

Complex Changes in the Suckling Rat's Small Intestine by the End of the Third Week of Life

HALLIDAY¹ has demonstrated that, in the suckling rat, the absorption of antibodies originating from milk ceases relatively abruptly on the 19th–20th day of life. This is followed by the temporary decrease of γ -globulin level and temporary increase of β -globulin level^{2,3}. During the absorption of antibodies, cells containing each one large supranuclear vacuole^{4,5} with eosinophilic inclusion bodies inside^{6,7} can be found in the ileum. No such cells are present in adult animals. By the end of the third week of life, the activity of several enzymes^{8,9} and the rate of cellular migration¹⁰ changes in the intestinal epithelium.

In the present study, the temporal relations of the morphological, enzymic and functional changes taking place in the epithelium of the small intestine, first of all in the ileum, were examined.

Material and method. Albino rats were used throughout. From each age group, 5 rats originating from at least 2 litters were killed. The small intestine was excised, spread, and cut into halves. The duodenum was thrown away and a portion of ileum of identical size was cut out for histological examination. The proximal and distal parts of the intestine were examined separately. The intestinal specimen was slit open, washed in saline and the epithelium was rubbed off using neutral saline containing 0.2% EDTA. The suspended scrapings were frozen and homogenized by grinding. Enzyme assays were carried out in neutral phosphate buffer, using pooled homogenates from 5 animals.

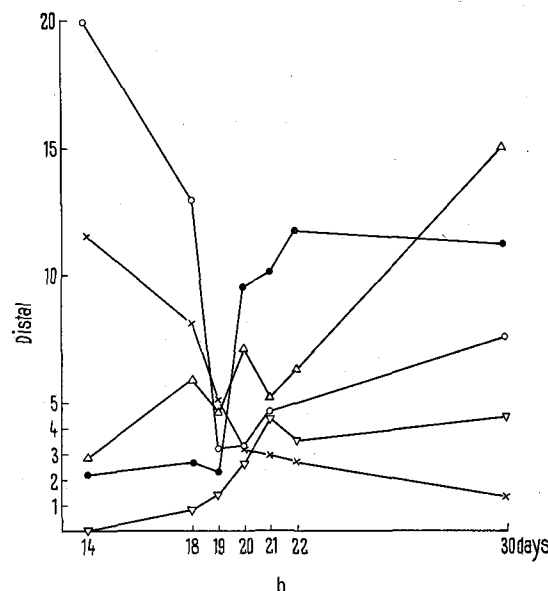
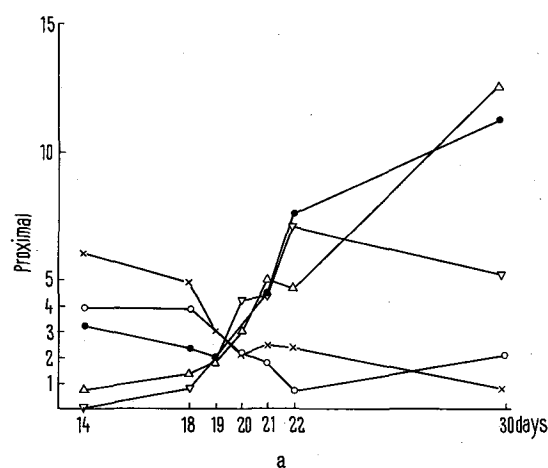
Amylase and invertase activities were determined by Nelson's method; proteolytic activity with casein, spectrophotometrically at 280 nm; lipase with tributyrin by titration; lactase with *o*-nitrophenyl- β -galactoside¹¹.

Results and discussion. The proximal and distal parts of the small intestine of suckling rats differed in colour. The proximal part was milky white, the distal part

yellowish brown⁶. This colour difference was shown also by the respective homogenates and tended to diminish slightly after the 14th day. The colour of the ileum was still distinctly brown at 18 days, and greyish at 20 days of age and in older animals. The ileum of 19-day-old rats was of transitory colour.

The results of histological examinations are summarized in the Table. Cells containing supranuclear vacuoles gradually disappeared from the intestinal epithelium between the 18th and 21st day; they were seen for longer at the tips than at the base of the villi. The eosinophilic inclusion bodies disappeared earlier than the vacuoles. In the materials examined, they were found only sporadically after the 18th day. The appearance of the above phenomena varied individually for 1 or 2 days.

The changes of hydrolytic enzyme activity in relation to age are shown in Figures 1a and 1b. Lactase activity



Distribution of ileal epithelial cells containing supranuclear vacuoles as assessed in groups of 5 rats of various ages

Age in days	14	18	19	20	21	22	30
+++●	+++●	+++●	+++	+	+	—	—
+++●	+++●	+++●	++	±	±	—	—
+++●	+++●	+++●	++	±	—	—	—
+++●	++	+	—	—	—	—	—
+++●	++	+	—	—	—	—	—

Supranuclear vacuoles: —, absent; ±, limited to tips of villi; +, limited to apical third of villi; ++, over apical and middle third of villi; +++, over the entire length of villi; ●, many inclusion bodies present in the supranuclear vacuoles.

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¹¹ The generous gift of SERVA Entwicklungslabor, Heidelberg (Germany).

