The Villus Architecture of the Small Intestine in the Tropics: a Necropsy Study

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PLATES LX AND LXI

Previous studies of intestinal biopsies from apparently healthy people living in the tropics have shown abnormalities of villus architecture (Baker et al., 1962; Sprinz et al., 1962; Banwell, Hutt and Tunnicliffe, 1964; Lindenbaum, Kent and Sprinz, 1966). It therefore seemed appropriate to undertake post-mortem study of the villus architecture along the length of the small intestine. The usefulness of necropsy material for such a study has been demonstrated previously (Chacko et al., 1965; Creamer and Leppard, 1965; Loehry and Creamer, 1966; Wilson, 1966).

MATERIAL AND METHODS

Intestines were obtained within 6 hr of death from stillborn foetuses and subjects dying of diseases other than those of the gastro-intestinal tract. Only those showing an adequate state of preservation were included. Intestines from 19 foetuses, 12 neonates (0-30 days), 4 infants (1-12 moth), 9 children (1-12 yr) and 23 adults were examined. In 41 cases the entire intestine including the duodenum was obtained, but in 27 only the jejunum and ileum were available. Two of the adults were Europeans who had been resident in India for many years. The remainder were all Indians.

Immediately after removal, the intestine was opened and rinsed gently in 4 per cent. formaldehyde to remove the contents. After thorough fixation, the mucosa of the small intestine was examined under a dissecting microscope at 11 equidistant sites, starting with the first part of the duodenum and ending with the terminal ileum. When the duodenum was not available the proximal end of the jejunum was taken as site 2.

In some areas a layer of mucus covering the surface made it difficult to see the details. In such cases light superficial staining with a very dilute solution of toluidine blue was found useful in bringing out the details. The terms used to describe the various types of villus structure have been defined previously (Baker et al., 1962). For graphic representation, the changes in mucosal architecture were graded from 1 to V. Finger-like villi were graded as I, tongue-shaped villi as II, leaf-like villi as III, ridges as IV and convolutions as V. Where there were mixtures of various types, as was often the case, they were graded between the two types depending on their relative proportions.

RESULTS

The greatest degree of abnormality (highest numerical grading) was found proximally with a tendency for the changes to become progressively less marked distally. In the duodenum and jejunum the crests of the valvular convolvents often showed a more severe change than was seen in the troughs between these crests. In the ileum where the folds are wider apart this difference was less marked.

In the troughs between valvular convolvents, the ridge-, leaf- and tongue-shaped villi usually showed an arrangement in transverse rows with their broad surfaces at right-angles to the long axis of the intestine. On the crests, however, they were often arranged parallel to the axis of the intestine as described by Creamer and Leppard. The arrangement on the sides of the mucosal folds was irregular.

Adults. The duodenum was available in 11 cases, out of which 3 showed a convoluted

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pattern and 6 showed convolutions mixed with other forms. The most proximal part of the jejunum showed convolutions with other forms of villi in 7 out of 23 cases (fig. 1). In many cases the changes in the mucosa became progressively less marked at more distal levels of the intestine, and in 8 cases finger-like villi were predominant at site 11. The 2 specimens obtained from European patients had leaf-like villi with occasional ridges in the proximal jejunum. In one of these, finger-like villi were present from site 4 onwards, which was more proximal than in the case of any Indian subject in this group.

*Children.* The changes seen in the children were similar to those found in the adults.

![Diagram of villus architecture in various age groups](image)

**Fig. 1.**—Mucosal villus architecture of the small intestine in various age groups. The grades are shown on the ordinate: I = fingers; II = tongues; III = leaves; IV = ridges; V = convolutions.

Figs. 2-5 illustrate the progressive diminution of changes from the jejunum to the ileum seen in a 6-year-old boy who died of myocarditis of unknown aetiology. The upper jejunum showed convolutions on the crests of mucosal folds (fig. 2), and the troughs in between the folds showed a mixture of leaf-like villi and convolutions (fig. 3). The mid-jejunum showed leaves and tongues (fig. 4) and the terminal ileum showed leaves and occasional finger-like villi (fig. 5).

