PROCEEDINGS OF THE NUTRITION SOCIETY

ONE HUNDRED AND EIGHTY-FIRST SCIENTIFIC MEETING
DEPARTMENT OF PHYSIOLOGY, SOUTH PARKS ROAD, OXFORD

15 and 16 JULY 1966

ABSORPTION OF NUTRIENTS FROM THE INTESTINE

15 July, First Session

Chairman: H. M. SINCLAIR ESQ., MA, DM, BSc, FRCP, *Magdalen College, Oxford*

The structure of the small intestine and some interesting relations to its function

By MARGOT SHINER, *Medical Research Council Gastroenterology Research Unit, Central Middlesex Hospital, Park Royal, London, NW* 10

The method of peroral small intestinal biopsy has contributed much to our understanding of the microscopic appearances of the intestinal mucosa in health and disease.

In health (Pl. 1) the small intestinal mucosa can be roughly divided into an epithelial component, comprising the covering cells of villi and the crypt cells, and a stromal, vascular, nervous and cellular component. It would be fair to say that no one has as yet made a thorough study of the vascular and nervous supply to the mucosa. An increase in collagen fibres, chronic inflammatory cell infiltration and oedema can often be seen in mucosal biopsies but its specific significance is as yet unknown. As to the epithelial component, it is known that the columnar epithelium of the crypts of Lieberkühn are the precursors of the villous epithelium. They undergo mitosis and are thought to be the undifferentiated component of the crypt-villous epithelium. Newly formed cells move up the villus in stepwise fashion. It follows that the youngest of the absorbing cells are situated at the lowest portions of the villi and the oldest and most mature cells at the tip of the villi from whence they are extruded as they come to the end of their life span (24–48 h). Other cell components of crypt cells are the goblet cells, the argentaffin cells and the Paneth cells of which only the first two varieties can be found amongst the columnar cells of the villi. The argentaffin cells are of course part of the endocrine systems of the body and they produce 5-hydroxytryptamine. The Paneth cells are exocrine secretory cells whose exact functional significance is unknown.

One arrives then at the villous cells which concern us mainly in absorption. These are highly differentiated tall columnar cells with an interesting brush border (Pl. 2*a*) composed of microvilli, numbering between 1000 and 3000 to each cell. Their basally situated, oval-shaped nucleus (Pl. 2*b*) is surrounded by cytoplasm which contains the usual components—the granular and agranular endoplasmic

reticulum, mitochondria, Golgi apparatus, lysomes and others. These cells are limited below and on either side by a folded trilaminar membrane which is more or less closely apposed to the adjacent cell membrane laterally. Basally the cell connects to the so-called basement membrane through which it makes contact with the blood, lymph and nervous supplies of the villous stroma.

Most active absorption of nutrients proceeds through villous epithelium along the sides and tips of each villus. It seems reasonable to attach great importance to the normal shape of the villi in that it offers an enormous surface of absorbing cells to the luminal juices and nutrients bathing them. It is, however, equally important to consider the size of each cell and its degree of maturity because disturbance of either factor will lead to malabsorption. Thus, in certain malabsorption states, such as idiopathic steatorrhoea (Pl. 3) we observe that not only the surface area for absorption is reduced by simple reduction or disappearance of villi, but also each cell is altered, becoming shorter than normal. Histochemical techniques have shown a reduction in certain enzymes, such as succinic dehydrogenase, esterase, acid phosphatase, leucine aminopeptidase, monoamine oxidase and TPN and DPN diaphorase, and mucosal assays have demonstrated reduction of other enzymes, such as the lactases, maltases and invertases. Malabsorption in idiopathic steatorrhoea is most likely the result of insufficient absorptive area as well as a reduction in cellular enzymes, but the cause of the structural malformation of villi and cells probably resides within the crypt cells, although the adverse influence on the crypt cells is unknown. Histologically we observe an elongation and increased tortuosity of the crypts with probably some increase in the number of mitoses.

At the ultrastructural level (Pl. 4*a*) the reduced height of the surface epithelium in idiopathic steatorrhoea can be confirmed. In addition the nuclei appear smaller and rounder with more irregular outlines. A curious abnormality can often be seen in the microvilli which appear sparser, shorter and often broader. The impression gained is that of a sick but viable cell. It would be of great interest to know more about the morphological alteration of surface and crypt cells in idiopathic steatorrhoea at the ultrastructural level and to relate this to such cytotoxic drugs as aminopterin, since at the light microscopic level similar changes can be observed in both. It is worthy of notice that although, in idiopathic steatorrhoea, the morphological abnormality of the surface cell is associated with reduction of cellular enzymes, it is possible to have a structurally normal cell and still demonstrate a reduction or absence of enzyme, such as can be found in hypolactasia.

