INVITED ARTICLE

Small Bowel Morphology in Chronic Infantile Diarrhoe.

by

PITONO SOEPARTO and I WAYAN GIRI

(From the Department of Child Health and Department of Pathology School of Medicine, University of Airlangga, Surabaya).

Before the introduction of in vivo intestinal biopsy techniques, relatively little was known about the morphology of human intestinal mucosa under normal condition, and still less about its pathological states.

The first intestinal biopsies were carried out with a modification of the rigid gastric biopsy tube (Shiner, 1956) and it was only after the introduction of the much more flexible biopsy capsule (Crosby and Kugler, 1951) that the technique of intestinal biopsy became extensively used throughout the world (Greene et al., 1974; Townley and Bernes, 1973). In 1962, Read and his colleagues produced a modification of Crosby's capsule, and a paediatric version of the modification is now widely used for small intestinal biopsy in children (Marketed as Watson Capsule).

A modified version of the paediatric Crosby Capsule with two part holes, which provides two smaller biopsies at one time, may be useful when the presence of a patchy lesion is suspected.

It has been recognized that intestinal biopsy has important limitations. In the first place only the mucosa and at most the superficial part of the submucosa are included in the material sampled.

This mean that only disease which primarily or predominantly effects the mucosa is likely to be detected. Secondly biopsy is only likely to be of value in those disease in which the lesions are

Received 14th Mei 1980.

sufficiently diffuse to be sample on a random basis. The possibility of sampling error must always be considered when a biopsy is found to be normal against clinical expectations.

Thirdly the difficulty of difining the limits of normality in morphological terms, (Lee and Toner, 1980)

The dissecting microscope is helpful in diagnosing a patchy enteropathy. Patchy lesions is chiefly associated with cow's milk sensitive enteropathy and post enteritis syndrome. There is a close relationship between dissecting microscopic appearances but this is not absolute. Nevertheless, examination of small intestinal biopsy specimens with the dissecting microscope is as important as examination with the microscope and should not be omitted.

Abnormal appearances are broadly grouped under two headings : a flat mucosa and a ridged or convoluted mucosa (Walker Smith, 1979).

Classification of dissecting microscope appearance

(J.A. Walker Smith, 1979)

Group I. Flat mucosa :

a. Flat and barren.
b. Flat mosaic.

Group II. Thickened ridges :

a. Short.
b. Taller.

Group III. Broad villi :

a. Long thin ridges like villi and tongue like villi.
b. Tongue and leaflike villi with occasional finger like villi.
c. Leaflike and finger like villi.

It cannot be over emphasized that mucosa abnormality must always be assessed against the background of the normal variation in any particular community.

In the tropics, under dissecting microscope fingers villi are much less conspicuous than in "temprate" biopsies, the leaf villous is the predominant form and is quite often accompanied by short ridges and even on occasion a convoluted pattern (Lee and Toner, 1980).

Histologically, the villi tend to have a pyramidal shape, being broader at the base than the apex.

They are also significantly shorter than their temperate counterparts. In terms of villous height, at least half of all tropical biopsies would be regarded as abnormal by temperate standards (Lee and Toner, 1980).

Consequently in our series of biopsies we tend to follow a more rigid criteria in interpreting a biopsy as being abnormal.

Light microscopy : small intestinal biopsy sections are routinely examined with the light microscope.

At present an unsatisfactory situation exists in relation to histological terminology. Many authors use the terms flat, abnormal (but not flat), and normal to describe the appearances seen.

The differential diagnosis of any child under two years with chronic diarrhoea and failure to thrive is an important problem. In these circumstances the following diagnosis need to be considered,

namely post enteritis syndrome, coeliac disease, cystic fibrosis, giardiasis and cow's milk protein intolerance as well as an anatomical abnormality of the small intestine. Chronic diarrhoea without failure to thrive needs to be distinguished from toddler's diarrhoea in which there is chronic diarrhoea but not failure to thrive (non specific diarrhoea, irritable colon syndrome), the small intestine of which is morphologically normal.

Sometime long term follow up is the only way to establish the diagnosis definitely. In view of this, when symptoms have been present for three weeks or more and there is doubt about the diagnosis, a small intestinal biopsy should be considered.

In the tropics, coeliac disease, and perhaps cystic fibrosis are rare, post enteritis syndrome, giardiasis and cow's milk protein intolerance, and malnutrition following gastroenteritis are on the other hand much more common.

The above group of disorders in which the lession may be patchy, the demonstration of an enteropathy is nonspecific. However, the finding of mucosal abnormality is diagnostically useful in such patients because it indicates the presence of pathology in the small intestine. Some disorders in this group e.g.: Cow's milk protein intolerance, may be diagnosed by serial biopsy related to the dietary protein withdrawal and challenge.

Postenteritis syndrome :

In clinical practice two main groups of problems has been observed following acute gastroenteritis in infancy (delayed recovery) namely an acute intolerance to the increasing concentration of milk, and a more chronic problem with persistent diarrhoea and failure to thrive.

The last categories (persistent diarrhoea and failure to thrive) were grouped together as the post enteritis syndrome.

Some patients with post enteritis syndrome show mucosal abnormality (post enteritis enteropathy). In the remainder the small intestinal mucosa was normal. (Table 1).