*Infants.* The changes in this group were identical with those seen in the children. In one 58-day-old male infant who died of a lung abscess there were ridges and leaves in the proximal jejunum (fig. 6). The ridge-like villi were arranged in parallel rows at right-angles to the long axis of the intestine.

*Neonates.* In this age-group finger-like villi occurred more often than in any of the older age-groups, but even in this group, leaf- and tongue-shaped villi were present proximally in more than half the specimens (fig. 1).

*Foetuses.* Most of the specimens showed finger-like villi throughout the intestine (fig. 7). Tongue-shaped villi were, however, seen in 6 specimens, but showed no predilection for any special area of the intestine (fig. 1). Occasional leaf-like villi were seen in some of the older foetuses in the proximal part of the intestine.

**DISCUSSION**

This study has confirmed the previous observations from biopsy material that marked changes in villus architecture are common in adults living in the tropics, even though they have no apparent gastro-intestinal disease. The changes in the children were similar to those seen in the adults. Although the infants were a small group, the changes found were only
Fig. 2.—Specimen from 6-yr-old boy. Mucosa of upper jejunum showing a convoluted pattern at crest of one of the valvulae conniventes. ×25.

Fig. 3.—Mucosa of trough adjoining the crest shown in fig. 2. Note mixture of leaf-like villi and convolutions. ×20.

Fig. 4.—Same subject as fig. 2. Mucosa of mid-jejunum showing leaf- and tongue-shaped villi. ×40.
Fig. 5.—Same subject as fig. 2. Mucosa of terminal ileum showing leaf-like villi with occasional finger-like villi. ×40.

Fig. 6.—Mucosa of proximal jejunum from a 58-day-old infant showing ridge-like villi. ×20.

Fig. 7.—Intestinal mucosa of a foetus showing finger-like villi. ×55.
slightly less marked than in the children. The group of neonates included intestines with a range of villus architecture from finger-like villi to those with leaves.

The foetal intestines, with the predominance of finger-like villi at all levels, are in marked contrast to those in the other groups. This suggests that the changes in the older subjects are not due to a racial difference in villus anatomy but are acquired.

Baker, Mathan and Cherian (1963) described mucosal changes in albino rats that were very similar to those found in this study. Isolation of a segment of jejunum in these rats delayed or even with changes (Chacko, Mathan and Baker, 1968), suggesting that the passage of intestinal contents played a part in bringing about the alterations. The fact that the changes in the human intestine are most marked in the duodenum and upper jejunum and become less marked distally, also suggests that some damaging factor(s) to which the upper small intestine is exposed becomes neutralised or inactivated progressively. A similar distribution of lesions occurs in some cases of tropical sprue (Baker et al., 1962) and gluten-induced enteropathy (Rubin et al., 1960). The greater involvement of the more exposed crests of the valvulae conniventes and less severe involvement of the troughs further supports this idea of some damaging factor(s).

In 7 cases there was evidence of parasitic infestations, mainly hookworm, roundworm and pinworm. The part played by hookworm infestation is debatable (Sheehy et al., 1962), though Layriss e et al. (1966), in an area where tropical sprue does not occur, failed to show any significant change in the villi with heavy hookworm infestation. There is no evidence that roundworms or pinworms cause mucosal changes.

Six of the adult patients had malignant disease in different parts of the body, but their intestinal mucosa was in no way different from that of the other adults. Cremer (1964) suggested that mucosal abnormalities of the small intestine may be associated with malignancy, but the exact pathogenesis of such changes and their relationship to the malignancy is not clear.

The presence of occasional tongue-shaped and leaf-like villi even in foetuses suggests that these changes were developmental in origin, or that they were the result of damaging factor(s) during intra-uterine life. Alterations of the mucosal architecture have been described in fetal grafts used in the construction of an artificial urinary bladder (Goldstein et al., 1967) and the ingestion of amniotic fluid that contains urine might possibly contribute to the foetal changes.

