mean duration of diarrhoea before referral to us was 5 weeks, range 3–12 weeks. The perinatal histories were uneventful, a family history of allergy was recorded in 4 cases and one patient had a sib who had died of an undefined diarrhoeal illness at the age of 5 months.

On arrival at this hospital all infants weighed less than the 3rd centile for age and 15 were clinically marasmic; 8 weighed less than their birthweight and these developed symptoms at a mean age of 3 weeks and were referred to us at a mean age of 7 weeks. 4 patients were clinically dehydrated on arrival, and 11 were referred on intravenous fluids. The typical clinical appearance of these patients is illustrated by the 2 infants in the Fig.

Laboratory features. The laboratory investigations performed on these 17 patients are outlined in Appendix A. No pathogenic bacteria or parasites were recovered from stools, and viral studies were not performed. Urine microscopies and cultures were normal, and when performed, blood cultures...
were sterile. 6 patients had haemoglobins of <10 g/dl, and 4 had total white cell counts of >15 000/mm³ (15·0×10⁹/l), the predominant cells being neutrophil polymorphs. 4 infants were hyponatraemic (plasma sodium <130 mmol/l; <130 mEq/l), one was hypernatraemic (sodium >160 mmol/l), and 5 had a metabolic acidosis on referral. 3 were hypoalbuminaemic (plasma albumin <3·0 g/l). Hypocalcaemia was not a feature in any of the 17 infants. Plasma zinc level was low in 1 of 5 infants in whom it was determined, whereas plasma copper was normal in all 5.

Serum IgA and IgM levels were raised in 3 patients, and 4 had low levels of IgA; in 1 patient IgM was raised, in another IgG was raised. None of the patients had low serum concentrations of IgG or IgM.

Peroral jejunal biopsy performed in one case showed subtotal villous atrophy; this infant had received gluten (1–2 g daily) for 3 weeks before biopsy, but after a formal gluten challenge has been proved not to have coeliac disease.

**Comparison of clinical and laboratory features between category 1 and category 2 patients.** On the basis of the clinical and laboratory features it was sometimes not possible to clearly differentiate category 1 patients from category 2 patients at the time of referral. In a small proportion of infants, however, the diagnosis was almost immediately apparent (e.g. acrodermatitis enteropathica, ulcerative colitis, staphylococcal pneumonia). Diagnosis in category 1 patients was established either after more extensive investigation, or in retrospect (e.g. cows’ milk protein intolerance). None of the infants in category 1 subsequently proven to have coeliac disease presented the typical clinical appearances of the 2 patients in category 2 shown in the Fig. Some patients in category 1 (e.g. secondary disaccharide intolerance, cows’ milk protein intolerance), however, presented identical clinical features to the category 2 patients.

**Management.** The management of category 1 patients was according to the specific diagnoses which were
made. Correction of water and electrolyte imbalances was necessary in a number of these patients, and a few required a period of parenteral nutrition.

In the category 2 patients with diarrhoea dating from birth, long-term parenteral nutrition for periods varying from 1 to 9 months was necessary in all 6. None responded to the dietary regimen outlined in Appendix B, nor to any other artificial food formulae (e.g. elemental diets) or drugs (e.g. cholestyramine, corticosteroids, prostaglandin synthetase inhibitors, oral antibiotics).

After investigation and unsuccessful attempts to treat with a variety of the commercially available dietary formulae, the 17 patients in category 2 who presented after birth were treated with a diet which excluded all protein sources except for chicken, and the disaccharides lactose and sucrose. Total parenteral nutrition was not considered necessary in any of this group, but oral feeding was temporarily supplemented by intravenous nutrition in one case. In some of this group the infant’s condition precluded detailed investigation. The mean duration of hospitalization and weight gain was 29 weeks and 29 g per day respectively.

Details of the chicken-based diet, duration of treatment, and the scheme for reintroducing a normal diet are outlined in Appendix B.

Discussion

It is our experience and that of others (Avery et al., 1968; Hyman et al., 1971) that infants with protracted diarrhoea often present major problems in diagnosis and management. Because of delays in referral to experienced centres, the condition of the patients often precludes intensive investigation and an empirical approach based on theoretically possible diagnoses is necessary. Nevertheless, it should be stressed that every attempt to exclude medical and surgically remediable causes (see Table 3) should be made. In our series 3·6% of patients had an underlying surgical cause for their protracted diarrhoea, compared with 10% in the reported series of Avery et al. (1968).

