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The microvascular architecture of the glandular mucosa of rat stomach*

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INTRODUCTION

Cells of the gastric epithelium are responsible for secretory and protective functions. To subserve these functions, an intimate relationship between these cells and the mucosal microcirculation might be expected. Physiological studies indeed show a direct relationship between acid secretion and gastric mucosal blood flow (Lanciault & Jacobson, 1976); abundant evidence implicates a disturbed mucosal microcirculation in the pathogenesis of acute gastric ulceration (e.g. Moody, 1971).

While the vascular anatomy of the mammalian stomach has been previously investigated, more recently by Oka (1970), Rosenberg & Guth (1970), Hase & Moss (1973), Piasecki (1974, 1975) and Guth & Smith (1975), the precise arrangement of the gastric mucosal microcirculation has yet to be fully elucidated; in particular, the presence or otherwise of arteriovenous anastomoses in either the mucosa itself or in the submucosa remains in dispute.

In the present study, the microcirculation of the gastric mucosa of the corpus (terminology after Robert, 1971) of the rat stomach has been examined. The techniques utilized included scanning electron microscopy of vascular corrosion casts and of acid-digested tissues, *in vivo* microscopy of blood flow and conventional transmission electron microscopy.

MATERIALS AND METHODS

Adult male rats of Porton strain, fed on a diet of standard rat pellets and weighing approximately 250 g, were used. Animals were deprived of food for about 12 hours prior to experiments; they were first lightly anaesthetized with ether, then injected intraperitoneally at a dosage of 1 ml per 100 g body weight with an aqueous solution of 2 % tribromo ethanol (Aldrich, Milwaukee, Wisconsin) and 2 % tertiary amyl alcohol. Animals for *in vivo* experiments were anaesthetized with an intraperitoneal injection of 2 % chloralose – 10 % urethane solution in normal saline at 0·6 ml/100 g body weight (Bohlen & Gore, 1976).

Vascular casting

The procedure followed was essentially that described previously (Gannon, 1978; Rogers & Gannon, 1981). The abdominal aorta was ligated just proximal to the origin of the common iliac arteries, and the renal vessels were occluded. The thoracic

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aorta was cannulated, just proximal to the diaphragm, with polyethylene tubing (P.E. 90 Intramedic, Clay Adams, New Jersey). Blood was washed out with 0·9% saline (at 37 °C) containing 58·7 g/l of 40000 M.W. polyvinyl–pyrrolidone (Sigma, St. Louis), 10 I.U./ml Na heparin, (Glaxo, Melbourne) and 1×10^{-6} papaverine HCl (David Bull Laboratories, Melbourne). The posterior vena cava was cut within the thorax to allow blood and saline to escape. Care was taken with the stomach to avoid handling or exposing it to air, because to do so has been found to result in incomplete casts in other tissues (Rogers & Gannon, 1981). The casting medium was usually methyl methacrylate partial polymer (viscosity 2–5 centistoke at 20 °C) prepared as described elsewhere (Gannon, 1981). Mercox CL 2B (Vilene Hospital Ink and Chemical, Tokyo) was used for the partial cast preparations.

Venous partial casts were made, by retrograde cannulation of the hepatic portal vein near the liver, following completion of blood washout. The anterior mesenteric vein was ligated to prevent loss of casting medium into the intestinal vasculature, and the gastric venous system was partially cast in a retrograde direction. For these experiments the casting medium was Mercox injected by hand, with the stomach exposed to monitor the degree of perfusion. Prior to injection, the Mercox was allowed to partially polymerize at room temperature for 5 minutes, following addition of the catalyst paste, so that this high viscosity medium would not readily pass through capillaries. Arterial partial casts were made with the same casting mixture infused by hand through the aortic cannula.

The cast preparations were digested and prepared for scanning electron microscopy as described elsewhere (Gannon, 1978; Rogers & Gannon, 1981). Stereo paired micrographs were routinely taken, and viewed in a Wild ST4 mirror stereoscope.

