replenished, the blood. Here haemolysis, aplasia, and maturation arrest are common concepts. There seems good reason to believe that exactly similar mechanisms exist in the small intestine. Evidence has previously been produced to suggest that the mucosa in idiopathic steatorrhoea is flattened because of a maturation arrest of crypt cells (Creamer, 1962). In the present study some mucosae showed a small population of adult cells but an increased population of crypt cells. The rate of division is not in excess, but the number of cells dividing may be as much as three times that in health, so the output of cells from the crypts will be similarly increased. Loss must equal output if a steady state is to be maintained, and therefore the surface cells will be shed at a similarly increased rate. There is evidence of excessive cell death and desquamation on the villous tips of many of these specimens but no evidence of cell death in the crypts as is seen in flat mucosae from idiopathic steatorrhoea and other conditions. This seems to be analogous to haemolysis or haemorrhage, the crypts (marrow) hypertrophying in response to the excess loss. However, the other group of abnormal mucosae had crypts of a normal or shorter length than in health and a diminished mitotic rate. Here the small adult-cell population is probably the result of a small output of cells and represents a relative atrophy or hypoplasia. The patients in this group had chronic wasting illnesses such as pulmonary tuberculosis and temporal arteritis.

These observations introduce two factors of importance to absorption. The abnormal mucosae are considerably short of adult epithelial cells, so that the area available for absorption is diminished. It is important to realize that many of these specimens look comparatively normal on an ordinary histological section. If these findings applied to the whole mucosa the small-intestinal surface might be reduced to 25 to 12% of normal. There is, however, considerable variation in some conditions between the changes on the crests of mucosal folds to the more sheltered troughs in between them, and it is

unwise to generalize from a single peroral biopsy (Creamer, 1964). The second factor is the maturity of the adult epithelial cells covering the villi. In the changes akin to haemolysis the cells must pass through the adult population much faster than in health. If normal adult epithelial cells have a life of about two days, those on a "haemolytic" mucosa may last only a few hours and therefore the cells available for absorption will be younger than in health. This may mean that their enzymatic complement is below normal in addition to their small number.

Summary

Twenty specimens of small-intestinal mucosa showing variations in villous shape from fingers to leaves and to convolutions have been examined. As the villous shape becomes more abnormal the adult epithelial cells covering them are greatly reduced in number. It is suggested that the villous shape is plastic and remoulds to a more simple and economical shape as adult cells become fewer. There are two abnormal patterns of cell turnover associated with the diminution of adult epithelial cells; one is analogous with haemolysis and the other with hypoplasia.

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Small-intestinal Mucosal Dynamics and the Environment

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These observations were prompted by the finding of a very abnormal jejunal mucosa near the stoma of gastric operations where the environment of the cells was clearly deranged. The small-intestinal mucosa is normally in a state of rapid turnover and might be expected to respond to changes in the environment. It has previously been shown that the structure of villi is related to the size of adult epithelial cell population, so that as the available epithelial cells decrease in number leaf-shaped villi or convolutions are formed as a matter of economy (Creamer, 1964). This diminution of adult cells may result from a failure of output from the crypts or an excess loss from the surface.

The cells covering the villi have a luminal environment, but they also glide over a structure which represents an environment on the basement-membrane side, and either of these environments may be altered. In this study only changes in the luminal environment and the consequent effects on cell turnover have been examined.

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Materials and Methods

Eleven specimens of small-intestinal mucosa were examined from a variety of conditions. Details of the cases are mentioned in the results. Six of the specimens were surgical and five were obtained perorally. Cell counts and dissecting-microscope appearances were obtained as described previously (Creamer, 1964).

Results

Nine specimens were examined from patients in whom the environment of the small-intestinal mucosa was certainly abnormal. Four had gastric operations, two chronic intestinal obstruction from Crohn's disease, two chronic pancreatitis, and one the Zollinger-Ellison syndrome. All were abnormal under the dissecting microscope, having either leaf-like villi (grade 3) or flattened convolutions (grade 4). In all the specimens the same pattern was seen of a diminished ratio of adult cells to crypt cells and an increase in the length of the crypts

(Figs. 1 and 2). The length of the crypts tended to vary inversely with the ratio of adult cells, so that the smaller the number of adult cells the longer the crypts. The mitotic rate in these crypts (average 0.9%) was much the same as in health (average 1.1%). Estimates of the relative number of adult cells in each specimen showed a gross reduction in these

FIG. 1.—Diagrammatic representation of total mucosal height and adult-cell to crypt-cell ratio, crypt length, and the relative adult-cell population estimated for each specimen. N.=normal; P.G.=post-gastrectomy; O=chronic obstruction; C.P.=chronic pancreatitis; and Z.E.=Zollinger-Ellison syndrome.

cases compared with normal mucosae (Fig. 1). The grossest changes were seen in the two specimens of jejunum adjacent to a gastric stoma, where the environmental upset was probably maximal. Apart from this there was no difference between the changes induced by gastrectomy, obstruction, pancreatitis, or the Zollinger-Ellison syndrome. This last specimen was surgically obtained and the changes were diffuse over the whole area, about 1 cm. square.

FIG. 2.—Photomicrographs of mucosa from (A) jejunum near gastro-enterostomy stoma and (B) jejunum in Zollinger-Ellison syndrome. Note the short villous structure and long crypts in each specimen.