In category 1 patients the three commonest diagnoses were coeliac disease, secondary disaccharide intolerance, and cows’ milk protein intolerance. In 5 patients the latter diagnosis was made retrospectively when milk was reintroduced after a 2- to 3-month period of treatment with the chicken-based formula. The general condition of many of these infants on referral was so poor that the possibility of precipitating severe crises by cows’ milk challenges was not considered to be justified. A variety of other diagnoses was established such as primary sucrase-isomaltase deficiency, Shwach-

<table>
<thead>
<tr>
<th>Causes</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Coeliac disease</td>
<td>Lactose intolerance</td>
</tr>
<tr>
<td>Acquired sugar intolerance</td>
<td>Cows’ milk protein intolerance</td>
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<tr>
<td>Acquired protein intolerance</td>
<td>Soy bean protein intolerance</td>
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<tr>
<td>Enterocolitis</td>
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<td>Surgical</td>
<td>Malrotation</td>
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<td>Hirschsprung’s disease</td>
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<td>Blind loops</td>
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<td></td>
<td>After intestinal resection and other surgical procedures to gastrointestinal tract</td>
</tr>
<tr>
<td>Selective inborn errors</td>
<td>Congenital chloridor rhoea</td>
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<td>of absorption</td>
<td>Glucose-galactose malabsorption</td>
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<td>Extraintestinal infection</td>
<td>Sucrese-isomaltase deficiency</td>
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<td>Combined immune deficiency</td>
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<tr>
<td>Cystic fibrosis</td>
<td>Defective opsonization</td>
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<tr>
<td>Chronic inflammatory bowel</td>
<td>Ulcerative colitis</td>
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<tr>
<td>disease</td>
<td></td>
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<tr>
<td>Tumours</td>
<td>Neuroblastoma</td>
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<tr>
<td></td>
<td>Ganglioneuroma</td>
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<td></td>
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<td>Lymphoma</td>
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<tr>
<td>Antibiotics</td>
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<td>Adrenal insufficiency</td>
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<td>Histiocytosis X</td>
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<tr>
<td></td>
<td>Intestinal lymphangiectasis</td>
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<td>Intrauterine infections</td>
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man’s syndrome, acrodermatitis enteropathica, ulcerative colitis, ganglioneuroma, defective opsonization (Soothill and Harvey, 1976), and staphylococcal pneumonia (Harries and Francis, 1968). The opsonizing capacity of the serum of infants with protracted diarrhoea in whom a specific diagnosis is not immediately apparent should be assessed, since therapy with plasma infusions may result in prompt and complete control of the diarrhoea; defective opsonization may be a commoner cause of protracted diarrhoea than has been hitherto supposed, particularly when the diarrhoea is associated with frequent infections and eczema.

The most severely affected patients were those in category 2 who presented from birth. 4 of these 6 infants died, a mortality rate of 5% for the total series of 82 patients. Of particular interest in this group was the high incidence of sibs being similarly affected with protracted diarrhoea dating from birth, and the associated extraintestinal anomalies. 2 of the patients who died were sibs and both had absent corpora callosa. 2 others had sibs who had died at 1 week and 8 months after birth; 1 of these had a right dysplastic kidney and the other a ‘tissue paper’ like skin which exfoliated at intervals of 2 to
3 weeks. The latter patient was the infant with hypo-
plastic villous atrophy of the small gut as described
in the results section. None of the 6 infants in this
group had any of the currently recognized inborn
errors of absorption, but the familial pattern of
severe watery diarrhoea dating from birth may
indicate a genetically determined disorder of fluid
and electrolyte absorption. There was no clinical or
laboratory evidence of intrauterine infection, and
no history of intestinal disease in the parents.

