the increased output of epithelial cells and hypertrophy of the inter villous ridges.

SUMMARY

The injection of methotrexate in rats produced a period of epithelial cell aplasia in the small intestinal mucosa for the first three days followed by a period of increased cell production for three days as the mucosa regenerated. Studies of the three-dimensional mucosal structure showed that the period of cell aplasia produced merely stunted villi, whereas in the recovery phase there was hypertrophy of inter villous ridges and a convoluted mucosa.

REFERENCES


C. A. Loehry and B. Creamer

Part II Mucosal structure and dynamics in the lactating rat

It is now well established that the small intestine along with many other organs is considerably hypertrophied in the lactating rat (Souders and Morgan, 1957; Fell, Smith, and Cambell, 1963; Cambell and Fell, 1964). There is considerable hyperplasia of villi to almost twice their normal size, and these changes progress to a maximum at weaning, after which there is a gradual return to normal. Cambell and Fell (1964) have demonstrated how these intestinal changes are dependent on the increased food consumption during lactation.

Boyne, Fell, and Robb (1966), measuring mucosal and serosal surface areas in lactating and virgin rats, noted considerable 'branching and fusion' of villi in histological sections from the upper small intestine of the lactating group as well as increased height and surface area. From these studies it seemed possible to us that in the small intestinal mucosa of the lactating rat there might be a change in the dynamic state producing a primary increase in cell production to form the hypertrophied mucosa, and that the branching of villi noted by Boyne et al (1966) might in fact be due to hypertrophy of inter villous ridges, which had become prominent at the base of the tall villi in response to the increased cell output. The aim of the present experiments therefore was to study the dynamic state of the small intestinal mucosa in the lactating rat, and to relate this to the three-dimensional mucosal structure.

Methods

Dynamic State Four albino rats in the sixteenth day of lactation and four virgin controls of similar age and weight were injected intraperitoneally with 100 µc of tritium-labelled thymidine at the same time. Two lactating and two control rats were killed at eight hours, and the remaining rats at 24 hours after the injection. Sections were taken from the upper jejunum, and processed by autoradiography. The comparative rates of cell migration in the two groups were assessed by counting the cell column from the base of the villi to the uppermost labelled cell in 50 well orientated villi at the 24-hour period after injection of the isotope.

Structural Changes These were assessed on the sixteenth day of lactation in the jejunum (1) after autolysis and (2) by serial horizontal cross sections (Loehry and Creamer, 1969).

RESULTS

Dynamic State At eight hours after injection of the tritium-labelled thymidine the crypt cells showed labelling in both the lactating and virgin rats, but in the lactating group labelling was often seen at the base of the villi. At 24 hours the lower one third of villi in the virgin rats was labelled whereas in the lactating group the lower half of the considerably taller villi showed labelling. The mean height of the
Three-dimensional structure of the small intestinal mucosa related to mucosal dynamics

FIG. 1. Autolysed jejunal mucosa from a lactating rat. Note the prominent intervillous ridges (i) at the base of the villi. × 30.

FIG. 2. Horizontal cross sections near the base of the villi in the jejunal mucosa of a lactating rat (left) and a normal control (right). In the lactating rat some of the hypertrophied intervillous ridges have joined adjacent villi, while others produce the 'buttress'-like effect on the lateral surface of villi.

labelled villous cell column at 24 hours in the control rats is 20·1 cells (standard deviation 3·75) compared with a mean height of 47·1 cells (standard deviation 5·6) in the lactating group. The difference between the two groups is highly significant (p < 0·001).

STRUCTURAL CHANGES The autolysed appearance of the jejunal mucosa is demonstrated in Figure 1. Hypertrophy of the intervillous ridges is apparent at the base of the tall villi. These are especially prominent immediately adjacent to villi giving a 'buttress'-like appearance. Figure 2 compares a horizontal cross section near the base of villi from a virgin and a lactating rat. In the lactating rat many villi are joined by intervillous ridges and the 'buttress' effect is again demonstrated.
DISCUSSION

These experiments demonstrate an increased turnover state in the small intestinal mucosa of the lactating rat. The exact stimulus to this remains obscure, but as the hypertrophy is related to increased food consumption (Cambell and Fell, 1964) it is possible that it may represent a reaction of the mucosa to produce an increased surface area in response to an increase in work load, similar to that seen after intestinal resection (Loran and Althausen, 1966). It could be suggested that the crypts are stimulated in some way to step up the rate of cell production, and this, without a comparative increase in cell loss, would produce a hypertrophied mucosa. Whatever the mechanisms, however, the results are to produce an increased output of cells from the crypts and this is probably responsible for the enlarged villi and the increased prominence of the inter villous ridges.

SUMMARY

An increased rate of epithelial cell production was demonstrated in lactating rats. This caused hyperplasia of the villi and at the same time increased prominence of the inter villous ridges.

REFERENCES


Part III Mucosal structure and dynamics in the rat infested with the nematode Nippostrongylus brasiliensis

The histological changes in the upper small intestinal mucosa of rats infested with Nippostrongylus brasiliensis are now well established (Symons and Fairbairn, 1962; 1963). The histological appearances in severely infested animals are similar in many respects to those seen in coeliac disease, with reduced or absent villous projections, lengthened crypts, and an increase in mitotic figures. Symons (1965) has studied cell kinetics in infested animals by the use of tritiated thymidine, and has demonstrated an increased cell production in the crypts, and an increase in cell migration on the villi. Although there were changes in the progenitor cycle of cells before gross changes were apparent in crypt and villous morphology, Symons could not be sure whether the increased turnover state was due to a direct effect of the parasite or secondary to an increased loss of cells from trauma at the tips of villi. In another communication (Loehry, Croft, Singh, and Creamer, 1968) we have studied cell loss in infected animals by means of deoxyribonucleic acid loss and excretion of $^{59}$Fe. These experiments showed a considerable increase of cell loss on the ninth day of infection. It thus seems established that by this time the effect of the parasite is to produce a "flattened" mucosa with increased cell loss possibly stimulating increased production. The aim of this study was to relate this dynamic state to the three-dimensional mucosal structure.

METHODS

Male albino rats were infected by subcutaneous injection of 5,000 to 10,000 larvae of Nippostrongylus brasiliensis from a culture obtained by incubating faeces of an infected rat with active charcoal at 25°C. Animals were killed on the ninth day of infection and the small intestinal mucosa was examined by an autolysed technique and photographed under the dissecting microscope.

RESULTS

Figures 1, 2, and 3 are photographs of the autolysed upper jejunal mucosa taken respectively from a normal control rat, from one with a moderate infection (5,000) larvae, and from one with a severe infection (10,000 larvae). In the normal mucosa (Fig. 1) the triangular-shaped villi are apparent, many lying on their sides, and many crypts. In the mucosa from the moderately infected rat (Fig. 2) most of the villi are longer and shorter and many of the inter villous ridges have now hypertrophied. In the mucosa from the severely infected animal (Fig. 3) the mucosa is quite flat. Villous projections are practically absent, and the whole structure of the
Three-dimensional structure of the rat small intestinal mucosa related to mucosal dynamics. II. Mucosal structure and dynamics in the lactating rat.

C A Loehry and B Creamer

Gut 1969 10: 116-118
doi: 10.1136/gut.10.2.116

Updated information and services can be found at:
http://gut.bmj.com/content/10/2/116.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/