Finally, in relating function to structure of the small intestinal mucosa I should like to mention two separate fields of investigations which have interested me in recent years.

The first is that of fat absorption across the brush border of the villous cells. Current biochemical theories would indicate that fat is brought to the surface of the absorbing cells mainly in micella form (Hofmann & Borgström, 1962). This means that lipid in molecular form is absorbed across the brush border of the villous cells and might be an explanation of why fat absorption is such an extremely rapid process, for 1 min after exposure of the absorbing cells to predigested lipid

chyme, Jersild (1966) found lipid droplets already in the Golgi vacuoles above the nucleus. From my own electron microscopic observations I have also been impressed with the speed of lipid absorption by the cell. If most of the luminal lipid available for cellular absorption is in molecular form, this would be a very plausible explanation of why lipid droplets are so rarely seen in the region of the brush border, for the molecules are not sufficiently electron-dense to give us a positive picture. But lipid material of sizes varying from 50 to 500 Å or larger have been seen in the brush border on relatively rare occasions by a number of observers (Palay & Karlin, 1959; Lacy & Taylor, 1962; Rostgaard & Barrnett, 1965), who have variously placed the sites of entry of these droplets between or within the microvilli, and this would require entry either by micropinocytosis or by lipid diffusion through membranes of the microvilli or by either routes. I have been fortunate to observe dense droplets (Shiner, 1966), assumed to be lipid, within the microvilli of the absorbing cells after introduodenal feeding of linseed oil to rats (Pl. 4*b*). I believe that the importance of this observation lies not in the fact of recording a relatively rare phenomenon but in showing that lipid can be transported across the membranes of the microvilli. The enormous increase in surface membrane area provided by the microvilli would thus offer a plausible explanation for the rapid and efficient absorption of large quantities of lipid by the absorbing cells of the upper jejunum.

The other line of investigation pursued by my colleagues at the Wright-Fleming Institute of Microbiology and myself concerns the role of upper intestinal luminal bacteria in the absorption or malabsorption of fats. Our observations have confirmed those of others that in health the human upper jejunal luminal contents are virtually free from bacteria in the fasting state (Shiner, Waters & Gray, 1963; Drasar, Hughes, Williams & Shiner, 1966). This state is probably significantly influenced by the presence or absence of gastric acidity, for the latter tends to encourage the colonization of bacteria in both the stomach and jejunum. In certain diseased states of the small intestine associated with blind loops or diverticulitis, obstruction to the flow of luminal contents encourages the colonization of bacteria and this state has been linked to the frequent finding of steatorrhoea and anaemia in the affected patients, for after antibiotic treatment these symptoms may disappear. To add to these known facts, we have succeeded in demonstrating that (1) the jejunal colonization with bacteria in these patients bears certain resemblance to the flora normally found in the colon and faeces of healthy subjects and (2) the ability of certain anaerobes isolated from the jejunal juices of these patients to deconjugate bile salts in vitro (Drasar, Hill & Shiner, 1966). The faecal flora of normal subjects contains a numerical predominance of bacteroides. These are strict anaerobes and can be grown only with special techniques. Likewise the predominant organism isolated from the blind loop contents of our patients are the bacteroides and they are numerically far greater than the enterobacteria, to which the coliform group belongs, or the enterococci, such as *Streptococcus faecalis*. These last two groups of organisms have in the past been thought of as the important types and have been aetiologically related to the blind loop syndrome. In testing for bacterial ability to deconjugate bile we have found that, of a variety of luminal organisms tested, only

the bacteroides group could convert glyco- or tauro-cholates into cholates or deoxycholates. As shown by Hofman (1966), the deconjugated bile salts form poor micellar solutions with the hydrolysed products of digested fats, such as monoglycerides and fatty acids, and thus lead to faulty fat absorption by the intestinal cell and consequently to steatorrhoea.