Finally there were the 17 infants in category 2 who
had remained perfectly well until a mean age of 4.9
weeks, presenting usually with acute diarrhoea with
or without vomiting. These were all extremely ill and
marasmic on referral, and had previously been
unsuccessfully treated with a variety of dietary
formulae on the assumption of diagnoses such as
cows' milk protein intolerance and/or disaccharide
intolerance. All responded promptly to our protocol
using a chicken-based feed (details in Appendix B),
and were able to return to a diet containing cows'
milk approximately 3 months later. 5 infants who
originally fell into category 2 were subsequently
proved to have cows’ milk protein intolerance after
a period of successful treatment on the chicken-
based diet, and were therefore transferred to the
diagnostic category 1. Intolerance to cows' milk
protein may result in acute or more insidious and
chronic symptoms (Kuitunen et al., 1975), and for
this reason it is our policy to delay reintroducing
dietary gluten until after the successful reintroduc-
tion of cows’ milk protein (see Appendix B). In this
series a delayed response to cows’ milk protein was
not seen in any infant, and all are currently receiving
a normal diet except for 1 patient who remains on a
gluten-free diet awaiting a gluten challenge. From
our series and those of Avery et al. (1968), Hyman
et al. (1971), and Lloyd-Still et al. (1973), a com-
prehensive differential diagnosis can be formulated
for infants with protracted diarrhoea, as shown in
Table 3, which also lists conditions not included in
the present series that we have encountered in the
past.

Our results indicate that the chicken-based feeding
regimen (see Appendix B) is a highly effective form
of dietary treatment in those infants with protracted
diarrhoea of undetermined cause who present after
birth. It contains a hypoallergenic protein source,
esential fatty acids, and excludes the disaccharides
lactose and sucrose; carbohydrate is included in the
form of a glucose polymer, Gastrocaloreen. In some
infants carbohydrate was administered as glucose,
or a mixture of fructose and glucose, and was equally
effective. The formula provides all the essential
nutrients required for optimal growth, is a relatively
low osmolar feed, is well tolerated by infants, and is
cheap. After a few teaching sessions with a dietitian
before discharge from hospital, the parents of our
patients coped extremely well with the diet in their
homes. All the children thrived on the chicken-based
diet, and a proportion became overweight as a result of
their ravenous appetites and parental generosity with
regard to food demands. The dietary requirements
of marasmic infants with protracted diarrhoea are,
of course, greatly in excess of their actual body
weight; as they respond to dietary treatment and
begin to thrive their nutritional requirements per
unit body weight decline and appropriate reductions
are necessary to avoid excessive weight gain and
obesity.

In infants with protracted diarrhoea, in whom a
diagnosis is not readily apparent, we would recom-
end dietary treatment with the chicken-based
formula while awaiting the results of laboratory
investigations. Parenteral nutrition may be life
saving in marasmic infants and, unless there is a
rapid response to dietary treatment, should probably
be started at an early stage (Harries, 1971; Hyman
et al., 1971; Lloyd-Still et al., 1973). Complications
of parenteral nutrition, however, are far more likely
to occur in severely malnourished infants, particu-
larly septicaemia and hypophosphataemia (Harries,
1974). Hypophosphataemia may result in haemolytic
anaemia, and peripheral hypoxia leading to con-
vulsions and sometimes coma (Jacob and Amsden,
1971; Silvis and Paragas, 1972), and may also result
in defective phagocytic function, and thus predispose
to sepsis during parenteral nutrition (Craddock
et al., 1974). The somewhat traditional concept of
‘resting the bowel’ of infants with diarrhoeal states
continues to be attractive, but there is no good
evidence that this approach is therapeutically ben-
ficial. On the contrary, there is now good evidence
that intraluminal substrates exert a trophic effect on
the small intestinal mucosa and that this effect may
be mediated by certain gastrointestinal hormones
such as gastrin (Johnson, 1976). For these reasons
it is our policy to provide some oral feeds in those
infants with protracted diarrhoea who require
parenteral nutrition.

A variety of hyperosmolar ‘elemental’ diets are
currently available, and have been advocated in the
management of protracted diarrhoea in infancy.
These have a number of disadvantages such as their
high osmolality, their cost, and the fact that many
contain fat in the form of medium-chain triglycerides
thereby increasing the risk of essential fatty acid
deficiency. In our experience elemental diets are
rarely, if ever, indicated in the treatment of pro-
trated diarrhoea.

The pathophysiological mechanisms responsible
for the protracted diarrhoea in our patients have
not been defined in the present study, and are probably complex and multifactorial. The turnover of the epithelial absorptive cells of the small intestine is rapid, and a vicious cycle of malabsorption-malnutrition-exacerbation of malabsorption is an acceptable general concept to explain the continuing diarrhoea and malnutrition in many cases. Within this general concept, however, a number of specific pathophysiological mechanisms may act singly or in concert in the genesis of the diarrhoea and these will be briefly considered.