In the two operative specimens obtained from revision of gastric stomas larger areas of mucosa could be studied. In both these there was a striking difference between the villous structure on the crests of the mucosal folds and that in the troughs between. Each case showed a flattened convoluted pattern (grade 4) on the crests with a low adult-cell to crypt-cell ratio and long crypts, but in the sheltered troughs the villi were leaf-like (grade 3) and the ratio and crypt length more nearly normal (Fig. 3).

One surgical specimen of duodenum of normal appearance was examined. Here again a similar but less marked change was observed; in the troughs and on the sides of the mucosal folds the villi were normal in shape and height, but on the crests the villi were shorter, the crypts longer, and leaf-shaped villi were seen under the dissecting microscope. A similar appearance was seen in a surgical specimen of normal-looking ileum; on the crest of one particularly prominent fold the villi were leaf-like, while elsewhere they were finger-shaped.

Discussion

From the evidence presented there seems little doubt that the intraluminal environment can alter the pattern of cell turnover and the structure of villi. The common theme is a diminution in the adult cell population and a compensatory increase in the crypt-cell population. It seems reasonable to suppose that the adult cells are lost in excessive amounts because of physical, chemical, and perhaps bacteriological assault. The analogy to a haemolytic state in the blood seems complete.

In some cases the abnormality is most pronounced on the crests of mucosal folds where trauma is bound to be maximal. It is probable that peroral biopsy samples the crests of the fold more than the troughs, an observation which must make for caution in interpreting these biopsies as characteristic of the whole mucosa. Leaf-shaped villi are often found in duodenal biopsies from subjects in whom no other abnormality can be demonstrated. The liability of duodenum to trauma and the method of sampling would seem to explain this. The changes in the abnormal series were all much in excess of that seen in the normal duodenum.

Similar changes have been reported by Townley *et al.* (1964) in the dog, where jejunum was transplanted to the skin and subjected to physical and chemical trauma, and also in human ileum, where an ileostomy had been formed. Here the alteration in environment is gross. Of great interest are the reports of abnormal jejunal mucosae in Indians, Siamese, and Africans (Baker *et al.*, 1962; Sprinz *et al.*, 1962; Banwell *et al.*, 1964). Certainly many factors are operating here, but dietary variations and intestinal infestation are probably altering the epithelial environment. The rat when newborn has finger-shaped villi, but after weaning the villi are leaf-like (Baker *et al.*, 1963), suggesting that diet here has altered the environment. In man both hookworm and *Giardia lamblia* infestation have been reported to be associated with abnormal mucosal appearances and sometimes malabsorption (Sheehy *et al.*, 1962; Cameron *et al.*, 1962; Salem and Truelove, 1964).

In the present series the change in the intestinal environment is

obvious; partial gastrectomy, chronic pancreatitis, and obstruction all alter the luminal contents. The Zollinger-Ellison syndrome is accompanied by a large increase in gastric secretion,

FIG. 3.—Photomicrographs of jejunal mucosa near a gastrectomy stoma, (A) on the crest of a mucosal fold, and (B) in the trough beside it.

and Summerskill (1959) has shown that the pH in the jejunum may be as low as 2. The case studied had hypersecretion, atypical ulcers, and steatorrhoea; the jejunal pH was not measured, but by comparison with Summerskill's case was probably low.

In all these cases there was a diminution of the number of adult cells. While this may vary in some patients between the crests and troughs of the mucosal folds it is probably a factor in diminishing the absorptive capacity of the small intestine. Many of the patients studied had malabsorption, and Sprinz *et al.* (1962) showed that an impaired xylose absorption and low serum carotenes were common among the "normal" Siamese people they biopsied.

Summary

Specimens of small-intestinal mucosa from a variety of conditions with an abnormal luminal environment have been examined. In all the villous pattern was abnormal, with a small adult-cell population and an increased crypt-cell population. The abnormality in cell turnover corresponds to a "haemolytic" state with an increased loss of cells from the tips of the villi and an increased output from the crypts.

I am grateful to Mr. P. J. Leppard for technical assistance.

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Medical Memoranda

Perforating Wound of the Heart

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In Great Britain penetrating wounds of the heart are fortunately not common and perforating injuries must be even rarer. In the records of the Department of Forensic Medicine, University of Glasgow, we can find only 13 cases in the past five years. These were all fatal and only one reached hospital alive. In the U.S.A., where these injuries are more common, 12 to 37% of cases reach hospital alive, and of these 71 to 78% survive (Parmley *et al.*, 1958; Beall *et al.*, 1961; Vonberg *et al.*, 1961). However, if cardiac arrest occurs the mortality rate rises to 62% (Beall *et al.*, 1962). Only two cases in which recovery took place have been reported in the British literature over the past 10 years; of these one occurred abroad and in both the wounds

were penetrating ones (Pryer, 1953; Lawrie, 1955). Of two patients with perforating wounds described by Crastnopol and Mannix (1955) one died.

CASE REPORT

A young man aged 18 years was admitted to hospital at about 11 p.m. on 29 June 1963. He had been involved in a fight and had sustained three stab wounds inflicted with a long thin-bladed knife about 20 to 30 minutes previously.

On examination he was unconscious and severely shocked and his blood-pressure was not recordable. Three small stab wounds were noted in his chest and left upper arm. Two of these wounds proved to be of no consequence. The third wound was situated over the left sixth costal cartilage half an inch from the sternal border, and from it there was a continuous ooze of blood. There was an obvious left haemothorax. None of the classical signs of cardiac tamponade were present. No other injuries were noted. A rapid intravenous infusion of plasma was started with the aid of a Martin's pump.