
原 著

Effect of an Artificial Intestinal Valve
on Intestinal Adaptation in the Rat

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In the pediatric surgery such cases as long segment aganglionosis, microcolon, necrotizing enterocolitis and etc. require extensive intestinal resection. Improvement of the remaining intestinal absorption is essential in the long term post operative care of such cases⁴⁾⁵⁾⁷⁾⁸⁾.

In the adult surgery, extensive intestinal resection is often necessary in such cases as malignant tumor, thrombosis of the mesenteric artery and so forth.

In the previous paper⁵⁶⁾, we demonstrated significant improvement of intestinal adaptation by an artificial intestinal valve after total colectomy in a patient suffering from ulcerative colitis.

Based on the study of intestinal valve, the effect of the valve on the intestinal adaptation was studied in this investigation.

Experimental short bowel syndrome was produced by ileostomy in rats. Changes of the intestinal mucosa were studied in well adapted rats and poorly adapted ones.

Materials and method

Kyoto university Wistar rats weighing from 150 to 300g were used in this study. Except for the fasting group, rats were fed water and solid diet by Oriental Company ad libitum. Before operation 10 rats were contained as one group in metal cage. After the operation, each rat was put in a metal cage separately. The room was air conditioned at 20°C and 60% humidity.

Studies were done on the following four groups.

Group 1. as control group, 30 rats were used. They were fed water and solid diet ad libitum as mentioned above.

Key words : Intestinal valve, Short bowel syndrome, Scanning electronmicroscopic study of intestinal mucosa, Intestinal mucosa.

引索語 : 人工腸弁, 大量腸切除, 腸粘膜走査電顕像, 腸粘膜

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Group II, as fasting group, 30 rats were used. They were given only water ad libitum. Group III, this group was divided into two subgroups, namely group IIIa and group IIIb. Rats of group IIIa were performed ileostomy and total colectomy. Rats of IIIb received only ileostomy.

Operative procedure of ileostomy and total colectomy :

Under general anesthesia by intra-abdominally administered 5mg/100g body weight of Nembutal®, the abdomen was opened by midline incision. End-ileostomy was performed at 2 cm proximal to the ileocecal junction. Mucous surface was everted and fixed to the fascia by six 6-0 monofilament Nylon interrupted sutures.

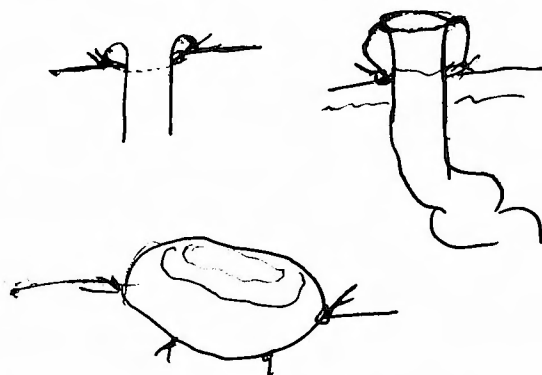


Fig. 1. Operative procedure of end-ileostomy. Mucosal surface is everted and fixed to fascia with 6-0 Nylon sutures.

Skin was closed by using adhesiva (Alon Alfa®). The mesocolon was ligated and separated down to the peritoneal reflex and colon was removed. The rectum was ligated and covered with peritoneum.

The fascioraphy was done with continuous 3-0 Nylon suture and skin was closed with adhesiva (Alon Alfa®).

Group IIIb, In the group IIIb, from 0.5 to 1.0 cm long midline incision was made, while that of the group IIIa was from 3 to 4 cm long. The ileum was exteriorized at 2 cm

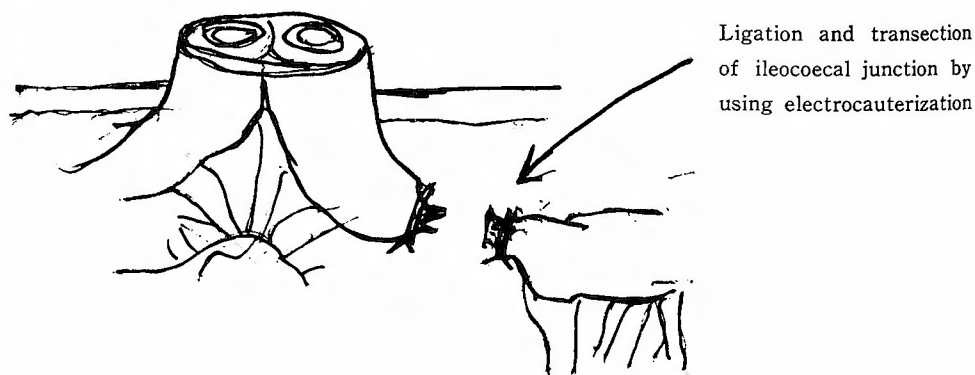


Fig. 2. Double burreled ileostomy and transection of terminal ileum by electrocauterization.

proximal to the ileocecal junction, a double barreled ileostomy was performed. The ileostomy was fixed to the fascia with from 6 to 8 interrupted 6-0 Nylon sutures. The skin was closed with adhesiva. The terminal ileum was double-ligated with 4-0 silk distal to the ileostomy adjacent to the ileocecal valve, and transected by electric-cauterization.

Comparison of the group III a (ileostomy only) and the group III b (ileostomy and total colectomy)

The operating time, blood loss, surgical death, hospital death of the two groups are shown in the Table 1.

Table 1. Comparison of Group III a (ileostomy and total colectomy) and Group III b (ileostomy)

	Operation time	Bleeding	Surgical death
Group III a	20~30min	0.5~1.0ml	12/24
Group III b	5~10min	trace	1/30

The mortality rate of rats with total colectomy was 50 per cent. The body weight curve of the surviving rats with total colectomy, however, was quite similar to the body weight curve of the rats with only ileostomy.

Of the 24 cases with total colectomy (group III a), 12 died of operative hemorrhage.

The rate of operative death of the rats with only ileostomy (III b) was quite low compared with the group III a. Of the 30 cases with ileostomy and colon transection (group III b) one died of post operative infection.

Complicated operative procedures and increased operative hemorrhage may explain the high mortality rate of the group III a.

Since the post operative studies such as histology and nutrition of the cases with total colectomy (group III a) excluding the operative death showed little difference to the group III b, the result of the group III b may well represent the total colectomy with ileostomy (group III a).

Effects of the remnant colon after ligation on the intestinal mucosa and serum biochemistry await for the further study. The overall difference of the two groups in this experiment, however, seems to be trivial enough to interpret the group III a as the same as group III b.

In both group III a and III b, ileostomy was made at as closest portion to the thoracic cage as possible in order to prevent contamination, microbial infection and loosening of sutures by licking.

Group IV : In addition to the ileostomy as in the group III b, intestinal valve was formed.

Operative procedure of the intestinal valve ; under the same anesthesia, the abdomen was opened by the midline incision. The terminal ileum was double ligated and transected by electric cauterization. The oral ileal stump was exteriorized as an end-ileostomy. Five centimeter proximal to the ileostomy, seromuscular layer was stripped circularly over the

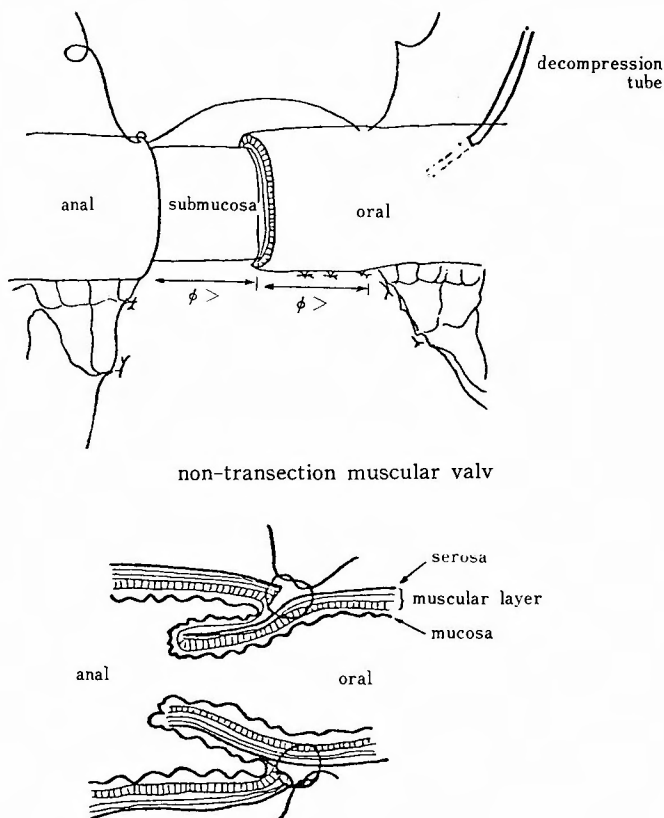


Fig. 3. Operative procedure of the artificial intestinal valve (muscular type).

length of 3 mm and muscular valve was performed by intussuscepting the proximal intestine into the distal lumen and fixing with 6 interrupted sutures. The intussuscepted length of the intestine was same as the diameter of the canal.