An acute enteric infection can cause damage to the small intestinal mucosa and may render the mucosa sensitive to foreign antigens such as cows' milk protein, and deficiency of IgA may predispose the infant to become sensitive to foreign protein (Harrison et al., 1976). In this context it is of interest that 4 of our 17 patients who presented after birth had reduced levels of serum IgA. As an entity, transient gluten intolerance (Walker-Smith, 1970) has not been unequivocally established, but it is our impression that infants with protracted diarrhoea benefit from temporary withdrawal of dietary gluten. Other foreign proteins such as soy bean protein may also play an aetiological role in some infants (Ament and Rubin, 1972).

Bacterial overgrowth of the small intestine is now established as a common phenomenon in infants with protracted diarrhoea in both the developing (Gracey and Stone, 1972; Heyworth and Brown, 1975) and developing (Gracey et al., 1969; Challacombe et al., 1974a, b) parts of the world. Both anaerobic (particularly Bacteroides) and aerobic (particularly E. coli and Klebsiella pneumoniae) species have frequently been isolated. These observations may indicate that bacteria, the toxins which they elaborate, or the 'toxic' products which they generate as a result of metabolism of intraluminal substrates may be of pathophysiological importance. For example, a variety of anaerobic bacteria possess enzymes which catalyse the deconjugation and 7-$\alpha$-dehydroxylolation of bile salts resulting in the production of free dihydroxy bile acids such as deoxycholate and chenodeoxycholate. In the experimental animal, deoxycholate inhibits the absorption of fluid and electrolytes in both the small and large bowel and in the jejunum inhibits monosaccharide absorption and mucosal (Na$^+$-K$^+$)-ATPase activity. At high concentrations this bile acid produces gross structural abnormalities of the jejunal mucosa (Harries and Sladen, 1972; Sladen and Harries, 1972; Guiraldes et al., 1975). Deoxycholate and other free bile acids are present in the duodenal contents of some infants with protracted diarrhoea (Gracey et al., 1969; Challacombe et al., 1974a; Schneider and Viteri, 1974), and may contribute to the pathogenesis of the diarrhoea. In addition to bile acids, bacterial production of hydroxy fatty acids may also contribute to the diarrhoea (Bright-Asare and Binder, 1973; Ammon et al., 1974). A variety of toxins elaborated by bacteria commonly found in the duodenum of infants with protracted diarrhoea (e.g. E. coli, Kleb. pneumoniae, Staph. aureus, Clostridium perfringens) inhibit fluid and electrolyte transport in the small gut of the experimental animal (Sulivan and Asano, 1971; Field, 1974; McDonel, 1974; Elias and Shields, 1976; Klipstein et al., 1976).

Further studies are required to clarify the pathophysiological mechanisms which operate in infants with protracted diarrhoea. We speculate that in a proportion of affected patients an acute infective insult renders the small intestine susceptible to intolerance of foreign proteins and/or bacterial colonization, and that this sequence of events is important in the pathogenesis of the diarrhoea and malnutrition. Malnutrition, whether primary or secondary to infection, probably plays an important pathophysiological role.

References

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Appendix A

Clinical and laboratory methods used for assessment and diagnosis of infants with protracted diarrhoea

Initial assessment

(i) Clinical. Historical evaluation of onset and duration of symptoms; relationship between withdrawal and/or introduction of different dietary constituents; family history of gastrointestinal disease; presence of blood and/or bile in vomit; presence of blood and character of stools; frequency of extra-intestinal infections; details of pregnancy and birth with regard to intrauterine infections and asphyxia; clinical assessment of degree of dehydration and nutritional status, and careful examination of the abdomen and anorectal region.

(ii) Laboratory. Haemoglobin, white blood cell and platelet counts; blood urea, plasma electrolytes, and acid-base status; plasma glucose, calcium, and magnesium, and serum proteins; blood cultures and clotting studies as indicated; stools for microscopy, culture, and reducing substances; urine for microscopy and culture, and amino acid chromatography. Erect and supine plain films of chest and abdomen.