An interesting and hitherto uninvestigated problem is that of the structural effects of the presence of deconjugated bile salts on the human small intestine. In rats it was shown by Dawson & Isselbacher (1960) that cholic acid exerts an irritating and destructive effect on the villous cells. Our own human intestinal biopsy work has indicated that villous abnormalities can be found in post gastrectomy steatorrhoea, blind loops and some patients with jejunal diverticulosis, but these changes are slight. Obviously, further work at both light microscopical and ultramicroscopical levels would be desirable.

The structure as well as function of the human small intestine is still relatively uninvestigated. Our knowledge of both is infinitessimal compared to our ignorance of the processes of absorption and digestion. Much work has been carried out and new insight has been gained during the last two decades yet the scope for future investigation into that field is unlimited.

REFERENCES

Dawson, A. M. & Isselbacher, K. J. (1960). *J. clin. Invest.* **39**, 730.
Drasar, B. S., Hill, M. J. & Shiner, M. (1966). *Lancet* i, 1237.
Drasar, B. S., Hughes, W. H., Williams, R. E. O. & Shiner, M. (1966). *Proc. R. Soc. Med.* **59**, 1243.
Hofmann, A. F. (1966). *Gastroenterology* **50**, 56.
Hofmann, A. F. & Borgström, B. (1962). *Fedn Proc. Fedn Am. Socs exp. Biol.* **21**, 43.
Jersild, R. A. Jr (1966). *Am. J. Anat.* **118**, 135.
Lacy, D. & Taylor, A. B. (1962). *Am. J. Anat.* **110**, 155.
Palay, S. L. & Karlin, L. J. (1959). *J. biophys. biochem. Cytol.* **5**, 363.
Rostgaard, J. & Barrnett, R. J. (1965). *Anat. Rec.* **152**, 325.
Shiner, M. (1966). *Gut* **7**, 107.
Shiner, M., Waters, T. E. & Gray, J. D. A. (1963). *Gastroenterology* **45**, 625.

EXPLANATION OF PLATES

Pl. 1. Light microscopic appearances of the normal human jejunal mucosa, showing villi and crypts of Lieberkühn, muscularis mucosae and a small amount of submucosa. Haematoxylin and eosin.

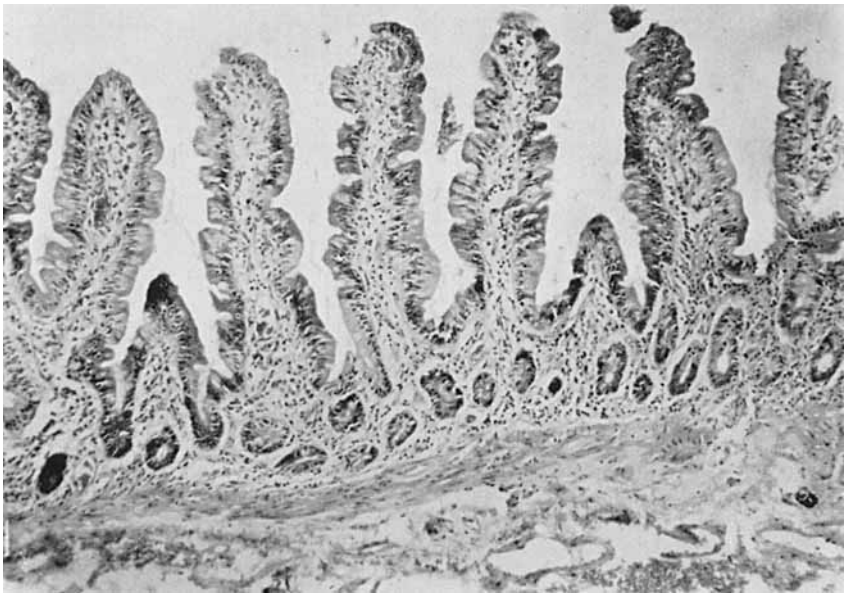
Pl. 2(*a*). Electron microscopic appearance of the upper half of two villous cells, showing prominent microvilli (M) in longitudinal section, mitochondria (MI), some lipid material (L) and the lateral or intracellular membranes (ME).

Pl. 2(*b*). Electron microscopic section through the lower half of two villous epithelial cells showing oval shaped muclei (N) separated by folded lateral plasma membranes (ME). MI, mitochondria.

Pl. 3. The jejunal mucosa in idiopathic steatorrhoea. Subtotal villous atrophy with hypertrophy of the crypts of Lieberkühn. Light microscopy. Haematoxylin and eosin.