In the previous study dogs were used and the intussuscepted length varied from one to two times the diameter of the intestinal lumen. In the rats, however, the length of the lumen was the maximum length to be intussuscepted, since the length over the diameter caused intestinal stenosis.

Laboratory examinations of the following items were studied :

- (1) Body weight curve.
- (2) Hematology.
- (3) Serum biochemistry.
- (4) Macroscopic observation of the intestinal mucosa.
- (5) Scanning and transmission electron microscopic study as well as optical microscopic study.

- (1) Body weight curve : Body weight was measured every morning between ten and

eleven o'clock.

(2) Hematology : Blood specimen was obtained by cardiac puncture. Erythrocytes and leucocytes were counted by Thoma's method. Hemoglobin was measured as hematin-HCl.

(3) Serum protein was measured with protein refractory densitometer.

(4) Electrolytes were measured with Hitachi' Model 205-0500 digital flame photometer combined with digital recorder J-301.

(5) Macroscopic study of the intestinal mucosa : Under general anesthesia with intraperitoneally administered Nembutal®, the abdomen was opened and whole length of the intestine from the Treitz' band distal to the peritoneal reflex was excised. The intestine was sharply dissected from the mesenterium as soon as possible without hemostatic procedure. The external diameter of the resected intestine was measured and five mm long specimens were obtained from the jejunum, jejunoileal junction and the terminal ileum.

1, Each segment was longitudinally opened and observed in reference to height, width and length of the villus. Thickness of the intestine was also measured.

2, A portion of each segment was fixed in 10% formaline, and prepared for hematoxylin-eosin stain.

3, Another portion of the each segment was prepared with glutal aldehyde for further study by electron microscopy.

(6) Scanning electron microscopic study of the intestinal mucosa : Under general anesthesia, the abdomen was opened and the intestine was resected and prepared after the same method as described in reference⁴⁷⁾.

The resected specimen was carefully washed by 4°C saline solution jet stream using 20 ml syringe with 21 G needle. The specimen was trimmed to 5×5mm square and fixed in 2% glutar aldehyde for two hours. After the specimen was placed in 0.1 M phosphate buffer (pH 7.2) for 30 minutes, it was fixed again in 4°C osmic acid for two hours. Stepwise dehydration was done for 60 minutes each using 60%, 70%, 80%, 90% and absolute alcohol.

Absolute alcohol was replaced with mixture of absolute alcohol and isoamyl acetate for 30 minutes and then it was replaced with isoamyl acetate for 30 minutes. The specimen was then dried by critical point dryer, Hitachi HCP-1.

The dried specimen was ion coated with gold parazium using Ion Coater (Eiko Engineering Co. IB-3) at under 0.1 torr, 5.5mA for 5 minutes.

Transmission electron microscopy : The specimens were fixed in the same manner as the SEM. After dehydration, specimens were embedded in Epon. Specimens were sliced with Porter Blum MT-2 ultra-microtome and double stained with Pb-citrate and uranyl acetate. TEM Hs-70, Hu12A were used.

Result

1) Body weight curve :

(1) Fasting group. During the first seven days' fasting, body weight decreased by 20% of the original. After the 14th day, rate of body weight-loss slowed down. Some of the rats survived for 28 days by only water.

Ten rats (33%) of the fasting group died between the 10th and the 14th day. The other rats were sacrificed accordingly for the studies.

Overall body weight loss curve during the first two weeks was linear.

(2) Group with ileostomy : Body weight loss during the first five post-operative days was similar to the fasting group.

Rats started to eat solid diet at between the second and the fifth post operative days. Although they started to eat, diarrhea continued and body weight decreased.

Ten of the rats (33%) of this group also died by the 14th post operative day. Twelve (40%) of this group, however, survived over 21 days and body weight loss stopped after the 14th day. Nine rats (30%) survived over 56 days and maintained constant body weight (60% of the original body weight).

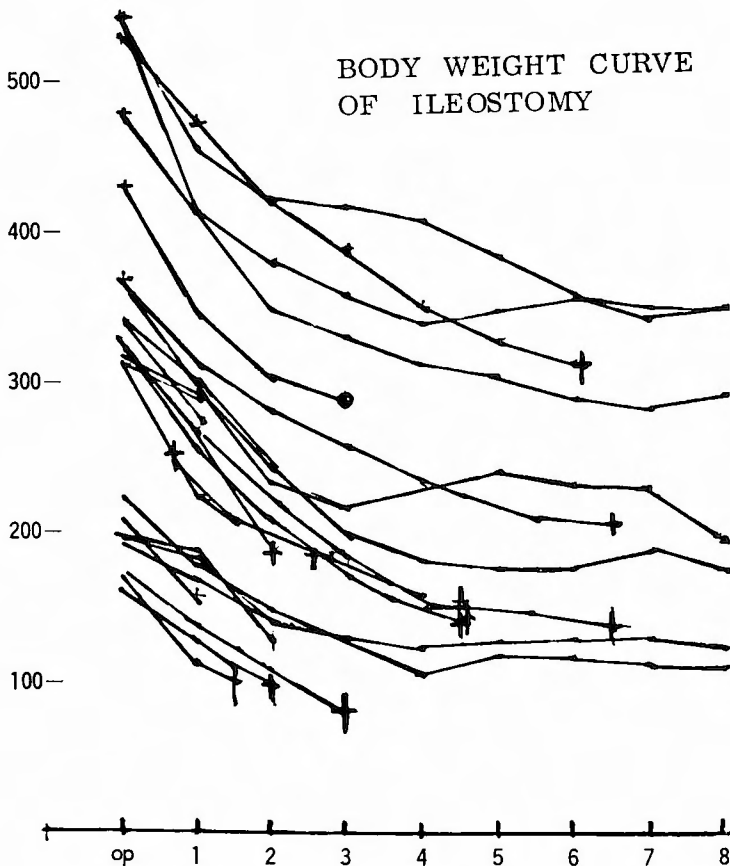


Fig. 4. In the First 2 weeks body weight loss rate is rapid.
Non of this group shows body weight recovering tendency

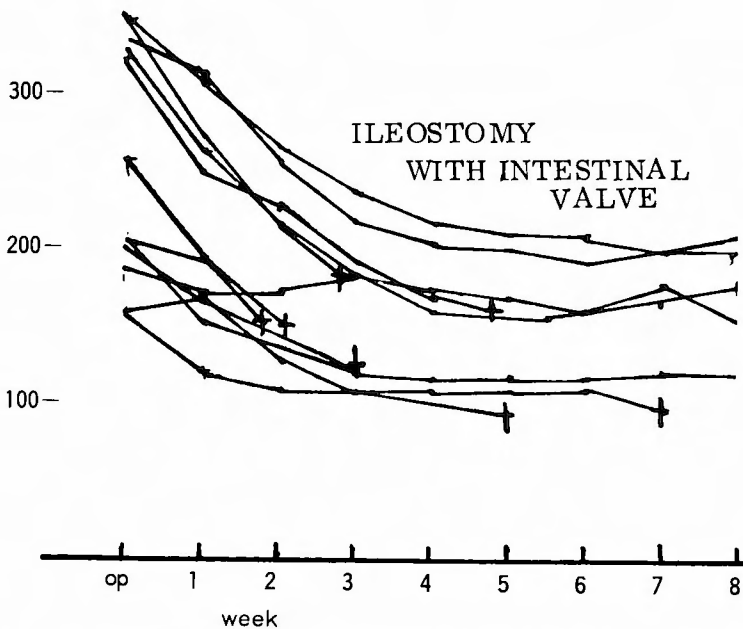


Fig. 5. First 2 weeks, body weight loss rate is almost same as "ileostomy only". After 5 weeks, some rats show "increase" of body weight.

The maximum survival period was 220 days, when it was sacrificed.

Body weight loss of the rats with ileostomy had little relation to the amount of food intake. Increased food intake resulted in only increased feces but body weight loss was not affected by the amount of food to be ingested.

Body weight curve, however, seemed to be affected by the improvement of diarrhea.

(3) Ileostomy and intestinal valve : During the first seven post operative days, body weight loss was somewhat moderate compared with the two former groups. Rats of this group also started to eat between the second and the fifth post operative days. Body weight loss rapidly decreased during from the 14th to 21st days. Fourteen rats of this group showed body weight increase during from the 28th to the 40th post operative days.