TABLE 1 : *Patients with post enteritis syndrome*

Total patients	Age	Abnormal mucosa on dissecting microscope
85	< 2 years	54 (63,5%)

Cow's milk sensitive enteropathy :

Food allergy or dietary protein intolerance may play a role in the genesis of post enteritis enteropathy

The most common food protein causing intolerance in children is cow's milk. Jejunal mucosa of very young infants previously fed a cow's milk protein based formula and who contact infective enteritis suffers damage when rechallenged with cow's milk protein (Sumithan, 1979).

Clinically there seem to be two syndromes of cow's milk sensitive enteropathy : a primary and a secondary.

In the primary there appears to be no predisposing factors, but in the secondary it follows acute gastroenteritis.

TABLE 2 : *Patients with cow's milk sensitive enteropathy (CMSE)*

Number of pat.	A g e	C M S E
64	< 2 years	27 (42.2%)

When present, the enteropathy can be shown to be cow's milk sensitive by serial biopsies related to withdrawal and challenge with cow's milk.

Unlike the gluten sensitive enteropathy of untreated coeliac disease, cow's milk sensitive enteropathy is of variable severity in proximal mucosal biopsy, and patchy in distribution, while a flat mucosae indistinguishable from the mucosal appearance found in coeliac disease, may occur.

In our series of cow's milk sensitive enteropathy lesser degrees of mucosal abnormality were more often found.

Malnutrition

During the active phase of the disease the jejunal mucosa may appear flat under the dissecting microscope and presents the histological features of crypt hyperplastic subtotal villous atrophy. There is increased leucocytic infiltration in the lamina propria.

An improvement in the nutritional status leads to marked improvement in mucosal morphology.

We were able to investigate 33 patients presenting with chronic diarrhoea and severe malnutrition (kwashiorkor, mixed type, marasmus). (Table 3).

There seems to be no correlation between the severity and type of malnutrition with the morphology of the small intestine.

The histopathological findings were evaluated according to Shanti Ghosh et al., 1972 :

Grade I : The majority of villi were shortened, broadened and clubbed at the tips and the epithelial cells are irregular. Cellular infiltration is more marked as compared to normal.

Grade II : The blunting of villi is greater with basal fusion as well as fusion at the tips. The epithelial cells are shortened with irregularity placed nuclei. The glandular layer is thickened and inflammatory cells are increased.

Grade III : There is a complete absence of villi except for the presence of short knoblike structures. Surface epithelial cells are irregular and often cuboidal. The mononuclear infiltration of the lamina propria is dense.

TABLE 3 : *The correlation of Malnutrition and morphology of intestinal mucosa.*

Type/Grade	Kwashiorkor	Mixed	Marasmus
Grade I	6	7	4
Grade I-II	1	—	1
Grade II	8	1	—
Grade III	5	—	—

Giardiasis

The parasites is usually found on histology within the intestinal lumen or adherent to the epithelial surface although it is doubtful if parasites can actually invade the epithelial surface.

Minor villous abnormalities associated with increase in leucocytic cells — especially eosinophils — have been reported, especially in tropically acquired cases with malabsorption. Frank villous atrophy has not been observed.

It thus seem improbable that disturbance in villous architecture are responsible for the malabsorption in giardiasis.

Of 28 infants below 2 years of age with chronic diarrhoea and malnutrition studied in Surabaya, giardia lamblia was found in duodenal juice of 5 patients (± 18%).

The significance of this finding of giardia lamblia in causing chronic diarrhoea and malnutrition in these patients needs however to be further investigated.

REFERENCES

1. CROSBY, W.M.; KUGLER, H.W.: Intraluminal biopsy of the small intestine: the intestinal biopsy capsule. Am. J. dig. Dis. 2 : 236 (1957).
2. GOSH, S.; DAGA, S.; KASTHURI, D.: MISRA, R.C.; CHUTTANI, H.K. : Gastrointestinal function in iron deficiency states in children. Am. J. Dis. Child 123 : 14 (1972).
3. GREENE, H.L.; ROSENSWEIG, N.S.; LUFKIN, E.G.; HAGLER, L.: GOZANSKY, D.: TAUNTON, O.D.; HERMAN, R.N. : Biopsy of the small intestine with the Crosby-Kugler Capsule. Experience in 3866 per oral biopsies in children and adults. Am. J. dig. Dis. 19 : 189 (1974).
4. LEE & TONER : Biopsy Pathology of the Small Intestine pp. 4-21 (Chapman and Hall, London 1980).
5. READ, A.E.; GOUGH, K.R.; BONES, J.A.; MC CARTHY, C.F. : An improvement to Crosby per oral intestinal capsule. Lancet i : 894 (1962).
6. SHINER, M. : Jejunal biopsy tube. Lancet i : 83 (1956).
7. SUMITHRAN, E.; IYINGKARAN, N.; ROBINSON, M.J.; LAM, S.K.; PUTHUCHEARY, S.D.; YADAV, M.: Effect of cosa of young infants recovering from acute infective enteritis. Proceeding of the International conference on infant nutrition and diarrhoeal disease and workshop on postgraduate paediatric education. Kuala Lumpur 9th — 16th November 1979.
8. TOWNLY, F.R.W.; BARNES, G.L.: Intestinal biopsy in childhood. Arch. Dis. Childh. 48 : 480 (1973).
9. WALKER SMITH, J.A. : Disease of the Small Intestine in Childhood. 2nd ed., p. 56., 139. (Pitman Med., London 1979).