Variation of Small Intestinal Morphology With Age

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Walker-Smith, John (1972). *Archives of Disease in Childhood*, 47, 80. **Variation of small intestinal morphology with age.** A study of small intestinal three-dimensional morphology from 85 childhood necropsies, using the dissecting microscope, has shown that there is a variation in morphology with age. While finger-like villi occurred frequently in the small intestine of neonates, particularly in the ileum, broader villi occurred more frequently in children aged between 5 months and 5 years, particularly in the proximal small intestine. However, in children over the age of 5 years, finger-like villi were observed more frequently, right along the length of the small intestine. This alteration in morphology in the early weeks of life is probably due to some change in the luminal environment developing shortly after birth, and it is suggested that bacterial colonization of the small intestine, and the response of the host to this, is responsible for these changes.

Newborn bandicoots, rats, and pigs have a small intestinal mucosa characterized by finger-like villi, but this appearance rapidly changes from about the age of 10 days to broader leaf-like forms (Van Lennep, 1962; Baker, Mathan, and Cherian, 1963; Kenworthy and Allen, 1966). Dissecting microscope examination at necropsy of small intestine which has undergone autolysis of its surface epithelium, leaving the basement membrane as its surface, is a useful way to study the three-dimensional mucosal morphology along the length of the small intestine (Creamer and Leppard, 1965; Walker-Smith, 1969; Creamer, Dutz, and Post, 1970). Using this method of examination the three-dimensional small intestinal morphology of children of varying age who were free of small intestinal disease was therefore studied at necropsy in order to determine whether or not there was any variation in human intestinal morphology with age.

Materials and Methods

Small intestine obtained at necropsy from 85 childhood necropsies performed at the Royal Alexandra Hospital for Children was allowed to stand in running water for 24 hours and then stained with ink and examined under the dissecting microscope (Walker-Smith, 1969). Small intestinal mucosal disease was not present in these children.

For the purposes of this report the appearances seen

were divided into finger-like villous cores (Fig. 1), and broader forms, i.e. long thin ridges, tongues, and leaves (Fig. 2). Specimens were taken from the duodenum and at 50 cm intervals from the duodenojejunal flexure. The appearances seen were grouped together according to the age of the child at death.

Results

The dissecting microscope appearances in the duodenum, proximal jejunum 50 cm from the duodenojejunal flexure, and distal ileum 50 cm proximal to the ileocaecal valve in the various age groups are indicated in Fig. 3. Finger-like villous cores were seen in the duodenum and right along the length of the small intestine in 2 neonates under 1 week of age and 1 neonate aged 2 weeks. In the remaining children under the age of 10 years the duodenal mucosa was characterized by broader forms (long thin ridges, tongues, and leaves). The jejunum was characterized by finger-like villous cores in 5 neonates under 1 week of age and 2 children aged 3 months and 5 months, respectively. Up to the age of 5 years, all remaining specimens were characterized by broader forms. Finger-like villous cores were most often seen in the ileum of all neonates, but the frequency of this finding in the ileum decreased thereafter up till the age of 4 years, when all ileal specimens were then found to be characterized by finger-like villous cores. Similarly in jejunal specimens taken from children 4 years and over, finger-like villous cores were seen with

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FIG. 1.—Dissecting microscope appearances characterized by finger-like villous cores. ($\times 40$.)

FIG. 2.—Dissecting microscope appearances characterized by broader villous cores (tongues and leaves). ($\times 40$.)

FIG. 3.—Dissecting microscope appearances in the duodenum, jejunum, and ileum of 85 children grouped according to age.

increasing frequency. The duodenum of 3 out of 4 children over 10 years of age was characterized by finger-like villous cores.

Thus finger-like villous cores were not seen, in the duodenum between the ages of 1 month and 10 years, in the jejunum between the ages of 5 months and 5 years, and were found less commonly in the ileum between the ages of 1 month and 4 years.

Studies along the length of the small intestine showed the typical transition from broader forms proximally to narrower forms distally in many of the younger children (Fig. 4).

Discussion

This study demonstrates a variation in three-dimensional mucosal morphology with age. Finger-like villous cores were most often seen in neonates and in children 4 years and older. They were also seen more commonly in the distal intestine.

Taking into account observations that histologically normal biopsies from the proximal small intestine in children are characterized under the

FIG. 4.—Distribution of dissecting microscope appearances along the small intestine in a child of 5 months.

dissecting microscope by broader villi than those seen in specimens from control adults (Burman, 1965; Walker-Smith, 1967; Shmerling, 1969) and reports that finger-like villi occur along the length of the small intestine in fetuses (Baker *et al.*, 1962), certain conclusions may be drawn.

These are: (1) that several days after birth there is a change in villous morphology, with a widening of intestinal villi to adopt broader forms, (2) that this change persists for several years, and (3) later in childhood, probably between the ages of 4 and 10 years, in those living in Australia at least and probably in those in Europe and North America, the villi become narrower again. At that time finger-like and narrow leaf-like villi are more often seen in the proximal small intestine and finger-like villi distally. A trend for broader villi to be present proximally, especially in the duodenum, persists in adult life (Loehry and Creamer, 1966).

In the neonates broad villi were most often seen only in the proximal small intestine, but later in the first year of life broad villi were found along the length of the small intestine in a majority of children. Baker *et al.* (1963) have observed similar changes in rats. They noted that rats at birth had finger-like villi for the full length of the small intestine, but within 10 days the villi became broader. These changes had a similar progression and distribution to those observed in the younger children in this necropsy study. They were most obvious proximally and spread distally. In the adult rat, ridges were seen instead of fingers proximally, and broad villi usually extended right along the small intestine, though becoming narrower and leaf-like distally. Gleeson *et al.* (1970) have

shown experimentally in the rat that if the jejunum were bypassed, the ileum changed from adult leaf-like villi to finger-like villi.

It follows from these observations in the rat, coupled with the fact that the change in morphology found in this study also began proximally and spread distally, that the change in morphology in both the rat and the human is due to some alteration in the luminal environment, developing shortly after birth, coinciding with the ingestion of food. Contact with food proteins, bacteria or bacterial products in the food, or bacterial colonization of the small intestine seems to offer the most likely explanation for this change. The change back to narrower villi, i.e. fingers and leaves in adult life, is harder to explain and suggests the disappearance of some intraluminal substance or the development of tolerance to it.

Variations in small intestinal flora with age or variation in host response to such flora could account for changes in intestinal morphology described here. Gorbach *et al.* (1967) have noted that normally the upper gastrointestinal tract of man contains low concentrations of predominantly Gram-positive micro-organisms. Schaedler, Dubos, and Costello (1965) have shown that the small intestine of the neonatal rat, sterile at birth, rapidly becomes colonized with bacteria shortly after birth.

The change to broader forms observed in the younger children is probably a sequel to contact with bacteria or indeed to bacterial colonization of the proximal small intestine. Host response may have a role to play as well, since it is well known that infants and toddlers are more susceptible to enteric infections than adults and, when they have such illnesses, these are often severer than in adolescents and adults.

Recently published observations of Kenworthy (1971) using germ-free pigs are of much interest in relation to the above hypothesis. He has compared small intestinal morphology in germ-free pigs, suckling pigs, and weaned pigs, all killed at 30 days, and has established that the change in villous morphology in the young piglet is not a direct function of age, but concludes that intestinal microbes and the digesta which these use as a substrate are the most important determinants of mucosal morphology.

Further studies of the bacteriology of the small intestinal contents of children of varying ages coupled with morphological study in such children should establish the relation between bacterial flora and morphology in the small intestine of the developing child.

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