Townley, Cass and Anderson (1964) produced mucosal changes in the intestinal mucosa of dogs by irrigation with hydrochloric acid. The foetus starts producing hydrochloric acid from the 4th or 5th mth (Dudin, cited by Smith, 1929) and this may be a contributory factor. However, if gastric acid of itself plays an important part, changes in the mucosal architecture should be seen in all foetuses, and this is not so.

The marked changes occurring in the neonatal period suggest that the principal exposure of the intestine to damaging factor(s) is at or soon after birth. The main differences in the luminal environment at this time are the ingestion of colostrum and breast milk and the change-over from a sterile to a non-sterile state.

Kenworthy and Allen (1966) and Kenworthy (1967) emphasized the importance of bacterial flora in producing alterations in the villus architecture of germ-free pigs, and Sprinz et al. (1961) and Sprinz (1962) showed changes in the intestinal mucosa of germ-free guinea-pigs challenged with Enterobacteriaceae and Shigella flexneri. The role of bacteria in producing mucosal changes in man cannot be assessed at present. It may be relevant that in the tropics, where symptomatic bacterial infections of the intestine are common, biopsy studies have shown the highest incidence of abnormalities in clinically normal people (Sprinz et al., 1965; Burwell et al., 1964; Klipstein, Samloff and Scherk, 1966). The development of mucosal abnormalities in American Peace Corps volunteers within 6 mth of arrival in Pakistan and the lack of such changes in more protected Americans (Lindenbaum et al., 1966) also suggest that the intestinal flora may be a factor. One 51-day-old infant in our series showed well-marked ridges in the upper jejunum. This child died of a lung abscess and pericarditis, and the swallowing of infected sputum may have contributed to the development of the mucosal abnormality.
Various irritating factors in food have been blamed for the mucosal changes (Sprinz et al., 1962). Chillies and other spices are favourite food additives in South India and these may play some part in damaging the mucosa. However, in the breast-fed child, damaging factors from the food could be effective only if absorbed by the mother and excreted in the milk. Feeding large amounts of chillies to rats has not produced changes in villus architecture (Dr. K. N. Jeejeebhoy, personal communication).

As these abnormalities are most marked in areas where malnutrition is common, this has to be considered as an aetiological factor. Pigs (Platt, Heard and Stewart, 1964) and monkeys (Deo and Ramalingaswami, 1963), but not rats (Hill et al., 1968), kept on a protein-free diet develop marked mucosal abnormalities, but the relevance of these findings to human nutrition is doubtful as even the worst diet is not entirely protein-free. Unless there is some specific deficiency in the breast milk, it is difficult to blame malnutrition during the 1st mth of life. Two children in our study suffered from protein-calorie malnutrition, but their mucosal architecture was no different from that of the other children. The changes in kwashiorkor consist of leaf-like and ridge-shaped villi with increased cellular infiltration of the lamina propria (Burban, 1965). In the absence of normal controls from the population these observations are of doubtful significance. In Uganda the intestinal mucosa in children with kwashiorkor showed little improvement 1 yr after clinical recovery (Stanfield, Hutt and Tunnicliffe, 1965). This suggests that the appearances may not have been due to the kwashiorkor, but were "normal" for that population.

The response of the small-intestinal mucosa to injuries of various types appears to be stereotyped. No matter what the damaging agent(s), the villi change progressively from finger-like structures to tongues, leaves, ridges, convolutions and finally a flat mucosal surface. It is therefore possible that in different cases one or more of the factors discussed above may be responsible for the changes. Further work is needed to delineate the relative importance of these factors.

**SUMMARY**

A post-mortem study has been made of the mucosal architecture of the small intestine from 19 foetuses and 48 patients of different ages who had no apparent gastro-intestinal disease.

Most of the foetuses had only finger-like villi but within the 1st mth of life many subjects had leaf-like villi. With increasing age the degree of abnormality increased, reaching a maximum in the older children.

The most marked change was seen in the duodenum and proximal jejunum; there was a tendency for the abnormality to diminish distally.

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