

Epithelial Cell Migration in the Alimentary Mucosa of the Suckling Pig (35533)

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The small intestinal villus epithelium (SIVE) is replaced approximately every 48 to 72 hr in adult cats (1), rats (2, 3), and mice (4, 5). However, the SIVE of newborn rats and mice is replaced more slowly than in adults (2-5). The replacement times of epithelia in small intestine, cecum, colon, esophagus, and esophageal region of stomach of the suckling pig are reported here.

Methods. Each of 40 healthy suckling pigs was given an intraperitoneal injection of 0.7 μ Ci of tritiated thymidine/g of body weight (sp act 2.0 Ci/mmole) in the following manner. Twenty-five pigs received thymidine between 6 and 14 hr after birth (day-old pigs) and 15 pigs received thymidine 21 days after birth (3-week-old pigs). In each age group, at least 2 pigs, each from a different litter, were killed 1 hr after thymidine injection and at 24-hr intervals thereafter. This was continued for 5 days in the 3-week-old age group and for 11 days in the day-old group. Sections from mid-esophagus, esophageal region of the stomach, and the antimesenteric border at various sites in the intestine (Table I) were pinned flat on a card and placed in Bouin's fixative. Tissues were embedded in paraffin and sections 4 μ thick were cut. Radioautograms were prepared by dipping sections in NTB₃ emulsion (Eastman Kodak

Co., Rochester, N.Y.) and exposing them at -45° for 1 month. The radioautograms were then developed with Kodak D-19 developer and stained through the emulsion with hematoxylin and eosin. The position of the leading cohort of labeled epithelial cells in each section was recorded and from this the replacement time estimated. Replacement time was the time required for labeled epithelial cells to reach the villus tip or the luminal surface of the tissue. The lengths of 5 well-oriented crypts and villi in the jejunum (site 1, Table I) were measured in 8 pigs from each age group.

Results. The time for complete replacement of SIVE was approximately 3 times longer in day-old than in 3-week-old pigs (Table I). At 2 days postinjection, labeled epithelial cells had migrated to the base of the villi in the day-old group and to or near the villus tip in the 3-week-old group (Figs. 1 and 2). There were variations in replacement time between pigs in the same age group (Table I) and also between littermates. Villi at site 1 were $1029 \pm 211 \mu$ long (mean \pm standard deviation) and crypts $110 \pm 25 \mu$ deep in day-old pigs, compared to 494 ± 186 and $166 \pm 38 \mu$ respectively in 3-week-old pigs. The villus length/crypt depth ratios (V/C ratio) were

TABLE I. Replacement Time for Epithelia in Alimentary Mucosa of Suckling Pigs [range (days)].

Age group	Esoph- agus	Stomach (esophageal)	Duo- denum	Jejunum-ileum*				Cecum	Colon
				1	2	3	4		
1 day old	4-5	4-5	9-10	9-10	9-10	7-10	7-10	4-5	4-5
1 week old	4-6	4-6	3-4	3-4	2-4	2-4	2-4	2-3	2-3

* Sites 1-4 were distributed at equal distances throughout the jejunum-ileum, site 1 being cranial jejunum; and site 4, caudal ileum.

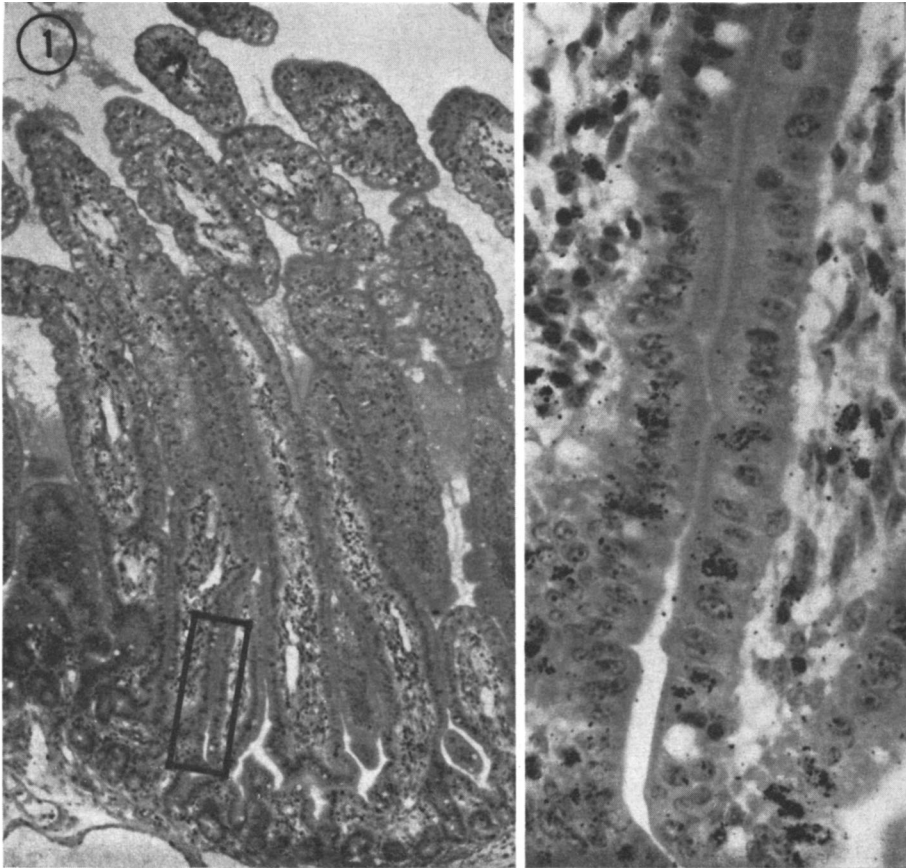


FIG. 1. (left) Jejunum of a 2-day-old pig 48 hr after injection of tritiated thymidine: radioautograph followed by H & E stain. ($\times C.55$). (right) from area in square showing labeled cells at villus base. ($\times C.350$).