Eleven out of the 14 rats survived for 250 days, when they were sacrificed.

Body weight loss of this group decreased almost simultaneously with the start of food intake. Food intake started during the second and the fifth post operative days just as the rats with ileostomy.

All of the rats with ileostomy only exhibited diarrhea. Some of the rats with ileostomy and intestinal valve, on the other hand, started to excrete solid feces mixed in the diarrhea.

Discussion on the body weight curve.

After operation, rats had from two to five days' fasting period regardless of the mode of operation. Retardation of food ingestion affected body weight loss, and operative damage to the rat seemed to affect the retardation of food ingestion. After this fasting period, food

intake and excretion of feces seemed to affect increase or decrease of body weight loss and even body weight gain.

The effect of each mode of operation is reflected in the course of the body weight curve.

Waterly diarrhea lasted longer in the rats with ileostomy only than the rats with intestinal valve and no body weight gain was observed even though food intake of the two groups showed little difference.

2) Hematological findings. Regardless of body weight curves, all of surviving rats uniformly showed decreased erythrocytes, leucocytes and hemoglobin.

3) Serum protein level was found to be slightly decreased in all post operative animals.

4) Change of electrolytes. Among the surviving rats, no difference of Na, K and Cl was noticed. The rats with ileostomy showed low Na level during 20 post-operative days body weight loss period.

Four weeks after the operation, all of the rats showed lowered Na, K and Cl, and recovered to constant values of from 90 to 96% of original level by the 12th week.

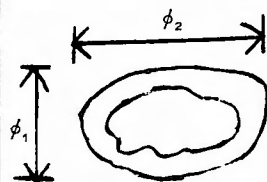
Rats of long term survival showed (1) hypochromic anemia, (2) hypoproteinemia at about 80-90% of normal value and (3) moderate lowering of Na, K and Cl levels.

5) Macroscopic study.

(1) Measurement of the intestinal diameter. No more than 0.1 mm of difference was noticed between the measurement of the intestine before and after fixation with formaline or glutaldehyde. The Table 2 shows measurement of hematoxyline eosin specimen.

Table 2.

	Jejunum		Jejunioileal junction		Ileum	
	ϕ_1	ϕ_2	ϕ_1	ϕ_2	ϕ_1	ϕ_2
control	2.2 ± 0.1	3.4 ± 0	2.5 ± 0.1	4.1 ± 0	2.5 ± 0.1	3.5 ± 0.1
4 days fasting	2.1 ± 0.1	3.3 ± 0.3	2.5 ± 0.1	4.1 ± 0.1	2.5 ± 0.1	3.5 ± 0.1
ileostomy	2.3 ± 0.1	3.4 ± 0.1	2.5 ± 0.1	4.0 ± 0.1	2.5 ± 0.1	3.5 ± 0.1
ileostomy with intestinal valve	2.8 ± 0.2	3.9 ± 0.1	2.5 ± 0.1	4.1 ± 0.1	2.5 ± 0.1	3.8 ± 0.1



Calibre measured in hematoxylin eosin stained gut.

Diameter of control group showed minimum value of jejunum, and maximum value at jejunioileal junction at the middle of small intestine and terminal ileum in between the former two.

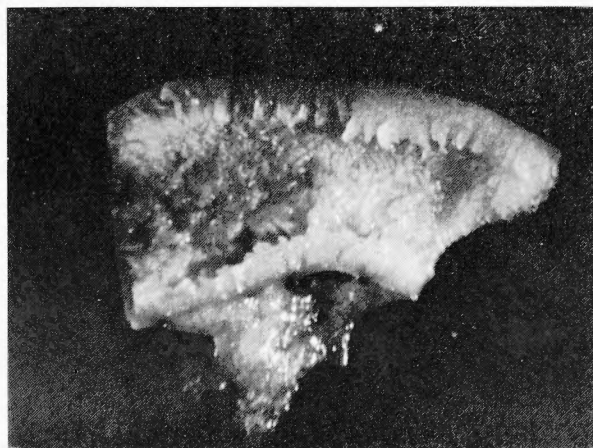
After 4 days fasting, no change of intestinal diameter was observed.

The jejunum of the rats with ileostomy was slightly enlarged but no calibre change

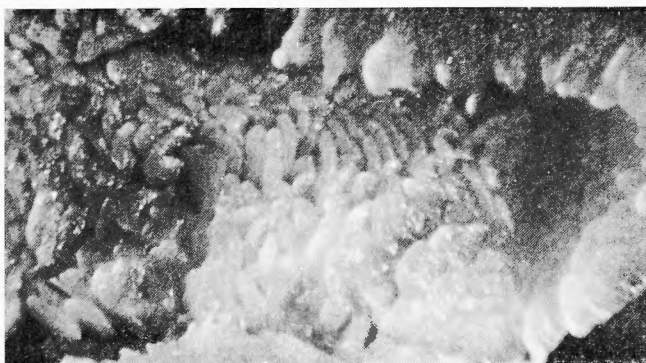
of jejunoileal junction and ileum was noticed.

The rats with ileostomy and intestinal valve showed marked dilation of jejunum, and long axis diameter of the ileum was increased by 0.3 mm. The jejunoileal Junction, however, showed no change of diameter.

(2) Mucosal surface. In all groups of control, starvation, ileostomy and intestinal valve, height of villi was maximum at the jejunum and gradually decreased down to the terminal ileum. The height of villi was presumed from the shadows of folds in scanning electron micrography. No specific change was observed in each group.



(a)



(b)

Fig. 6. Macroscopic appearance of ileal mucosal surface. Control rat. Villi are observed as "leaflet" type.

6) Scanning electron microscopic study of the mucosal surface.

(1) Control group : From the jejunum to the upper ileum, intestinal surface was covered with rod shaped or leaflet shaped villi.

By high power magnification of 2500 times or more, highly dense growth of microvilli on the luminal surface of mucosal epithelium was observed. The diameter of microvilli was about 0.1μ .

Close observation of the dense growth of microvilli revealed focal bushy growth of long microvilli. High power magnification showed significantly elongated focal growth of microvilli. This focal growth was composed on each mucosal epithelial cell unit. In other words, epithelial cells with elongated microvilli existed scattered on the villi.

Microvilli of a unit epithelial cell were of a same height.

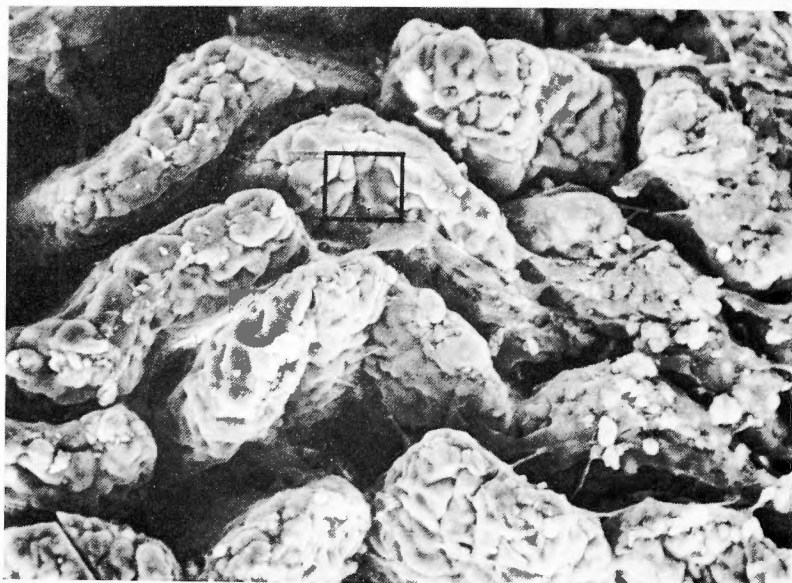


Fig. 7. (a) $\times 250$

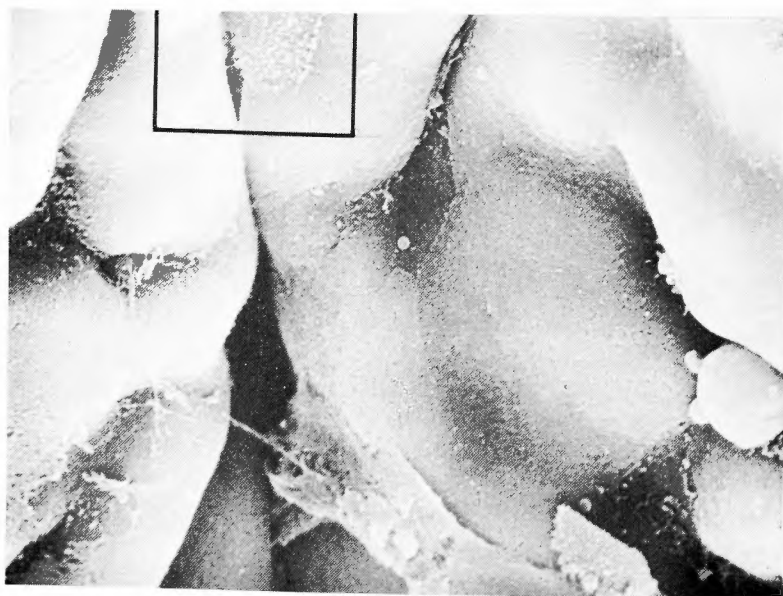


Fig. 7. (b) $\times 2,500$ Focal growth of elongated microvilli.