Fig. 1. Change of activity of hydrolytic enzymes (a) in the proximal and (b) in the distal part of the small intestine. Enzyme units: ×, Lactase (μ g transformed substrate \times $\text{mg}^{-1}/\text{min}^{-1}$); v, invertase ($10 \times \mu$ g liberated glucose equivalent \times $\text{mg}^{-1}/\text{min}^{-1}$); Δ , amylase ($10 \times \mu$ g liberated glucose equivalent \times $\text{mg}^{-1}/\text{min}^{-1}$); ●, lipase ($10 \times \mu$ g liberated butyric acid \times $\text{mg}^{-1}/\text{min}^{-1}$); ○, protease ($10 \times \mu$ g trypsin equivalent \times $\text{mg}^{-1}/\text{min}^{-1}$).

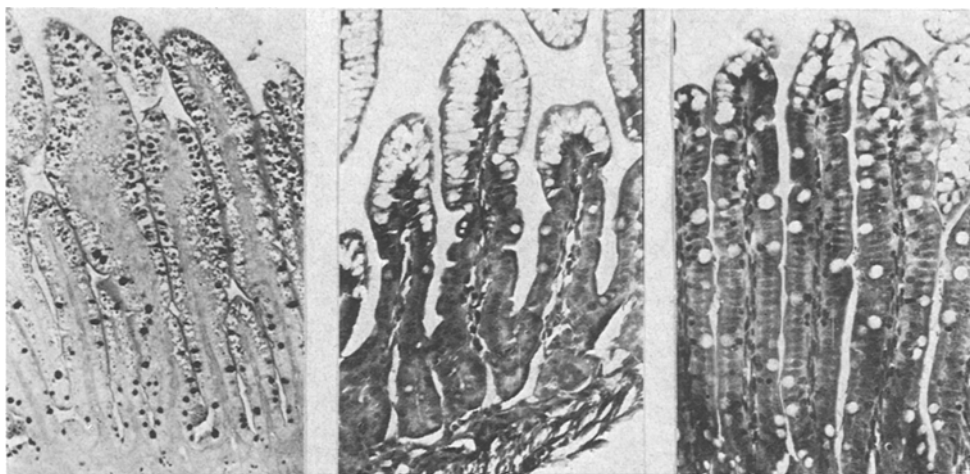


Fig. 2. Changes of the ileum of the suckling rat in relation to age. (a) Prior to the 18th day the intestinal villi are covered almost over their entire lengths by cells containing supranuclear vacuoles. The vacuoles often contain inclusion bodies. PAS reaction. (b) and (c) On the 19th and 20th days, cells with supranuclear vacuoles are seen exclusively at the tips of the villi and no inclusion bodies are present in the vacuoles. Haematoxylin-eosin stain.

tended to decrease, the activities of invertase, amylase and lipase to increase. The proteolytic activity rose again after an initial fall.

Our earlier studies¹² have shown that the small intestinal epithelium of the suckling dwarf goat was replaced by adult-type epithelium by the 72nd h and the adult-type cells were no longer able to absorb colostral proteins. The direction of differentiation of epithelial cells was found to have changed also in the rat's ileum. Cells containing invertase appeared first at the base of the villi¹³ and those containing supranuclear vacuoles were seen for the last time at the tips of the villi (Figure 2). The exchange of the ileal epithelium from suckling to adult type took place between the 18th and 21st days of life. This point of time fairly coincided with the cessation of antibody absorption on the 19th and 20th days¹. Simultaneously, the adhesion strength of intestinal epithelial cells increased and the hydrolytic enzyme activities had distinctly altered (Figure 1).

The yellowish-brown colour of the ileum appears to be due primarily to the inclusion bodies in the supranuclear vacuoles⁶. The disappearance of the yellowish-brown colour and of the inclusion bodies preceeds that of the vacuolized cells by 1 or 2 days (Table). The presence of plant rests in histological sections appears to indicate that the disappearance of inclusion bodies is related to the gradual superseding of suckling by intake of solid food.

In the distal part of the ileum, Peyer's patches well visible to the naked eye were found first on the 19th day. Accordingly, their appearance coincides with the beginning of changes in the serum immune globulin levels^{2,3}.

The above observations imply that in the rat's ileum multiple changes are taking place between the 18th and

21st day of life. The question arises whether or not the changes are limited to the ileum. Moog^{14,15} described enzymic and morphological changes in the proximal part of the small intestine of 16–18-day-old mice, which coincides with the cessation of antibody absorption in this species. The hydrolases studied by us showed changes also in the proximal part of the small intestine (Figure 1). Some changes perhaps extend to the entire organism.

We believe that these changes represent an important step in ontogenesis and their physiological significance is the preparation for weaning. There is no indication that in non-rodents the preparation for weaning actually manifests itself by such abrupt and pronounced changes as in rats.

Zusammenfassung. Die Zusammenhänge zwischen den histologischen Veränderungen und dem Wechsel des Enzymmusters im Darm der Ratte während des Überganges von Milch- zur Festnahrung werden beschrieben.

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The Control of Acoustic Input in the Medial Geniculate body and Inferior Colliculus by Auditory Cortex

The importance of sensory input control in the perceptive evaluation of information is known. In fact, a great number of experimental data suggest that the information coming from many afferent systems is controlled by centrifugal nervous pathways, and that centrifugal control may be a general principle of action of the central

nervous system¹. Within the acoustic system, together with the afferent pathway, anatomical data suggest a

¹ R. B. LIVINGSTON, in *Handbook of Physiology* (Eds. J. FIELD, H. W. MAGOUN, V. E. HALL; Am. Physiol. Soc., Washington, 1959), vol. 1, p. 741.