Subsequent assessment

When a specific diagnosis was not immediately apparent, and when the infant's general condition had stabilized the following investigations were performed in all cases: serum immunoglobulins, folate, cholesterol, and iron; plasma amino acids and organic acids; plasma and urinary catecholamines; 11-oxygenation index of urine; barium meal and follow through; sweat test; opsonizing capacity of serum. Serum trace metal levels (particularly zinc and copper) were determined in patients referred during the past 6 months.

The following investigations were performed only in those infants where they were considered to be indicated; barium enema, rectal pressure studies, sigmoidoscopy, and rectal biopsy; jejunal biopsy for histology and disaccharidase assays; duodenal intubation for pancreatic enzymes, bile salts, and culture of aerobic and anaerobic bacteria; blood levels of hormones such as vasoactive intestinal peptide, gastrin, and calcitonin; oral sugar loading.
tests and appropriate tests to exclude intrauterine infection.

Appendix B

Details of chicken-based diet, duration of treatment, and reintroduction of normal diet in infants with protracted diarrhoea of undetermined cause

Protein is provided as comminuted chicken (which contains some long-chain triglycerides), carbohydrate as Gastrocaloreen (a glucose polymer), and fat as Prosparol (an emulsion of long-chain triglycerides); carbohydrate can also be given as glucose, or as a mixture of glucose and fructose, up to a maximum concentration of 8–10%. The basic constituents of 100 ml of the full strength feed are shown in Table 4. Comminuted chicken 50 g, Gastrocaloreen 5 g, and 0·8 g of the metabolic mineral mixture (Table 5) are made up to 100 ml

(e.g. 1- or 2-hourly feeds) together with disaccharide-free complete vitamin supplements (i.e. 3 Ketovite tablets and 5 ml Ketovite liquid (Paines & Byrne, Greenford, Middx.) per day); any drugs must be administered orally free of disaccharides. The feeds are then slowly built up over a period of 10–30 days. This is achieved by first increasing the feeds to full strength, and then by adding Prosparol in 2-5 ml increments; Gastrocaloreen and calcium gluconate are also added to the feeds during this build up period to provide finally the requirements shown in Table 6. If this feeding regimen is tolerated and the patient begins to thrive, then the following modifications are implemented before discharge home. (i) The intervals between feeds are increased (e.g. 4-hourly × 5); (ii) introduction of suitable weaning solids appropriate for age (e.g. Robinsons baby rice mixed with 5% dextrose; milk-free mashed potato, and puree meat). The dietitian then spends two to three sessions with the mother teaching her the diet.

After a period of 2 to 3 months the patient is readmitted and reintroduction of disaccharides and cows' milk protein is attempted according to the following scheme.

Day 1. Lactose replaces the feed carbohydrate, initially in a concentration of 1%. If this is tolerated the concentration of lactose is increased on days 2, 3, and 4 to 3, 5, 7% respectively.

Day 5. If lactose is tolerated, a challenge (5 ml) of fresh pasteurized cows’ milk is given.

Day 6. If the milk challenge does not precipitate any symptoms, the volume of a suitable low solute cows’ milk formula is slowly increased over the next 4 days.

Table 4 Constituents of full-strength feed for treatment of protracted infantile diarrhoea of undetermined cause

<table>
<thead>
<tr>
<th>Constituents</th>
<th>Amount in 100 ml</th>
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<tr>
<td>Protein (contained in comminuted chicken)</td>
<td>3·75 g</td>
</tr>
<tr>
<td>Fat (contained in chicken)</td>
<td>1·65 g</td>
</tr>
<tr>
<td>Gastrocaloreen*</td>
<td>5·0 g</td>
</tr>
<tr>
<td>Sodium†</td>
<td>1·85 mmol</td>
</tr>
<tr>
<td>Potassium†</td>
<td>2·32 mmol</td>
</tr>
<tr>
<td>Calcium†</td>
<td>1·75 mmol</td>
</tr>
<tr>
<td>Other minerals†</td>
<td>—</td>
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<tr>
<td>Total energy provided: approx. 211 kJ</td>
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</tbody>
</table>

*Gastrocaloreen is a glucose polymer (Scientific Hospital Supplies, England).
†Sodium, potassium, calcium, and other minerals derived from the comminuted chicken and the metabolic mineral mixture.