Fig. 7. Ileal villi of control rat.

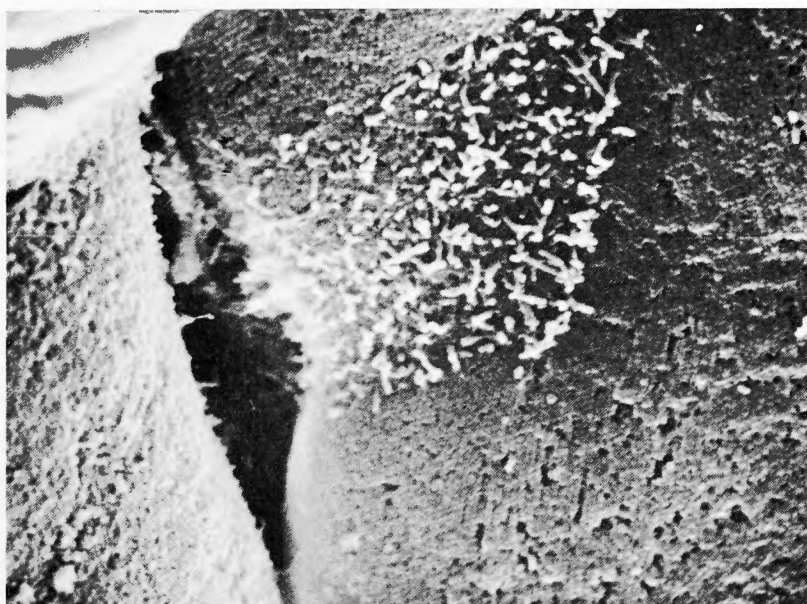


Fig. 7. (c) $\times 10,000$ Focal growth of elongated microvilli.

Fig. 7. Ileal villi of control rat.



Fig. 8. (a) $\times 500$ fasting

Fig. 8. Ileal villi of fasting rat. Moderately elongated microvilli cover the apical surface of the each villi homogenously.

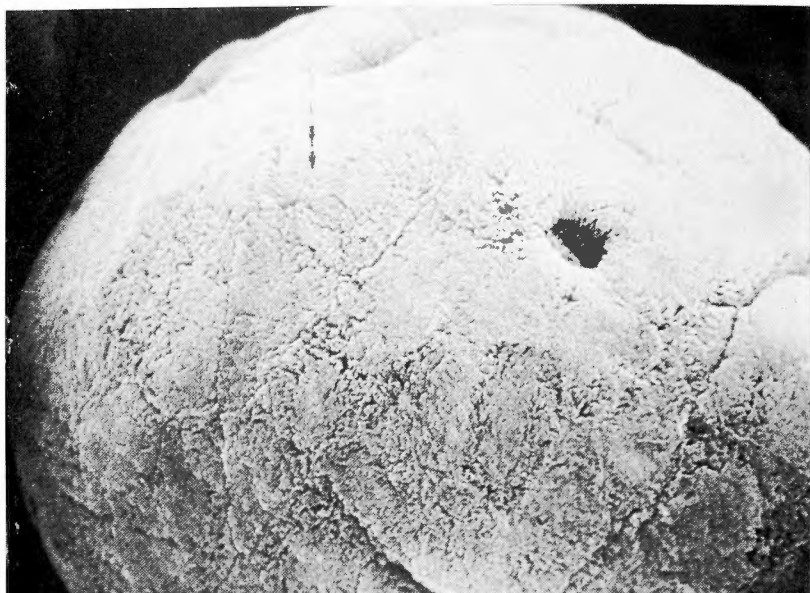


Fig. 8. (b) $\times 2,500$

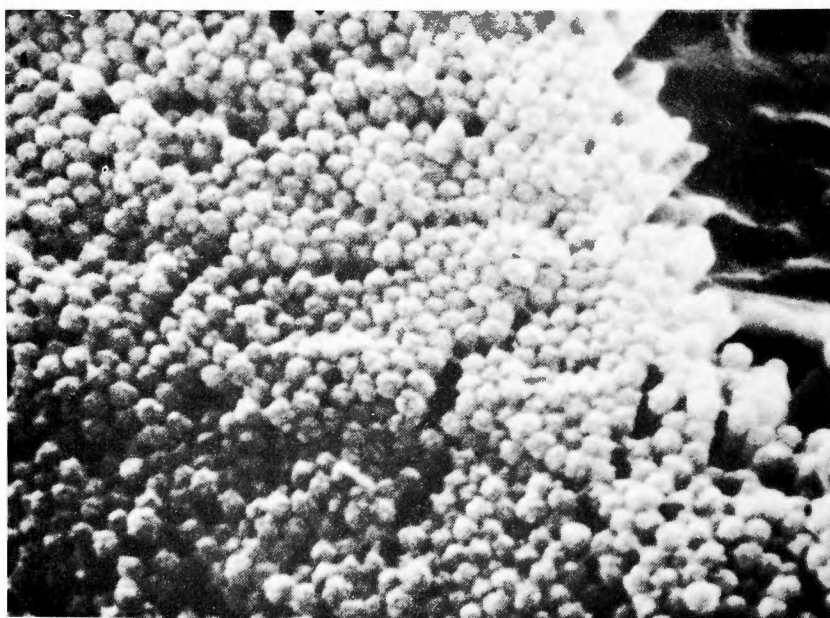


Fig. 8. (c) $\times 30,000$

Fig. 8. Ileal villi of fasting rat. Moderately elongated microvilli cover the apical surface of the each villi homogeneously.

The transmission electron microscope showed the length of the microvilli were about $1.0\ \mu$ and covered with glicocarix. The root of microvilli was continuous to the terminal web.

The mucosal surface of the fasting group : The villi were slightly thickend in width. High power magnification SEM showed elongated growth of microvilli, which resembled velvet. In the fasting group, scattered focal growth of elongated microvilli was not observed.

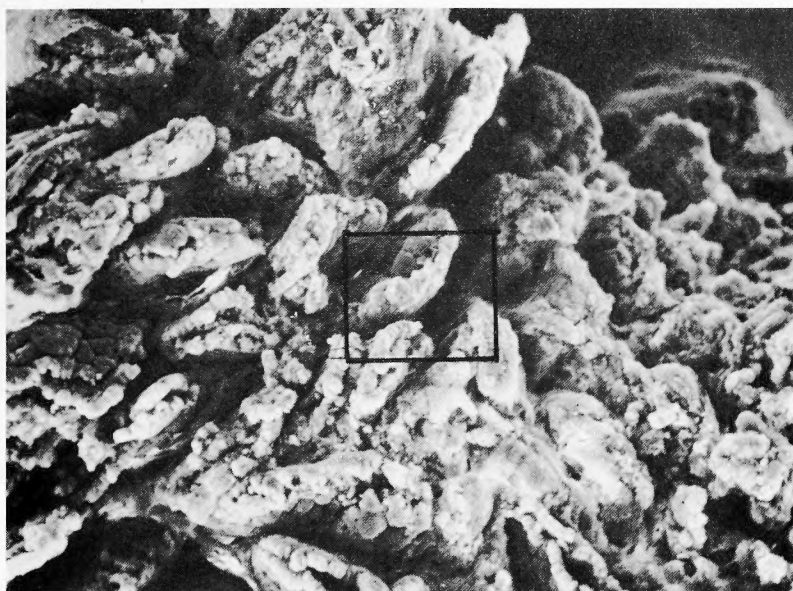


Fig. 9. (a)