9.4/1 in day-old and 3.0/1 in 3-week-old pigs (Figs. 1 and 2).

Epithelia in the large intestine were also replaced more slowly in day-old than in 3-week-old pigs. However, replacement times for the squamous epithelia in esophagus and stomach were similar for both age groups.

Discussion. The approximately 3-fold decrease in replacement time for SIVE, in 3-week-old as compared to day-old pigs, can apparently be explained by the shorter villi, deeper crypts, and the resultant 3-fold decrease in the V/C ratio, in 3-week-old pigs. In contrast to rats, where adults also have shorter replacement times but longer villi and higher rates of cellular proliferation than suckling (3, 6), it is not necessary to postulate an increased rate of cellular proliferation to explain the decreased replacement time

for SIVE in 3-week-old pigs. The decreased V/C ratio in 3-week-old pigs is assumed to be caused, at least in part, by an increased rate of cell loss resulting from exposure to the intestinal microflora (7).

The SIVE of the newborn pig and calf absorbs colostral proteins intact. This capacity is normally lost (closure) 24–36 hr after birth (8). El-Nageh (9) hypothesized that, in the calf, the first 1 or 2 generations of SIVE cells present after birth can absorb colostral proteins intact, that succeeding generations lack this capacity, and that closure occurs when the first 1 or 2 generations of cells are replaced. However, in the study reported here, 7 to 10 days were required for SIVE replacement in the newborn pig. It is suggested that closure precedes SIVE replacement in pigs.

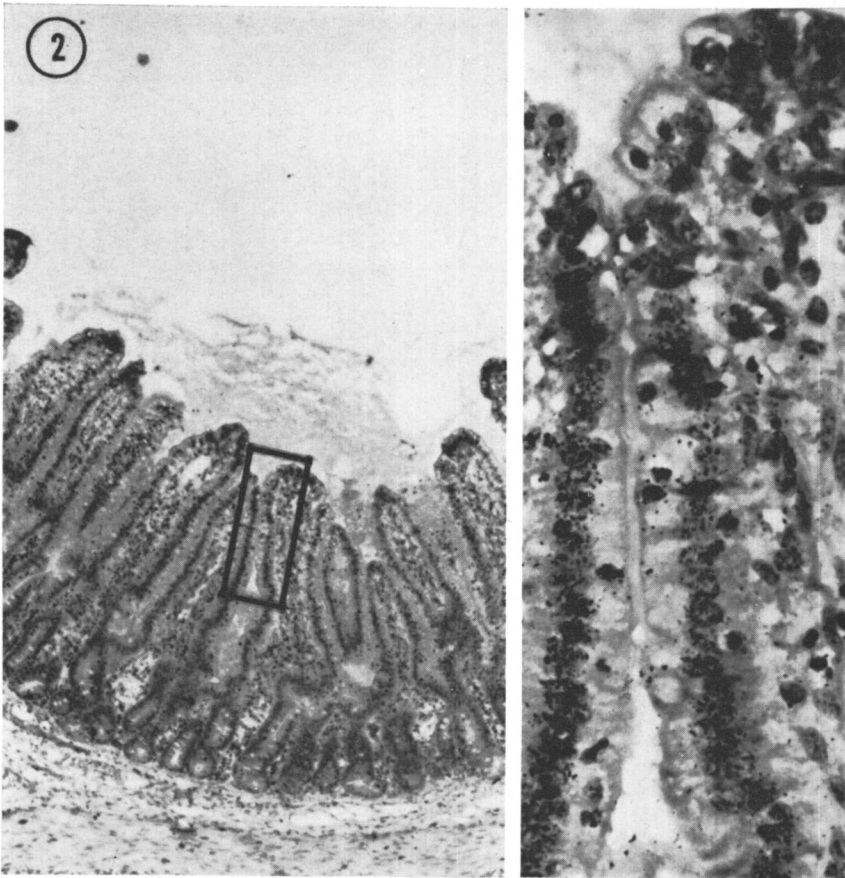


FIG. 2. (left) Jejunum of a 3-week-old pig 48 hr after injection of tritiated thymidine: radioautograph followed by H & E stain. ($\times C.55$). (right) from area in square showing labeled cells near villus tip ($\times C.350$).

As the replacement time for SIVE in day-old pigs is 7–10 days, the rapidly developing villous atrophy which occurs characteristically in transmissible gastroenteritis (TGE) (10) and occasionally in enteric colibacillosis (11) of newborn pigs must be the result of accelerated destruction rather than decreased production of SIVE. If production were to stop completely and immediately after infection in day-old pigs with either disease, without accelerated destruction, the villi should still be 70–80% of their normal length 2 days later. This conclusion with regard to TGE has also been expressed by others, based on observations of a different type from those reported here (10, 12).

The differences in V/C ratios and SIVE replacement times between day-old and 3-week-old pigs may contribute to the

marked decrease in the TGE case fatality rate with age (13).

Summary. The small intestinal villus epithelium in day-old pigs was replaced in 7–10 days, while that in 3-week-old pigs was replaced in 2–4 days. Decreased replacement time with age was associated with an increase in crypt depth and a decrease in villus length. Epithelia in the large intestine were also replaced more slowly in day-old than in 3-week-old pigs. Squamous epithelia in esophagus and stomach were replaced at similar rates in both age groups.

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