Pl. 4(*a*). Electron microscopic view of the upper part of villous cells in idiopathic steatorrhoea. Note the short and thick microvilli (M) and the extensive vacuolation (V) within the cellular cytoplasm. N, nucleus.

Pl. 4(*b*). Electron microscopic view of the brush border of a villous cell of rats after lipids have been ingested. The microvilli (M), seen here in oblique section, contain large numbers of dense staining droplets, assumed to be lipid material.

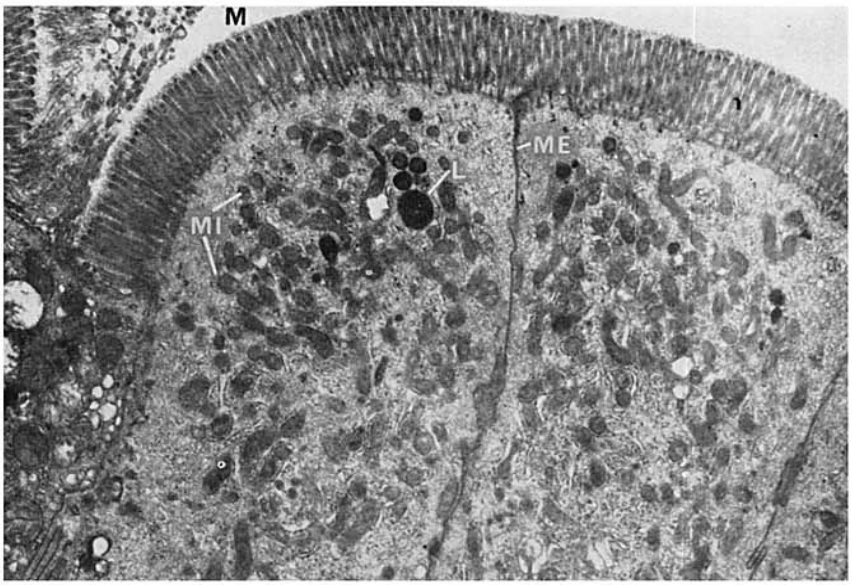


MARGOT SHINER

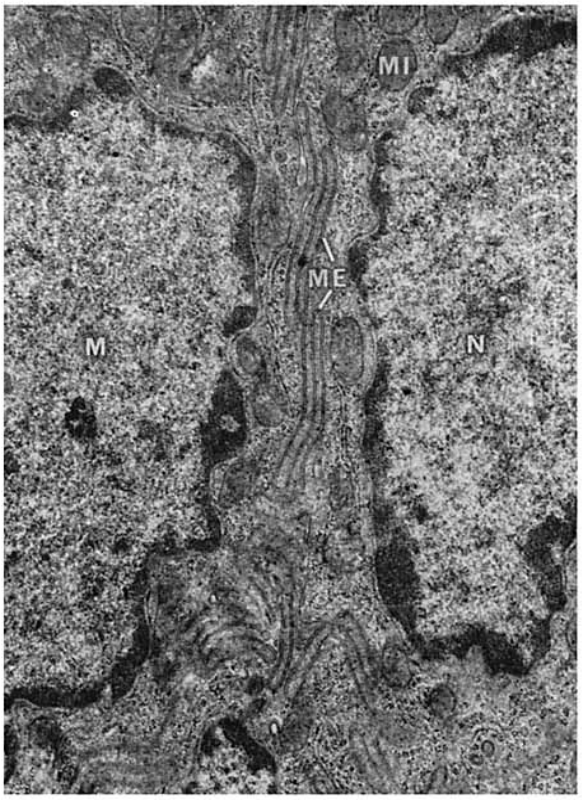
(*Facing p. 4*)

https://doi.org/10.1079/PNS19670003 Published online by Cambridge University Press

(*a*)