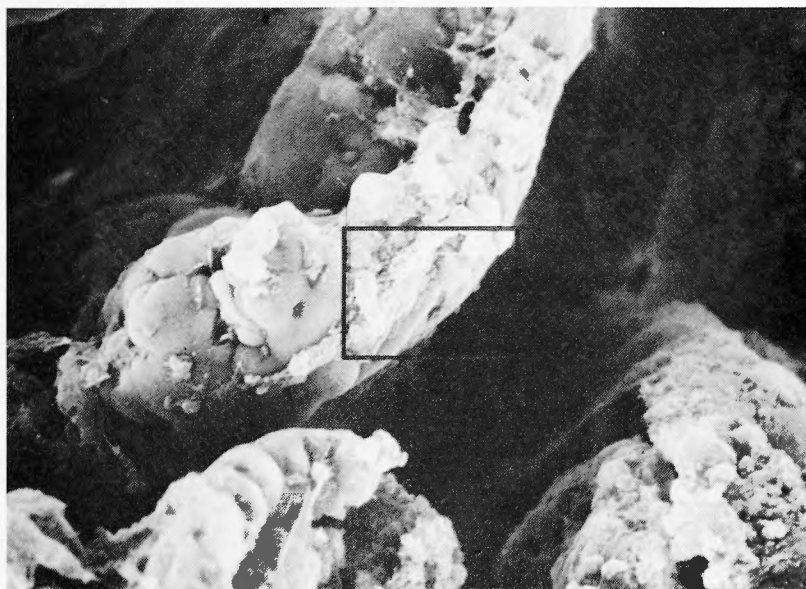


Fig. 9. (b)

Fig. 9. Jejunal villi of the long survival rat with ileostomy and the intestinal valve.

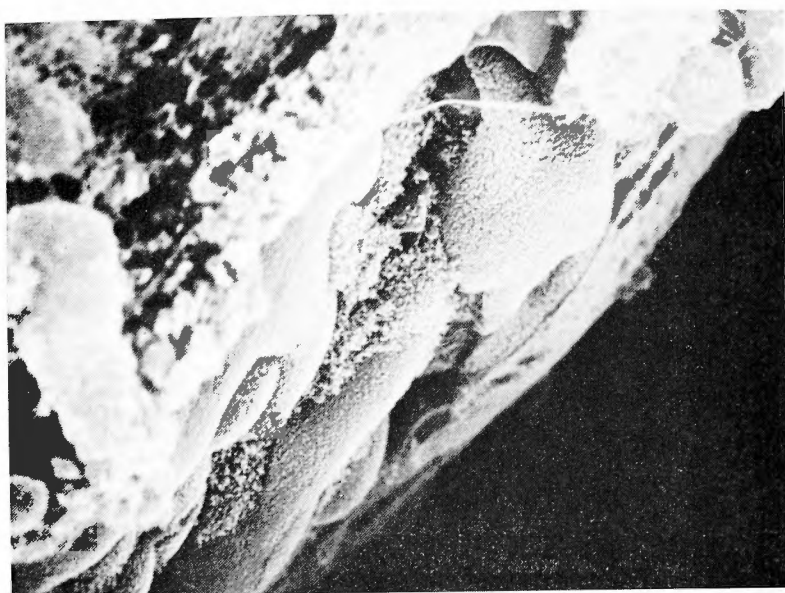
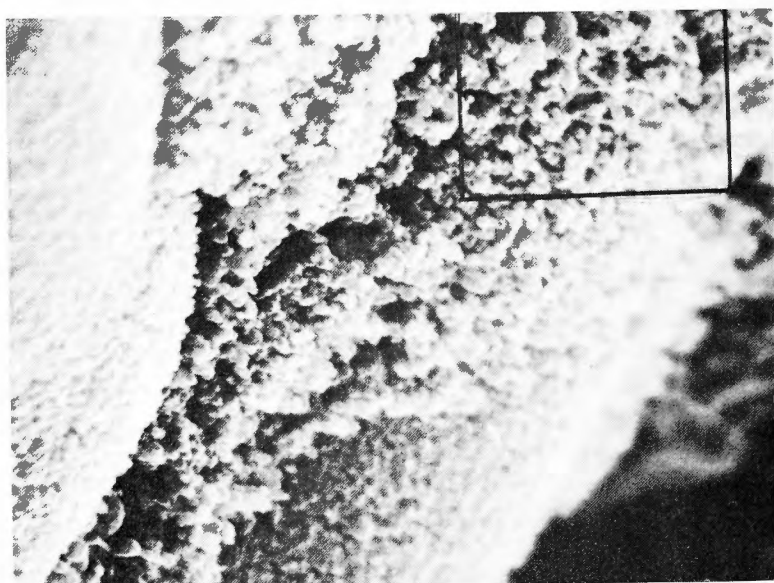
Fig. 9. (c) $\times 2,500$ Fig. 9. (d) $\times 10,000$

Fig. 9. Jejunal villi of the long survival rat with ileostomy and the intestinal valve.

Ileostomy group : In this group, high power S E M showed scattered focal growth of elongated microvilli just as in control. These focal growths gave irregular impression of surface. This change seemed to start from the top of villi to root of the villi and most prominent in the top region.

Ileostomy with intestinal valve group :



Fig. 9. (e) $\times 30,000$

Fig. 9. Jejunal villi of the long survival rat with ileostomy and the intestinal valve.



Fig. 10. (a) $\times 2,000$

Fig. 10. Surface of the jejuno-ileal villus of the long survival rat with ileostomy and the intestinal valve.

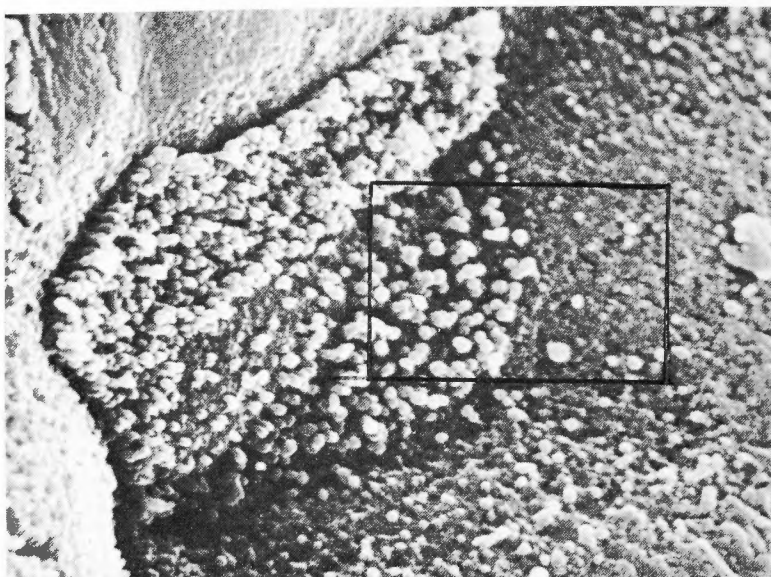


Fig. 10. (b) $\times 10,000$

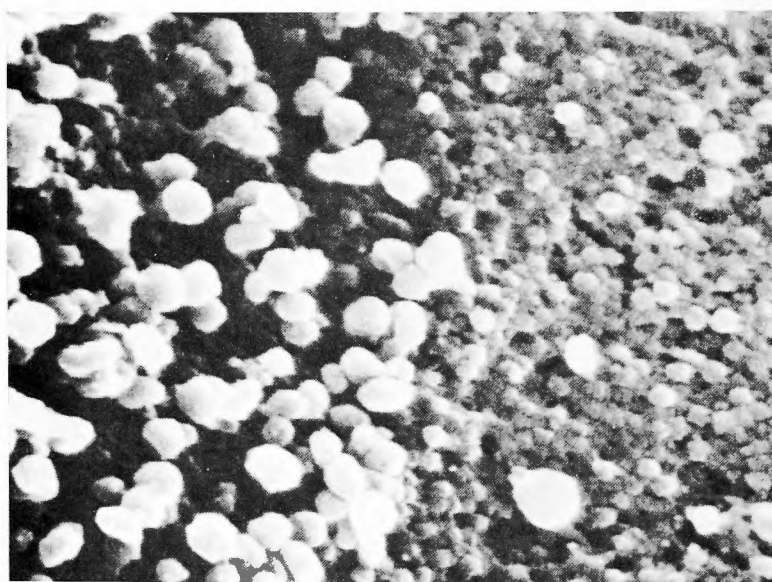


Fig. 10. (c) $\times 30,000$

Fig. 10. Surface of the jejuno-ileal villus of the long survival rat with ileostomy and the intestinal valve.