Conversion: SI to traditional units—Energy: 4·18 kJ ≈ 1 kcal.

Table 5 Composition of metabolic mineral mixture*

<table>
<thead>
<tr>
<th>Constituents</th>
<th>Amount (mg) in 1 g</th>
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<tbody>
<tr>
<td>Calcium</td>
<td>82</td>
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<tr>
<td>Potassium</td>
<td>83</td>
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<tr>
<td>Phosphorus</td>
<td>59</td>
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<tr>
<td>Sodium</td>
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<td>Magnesium</td>
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<tr>
<td>Iron</td>
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<tr>
<td>Copper</td>
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<tr>
<td>Zinc</td>
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</tr>
<tr>
<td>Manganese</td>
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<tr>
<td>Iodine</td>
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<tr>
<td>Aluminium</td>
<td>0·0002</td>
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<tr>
<td>Molybdenum</td>
<td>0·0015</td>
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</table>

*Scientific Hospital Supplies, England.

with water. Initially this formula is given as a quarter-strength feed with added sugar (5% dextrose), from which the added fat (Prosparol) is omitted, in a suitable volume as small frequent feeds
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so as to completely replace the chicken feeds. Sucrose is added to the diet (e.g. as fruit puree) before discharge. If lactose is tolerated then invariably sucrose will also be tolerated, since secondary lactose intolerance usually persists for longer periods of time than secondary sucrose intolerance.

Day 10. The patient is discharged home on a gluten-free diet and closely followed-up in the outpatient department.

If there is a family history of coeliac disease or if onset of symptoms followed the introduction of gluten-containing foods into the infant’s diet, then it is our policy to perform a small intestinal biopsy before and after a gluten challenge 1 to 2 years later (Packer et al., 1974). If there is clinical or biochemical evidence of deterioration on a gluten-free diet, a small intestinal biopsy is performed to exclude an enteropathy caused by cows’ milk protein, before returning the patient to a cows’ milk protein-free diet. If the patient thrives and does not fulfil the diagnostic criteria for gluten challenge as outlined above, gluten is introduced to the diet after approximately 3 to 6 months, and the patient is followed up at regular intervals for 2 years. If during this time there is any clinical or biochemical evidence of coeliac disease a small intestinal biopsy is performed.

Erratum

In the article on ‘Controlled trial of continuous positive airway pressure given by face mask for hyaline membrane disease’ by Allen et al., May 1977, pp. 373–378, the published values for CPAP and ventilation therapy on pages 374, 375, 376, 377, and in Table 3 (corrected version published below) were incorrect from the decimal point being sited one place to the left, resulting in the figures given being 10 times too small.

Table 3 Values (mean ±1 SEM) for mechanical ventilator variables when mean airway pressure was highest in the early-intervention and late-intervention groups. These values were obtained 2–4 hours after starting ventilation. PaO₂ was between 6·30 and 8·60 kPa (47 and 67 mmHg), PaCO₂ between 4·52 and 9·17 kPa (34 and 69 mmHg), and pH between 7·19 and 7·41

<table>
<thead>
<tr>
<th>Group</th>
<th>Early intervention (n=4)</th>
<th>Late intervention (n=7)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIO₂</td>
<td>0·85 ±0·03</td>
<td>0·89 ±0·02</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory frequency (cycles/min)</td>
<td>33·8 ±3·7</td>
<td>35·4 ±1·6</td>
<td>NS</td>
</tr>
<tr>
<td>Peak airway pressure (kPa)</td>
<td>2·0 ±0·28</td>
<td>2·6 ±0·27</td>
<td>NS</td>
</tr>
<tr>
<td>End-expiratory pressure (kPa)</td>
<td>0·3 ±0·11</td>
<td>0·27 ±0·11</td>
<td>NS</td>
</tr>
<tr>
<td>Inspiration : expiration ratio</td>
<td>0·62 ±0·12:1</td>
<td>1·79 ±0·26:1</td>
<td>&lt;0·02</td>
</tr>
<tr>
<td>Mean airway pressure (kPa)</td>
<td>0·91 ±0·08</td>
<td>1·76 ±0·25</td>
<td>&lt;0·05</td>
</tr>
</tbody>
</table>

Conversion: SI to traditional units—1 kPa ≈ 7·5 mmHg and 100 mm H₂O.