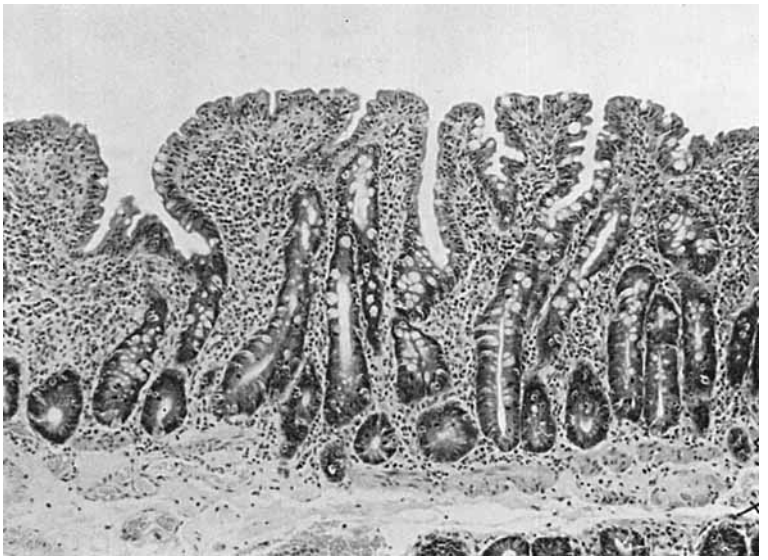


(*b*)



MARGOT SHINER

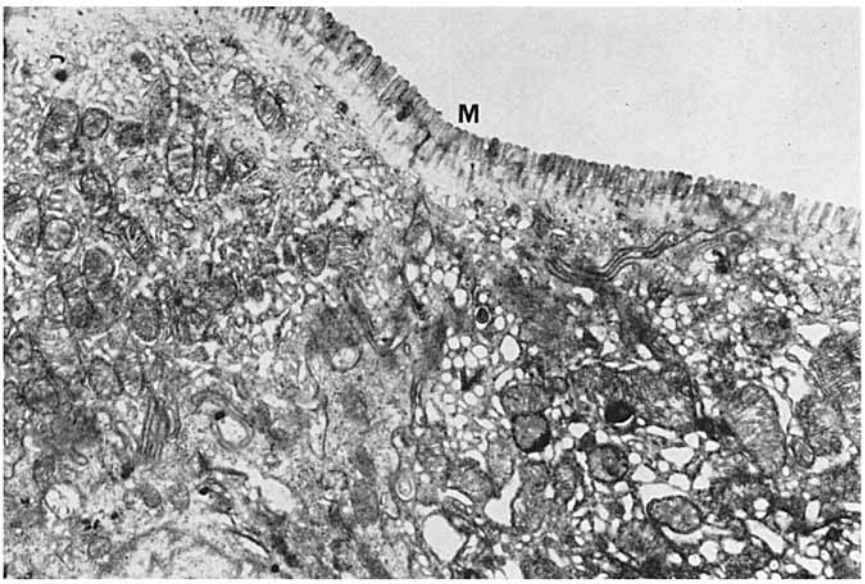
https://doi.org/10.1079/PNS19670003 Published online by Cambridge University Press



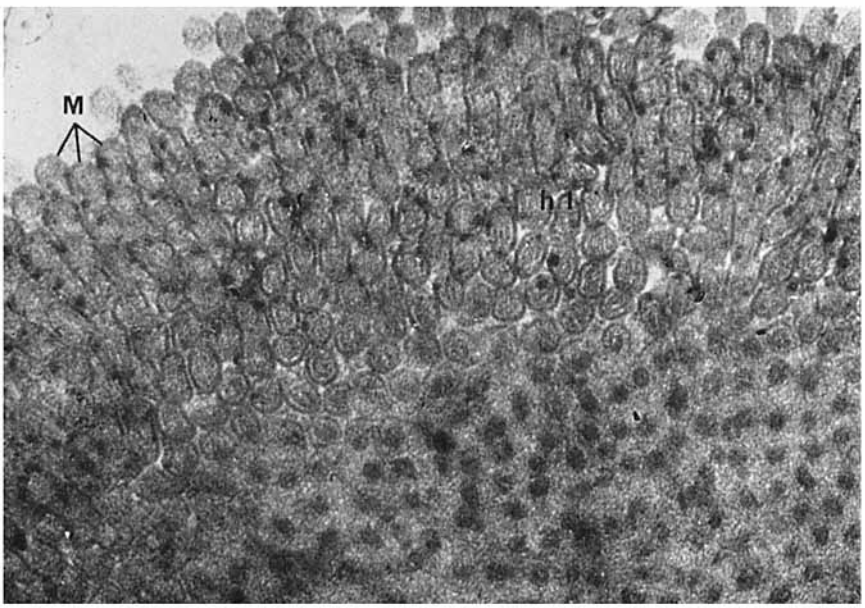
MARGOT SHINER

https://doi.org/10.1079/PNS19670003 Published online by Cambridge University Press

(*a*)



(*b*)



MARGOT SHINER

https://doi.org/10.1079/PNS19670003 Published online by Cambridge University Press