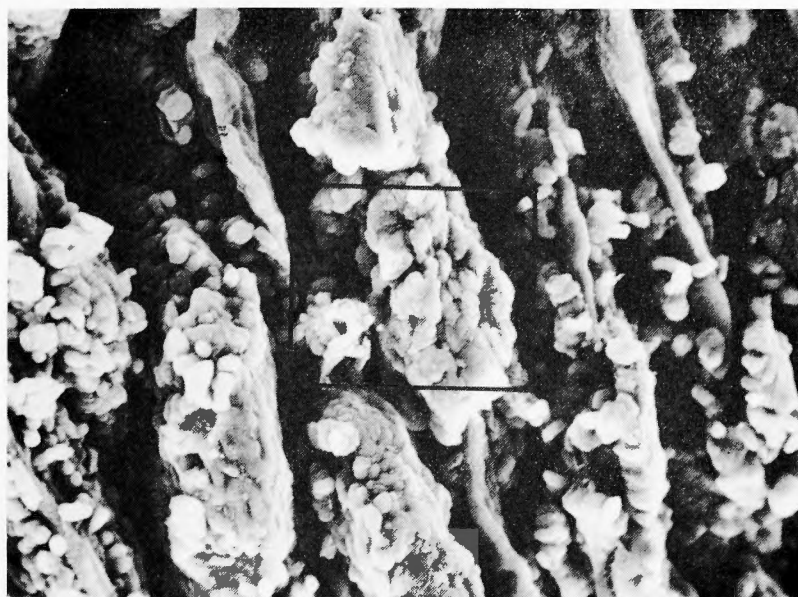


Fig. 11. (a) $\times 300$

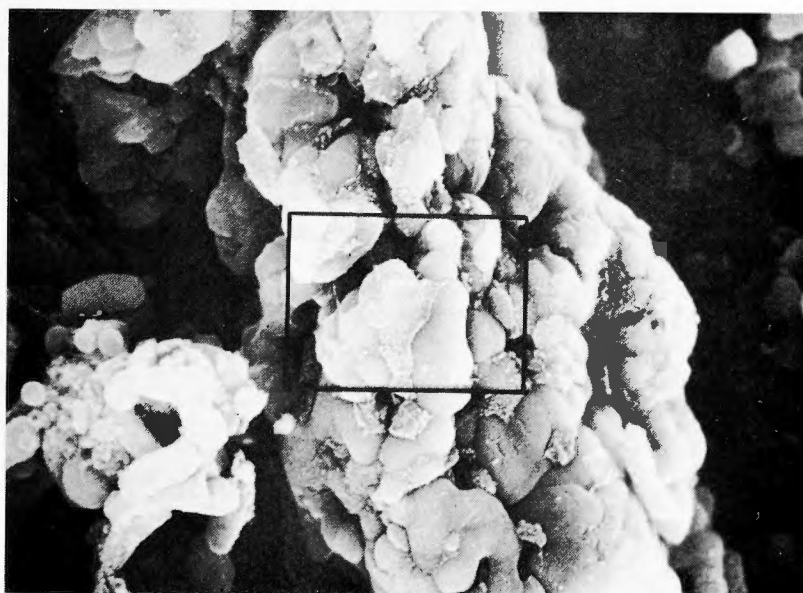


Fig. 11. (b) $\times 1,000$

Fig. 11. Villi of the terminal ileum of a long survival rat with ileostomy and the intestinal valve.

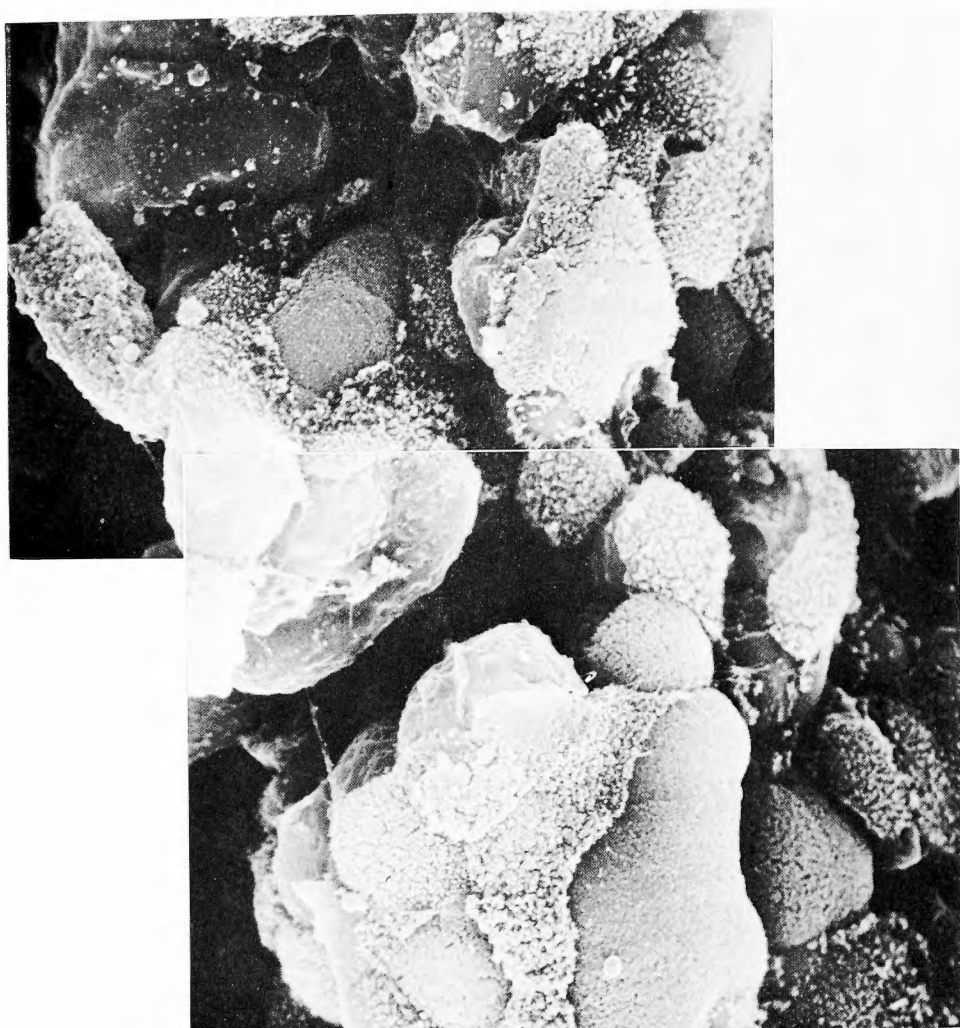


Fig. 11. (c) Apical part of a villus of the terminal ileal mucosa. Marked proliferation of the epithelial cells with elongated microvilli. distribution of the cell is not homogeneous unlike "fasting rat" but scatters part to part of the villous surface. $\times 3,000$

Low magnification S E M showed leaflet or rod shaped villi with deeper inter-leaflet spaces. Surface of villi was covered with 2 to 5μ high protrusions. These protrusions were most prominent along the top of the villi and decreased in number down to root. Much more protrusions were noticed in this group than in the group with only ileostomy. Microvilli were extremely elongated than other groups. The extent of elongation of the microvilli differed from cell to cell. The extent of elongation may be classified into three (1) very long. (2) medium and (3) moderate.

Elongated microvilli were, unlike the control group, often bent due to excessive elongation.

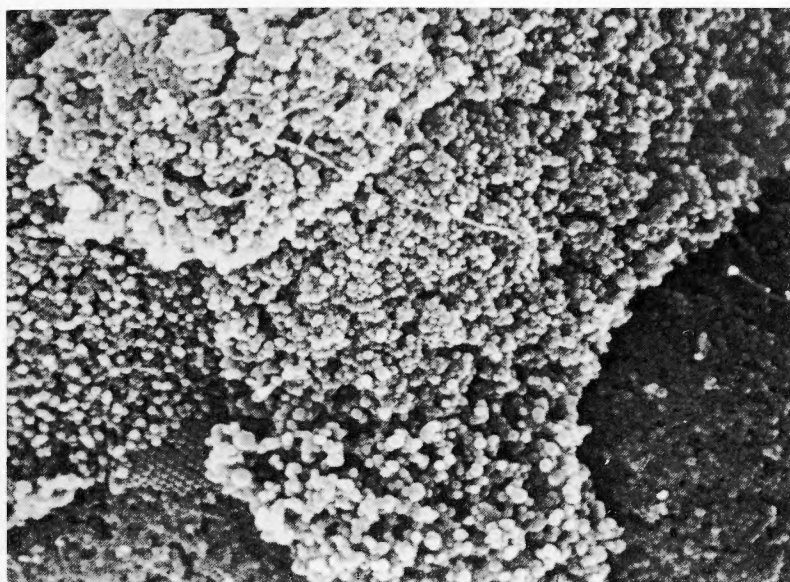


Fig. 11 (d) $\times 10,000$

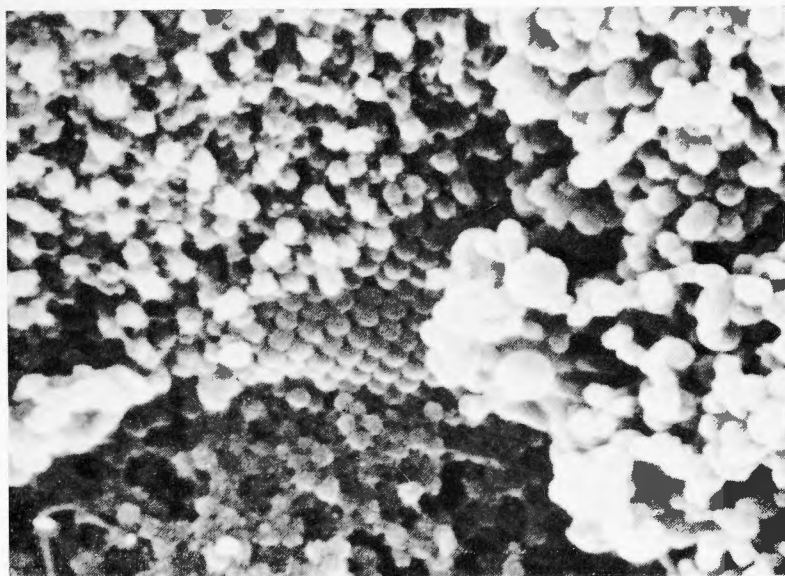
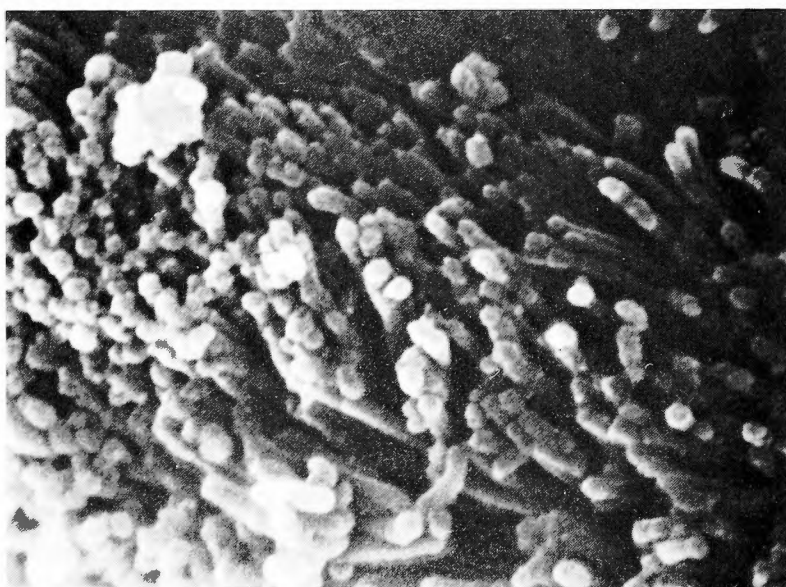


Fig. 11. (e) $\times 30,000$

Fig. 11. Villi of the terminal ileum of a long survival rat with ileostomy and the intestinal valve.



(a) microvilli of control $\times 30,000$

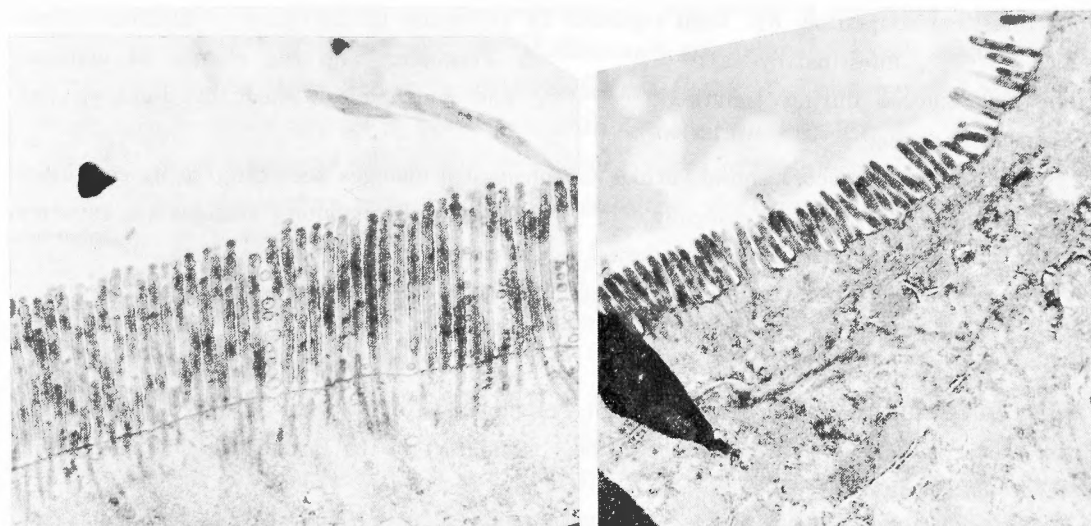


(b) elongated microvilli $\times 30,000$

Fig. 12.

These epithelial cells with elongated microvilli were observed in the cases with ileostomy and intestinal valve at 11th post operative day. At 21st post operative day, the appearance of such cells reached to the maximum.

It was quite interesting that this coincided with the period of decrease of body weight loss and beginning of body weight gain.



elongated microvilli

normal microvilli

Fig. 13. Transmission electron microscopy

Discussion

1. Effects of intestinal valve :

In our previous paper⁵⁶⁾⁶⁵⁾ we reported two effects of the artificial valve by telescoping anastomosis revealed by manometric study and clinical observations.

The first effect is anti-reflux effect. In the experiment on dogs, the intestinal valve functions almost the same as the ileocecal valve for anti-reflux purpose.

In the experiment, the artificial valve opened at less than 20 cm H₂O in the peristaltic direction. Passage in the anti-peristaltic direction, however, started at over 40 cm H₂O. No caliber change of the intestine proximal to the valve was observed.

This valve maintained the same function after two years and no stenosis due to cicatric constriction was observed.

The second effect was "slow down" of the intestinal transportation.

Intestinal stenosis may improve intestinal absorption. For this purpose, delicate control of the extent of stenosis is essential. Excessive stenosis easily causes ileus.

As a solution of this maneuver, function of the valve is quite satisfactory.

It was reported that significant difference of body weight gain is seen between the puppy with ileocecal valve preserved and not preserved after massive resection of the bowel⁵³⁾.

In our investigation reported here, the body weight study revealed obvious favorable effect of the intestinal valve on rats with ileostomy. It may be concluded that the intestinal valve accelerates intestinal adaptation in short bowel syndrome.

2. The change of intestinal musosa in the intestinal adaptation.

Intestinal adaptation has been reported in reference to starvation¹⁾, intestinal resection⁸⁾¹³⁾²⁰⁾²²⁾²⁸⁾, intestinal by-pass¹⁰⁾²²⁾²⁴⁾³³⁾³⁴⁾⁴⁸⁾⁶⁰⁾. Pregnancy and the change of maternal intestinal mucosa during lactation¹⁴⁾¹⁸⁾²⁴⁾²⁵⁾²⁶⁾, and biochemical effect of digestive and absorption changes¹³⁾²⁰⁾²¹⁾³⁰⁾³³⁾⁵¹⁾⁵²⁾⁵⁷⁾⁶⁴⁾.

The intestinal mucosa shows various morphological changes according to its conditions experimentally³⁾⁸⁾³³⁾³⁴⁾⁴³⁾ and clinically³²⁾⁴⁴⁾⁴⁵⁾. Three major contributory changes are expected in the intestinal adaptation to short bowel syndromes³⁰⁾.

- (1) Increase of intestinal caliber including thickening of the intestinal wall.
- (2) Enlargement of villi.
- (3) Elongation of microvilli.

These three altogether increase the surface of the intestinal lumen. These three changes are, in fact, observed and confirmed to be contributory to the improvement of the general nutritional condition.

MANGE et al⁴⁶⁾ confirmed close relationship between the height of villi and glucose absorption. It is quite important that morphological change has close relationship to the absorption of amino acid and sugar¹³⁾⁴⁶⁾⁵¹⁾⁵⁸⁾⁵⁹⁾⁶⁰⁾.

The relationships between intestinal mucosal surface and the absorption of various nutrients under such conditions as starvation, lactation and intestinal resection have been revealed¹⁾²⁾³⁾⁷⁾⁸⁾¹¹⁾¹²⁾¹⁴⁾¹⁵⁾¹⁶⁾¹⁷⁾¹⁸⁾¹⁹⁾²⁰⁾²²⁾²⁵⁾²⁶⁾³⁴⁾⁴⁴⁾⁵⁵⁾.

(1) In order to obtain increase of intestinal caliber, chronic dilatation of intestinal lumen produced and maintained by moderate stenosis is considered. The stenosis causes stagnation of the intestinal content and yet maintain sufficient circulation of the intestinal wall, just like the chronic intestinal stenosis with moderate proximal dilatation which is seen clinically.

The stenosis, however, must be kept moderate and must not be a complete obstruction.

The adaptability of each individual is better when the stenosis is produced gradually. Rapidly produced stenosis tends to become more obstructive than slowly produced stenosis of the same caliber. Rapidly produced intestinal obstruction not only retard intestinal adaptation but also cause intestinal dysfunction.

Introduction of valve mechanism instead of simple stenosis enables easier control of the desirable intraluminal pressure.

The valve opens of itself at or above a certain pressure, and enables smooth passage of the intestinal contents, hence the caliber of the proximal intestine is controlled as designated.

(2) Increased mucosal surface by thickening of the villi and its effect on absorption have been reported by many authors¹⁾³⁾⁸⁾¹⁴⁾¹⁶⁾¹⁹⁾²⁰⁾²⁵⁾³⁹⁾⁴⁴⁾⁵⁵⁾. Since macroscopic and optical microscopic observation of villi readily gave much information, morphological change of villi has been used as an important criteria for the study of intestinal adaptation. In order to use change of villi as criteria for intestinal adaptation, their normal change under various conditions and at various stages of life cycle had to be elucidated.

As R. M. CLARK reviewed¹⁶⁾ as to life cycle of epithelium of intestinal mucosa, they originate from Lieberkühn cells of crypt. Parallel with maturation, the cells migrate to the tip of villi and eventually drop off to intestinal lumen. CLARK et al also reported number of crypt and villi do not change in accordance with age and or starvation.

The volumic change of villi, occurs by thickening and increase of surface area of villi. In other words, the surface area of villi is increased by thickening and elongation of villi by increase of the composing cells.

Life span of the epithelial cells of intestinal mucosa is studied with isotope. Nuclei are labelled with H^3 -Thymidine. The measurement of distribution of labelled nuclei gives information as to their life cycle¹⁶⁾. FREY et al²⁹⁾ considered when labelled cells were distributed 50% at the root of villi and 50% at the tip of villi the life cycle was at the middle of the life span. The method is most reliable at present.

ALTMAN³⁾ et al reports height of villi is maximum at duodenum and gradually lowers along the passage to anus, namely jejunum, ileum and colon and explained the difference as due to the difference of life span of the cells.

Their experimental result of life span of epithelial cells were 41 hours at the duodenum and 17 hours at the terminal ileum.

The life span of the cells at the same portion does not change by intestinal resection, bypass^{33) 34)} or lactation^{25) 26)}.

The change of shape and size of villi, therefore, may be enhanced by change of the speed of mitosis at crypt and speed up of migration of cell from root to the tip of villi.

CREAMER et al¹⁹⁾ consider increased cell division decides the shape and width of the root of villi and prolonged life span of the composing cells affect the height of the villi. They confirmed it with morphological change of the intestinal mucosa of rats under starvation.

It was reported that normally observed rod shaped villi of the terminal ileum became leaflet shaped as villi of the jejunum and further flattened. Parallel with the morphological change, the volume and surface area of each villi gets decreased.

The condition of the mucosa reflects not much of the present disease but more of the symptoms to appear as the result of adaptation.

(3) Change of microvilli. SKELA et al⁵⁵⁾ investigated remnant intestine after massive intestinal resection and found little micromorphological change.

TILSON et al⁵⁹⁾ Studied mucosal epithelial cells of rats after massive intestinal resection and recognized elongation of microvilli in the jejunum and the ileum. The number of the microvilli per unit area, however, changed little, namely $71.8 \pm 0.9/\mu^2$ before operation, and $69.5 \pm 0.9/\mu^2$ after operation. The diameter of microvilli also showed no difference ($0.117 + 0.003\mu$).

As the result of the study, microvilli did not increase in size three dimensionally but only increased in length by 1.5 to 2 times the original length.

The increased surface area by elongation of microvilli is 1.5–2 times the original surface area.

Observation of villi and microvilli varies according to each author and the reason for the difference must be clarified.

For the above mentioned studies, transmission electron microscope was used. Specimens for TEM are several millimeters cubic. The specimen is ultra sectioned for only two dimensional observation. In other words, TEM enables only several millimeter wide linear change of the intestinal mucosa. This method is suitable only in a certain situation when changes of the microvilli is homogenous in extensive part of the intestinal segment.

When the change of microvilli occurs regionally varying from one portion of epithelium to another, study of extremely large number of specimens becomes necessary.

Scanning electron microscopic study is three dimensional at various magnification. The change of microvilli is readily observed even if it happens only in a limited area. In fact, the intestinal mucosa of long surviving rats with ileostomy or ileostomy and intestinal valve in our study exhibited regional change of microvilli which occurred by each epithelial cell unit.

The study revealed the change of villi and change of microvilli lining the villi varied from one epithelium to another.

The length of microvilli roughly differ in the jejunum and the ileum. Furthermore, the microvilli show difference of length by individual epithelial cells which they cover even in the same segment.

Limited size of the specimens of transmission electron microscope often cause to look over such observation.

For the enlargement of the size of villi, passage of intestinal content is essential²²⁾, Increased amount of diet enhances elongation of villi more significantly in the ileum than the jejunum. The phenomena is explained as due to the encouraging factor for microvilli growth by glucagon in the duodenal juice or pancreatine³⁾.

In the jejunum, in addition, the villi are physiologically tall and potential for further growth is small. The ileum therefore may have more potential for adaptational growth because physiological height is relatively low.

The most significant finding in our study was appearance of large number of epithelial cells with elongated microvilli in the rats with ileostomy with intestinal valve.

Suppose intra-luminal or humoral factors cause prolonged life span of the cells and elongate the villus and microvilli as the reports in the past⁵⁹⁾ adaptation must naturally occur uniformly and diffusely on all the epithelial cells in a segment. Taking the existence of such factors for granted, the mucosal change obtained in our study must presuppose existence of difference of individual epithelial cell in the specific reactivity to such factors. Only the difference of potential of cell reactivity may explain the mucosal adaptation of the long surviving rats with ileostomy and ileostomy with the intestinal valve.

Malabsorption is compensated by increased cell division and the hyperplasia which improve the absorption. For the cell adaptation, cells with specific reactivity work as a receptor and reactor of intestinal adaptation.

Intestinal adaptation may be readily controlled when the causing factors for such adaptation are clarified.

Conclusion and summary

The effect of intestinal valve by telescoping anastomosis was studied with Kyoto university Wistar rats.

For elucidating the intestinal adaptation, studies were done under the conditions of (1) fasting, (2) ileostomy with or without total colectomy, (3) ileostomy with intestinal valve, on body weight change, hematology, serum chemistry, and morphological change of the intestinal epithelium.

Results were as follows :

1) From the comparison of body weight curves, it may be concluded that the intestinal valve encourages the intestinal adaptation of rats with ileostomy of which absorptive function is lowered.

2) The intestinal adaptation is encouraged by intestinal valve by its stagnation effect of the intestinal content and by increased epithelial growth at the ileum which show marked increase of elongated microvilli.

3) In the well adapted rats, elongated microvilli appear as scattered focal growth. Diffuse elongation of microvilli is observed in rats under starvation. The length of elongation of the microvilli is shorter than in the well adapted rats.

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和文抄録

Short bowel syndrome に対する
intestinal valve の効果

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Telescoping anastomosis による intestinal valve の基礎的研究として, ラットを用いて, short bowel syndrome における intestinal adaptation に対する効果を検討した。① fasting, ② ileostomy, ③ ileostomy + intestinal valve の各群について, 体重曲線, 血液検査, 血清化学, 電解質検査, 腸粘膜上皮の肉眼的, 電子顕微鏡的観察を行ない, 次の結果を得た。

1) intestinal valve は ileostomy 群の体重減少を, 術後10~14日で止め, その後増加を来たさせる効果があった。

2) intestinal valve による intestinal adaptation

は, 腸内容通過速度の調節, 回腸における粘膜上皮の増殖, 特に elongated microvilli を有する細胞の増殖によるものと考えられた。

3) elongated microvilli の出現は, intestinal adaptation を来したラットでは, 絨毛上に島嶼状に広く認められ, starvation 群では絨毛上にビマン性に認められた。しかし後者の microvilli の延長度は前者に比し短かった。

以上, intestinal valve は intestinal adaptation に極めて有効なことが確認された。