Acid-digested tissues

The abdominal cavity was opened and flooded with the primary fixative (2·5% glutaraldehyde plus 2% paraformaldehyde in 0·1 M phosphate buffer at pH 7·4). The stomach was then removed, opened and washed in fixative. It was then cut into pieces between 2·5 and 10 mm^2. Fixation was continued for 2–3 hours. Tissues were washed in buffer (2×10 minutes) and then post-fixed in 1% OsO_4 for 2–3 hours. Next, the specimens were washed in distilled H_2O (2×10 minutes) and placed in 6 M HCl at 55–60 °C in an agitating water bath. The time of acid digestion was determined by observation, the process being stopped when the tissue appeared almost gelatinous; this was usually at 30–40 minutes. Digested samples were washed in distilled H_2O, dehydrated in ethanol and critical point-dried. The dried tissues were broken with forceps and mounted on stubs with broken surfaces exposed. This preparative procedure is a modification (Uehara, 1980; personal communication) of that used by Uehara & Suyama (1978). Stereo paired scanning electron micrographs were routinely taken.

Transmission electron microscopy

Finely diced gastric mucosal tissues were immersion-fixed in a phosphate-buffered formaldehyde–glutaraldehyde mixture for 1·5–2·0 hours and post-fixed in OsO_4 as described in the preceding section. Fixed tissues were dehydrated in ethanol, rinsed in anhydrous acetone, infiltrated in a 1:1 mixture of acetone/resin for 2–4 hours, and embedded in TAAB embedding resin. Blocks were trimmed to include appropriate areas, following light microscopic examination of toluidine blue-stained

thick sections. Thin sections were stained with lead citrate and uranyl acetate, and viewed in a Siemens 102 T.E.M. at 60 kV.

In vivo microscopy

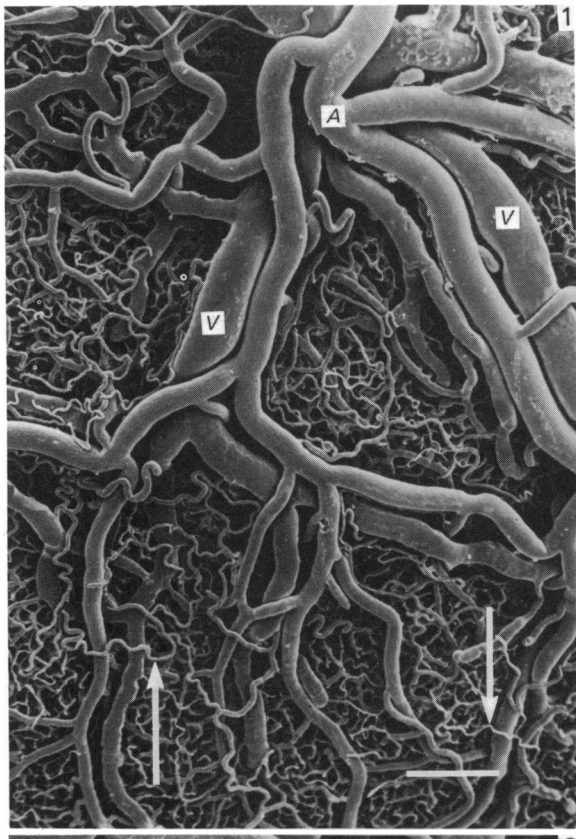
Rats were prepared according to the method used by Rosenberg & Guth (1970): after laparotomy, the submucosal aspect of the gastric mucosa was exposed for observation by dissecting away a small area of the muscularis externa of the ventral stomach wall under stereo-microscopic observation; bleeding was minimal and soon stopped. A suitably bent length of $\frac{1}{8}$ inch image conduit (American Optical Co., Southbridge, Mass., USA) was inserted through a longitudinal incision made with a micro-cautery apparatus in the antimesenteric margin of the duodenum; the conduit was passed through the pylorus into the stomach. The gastric area to be observed was stabilized between the bent end of the conduit and a 20 mm diameter metal disc which had an 8 mm diameter central aperture; the aperture was covered with a clear plastic film (Saran Wrap, Dow Chemical, Indianapolis). Both image conduit and stabilizing disc were clamped to a specially constructed plexiglass plate on which the animal was placed. For study of the luminal aspect of the mucosa, the ventral wall of the fore-stomach was opened by micro-cautery and the stomach contents were flushed out with warmed saline. The image conduit was placed against the dorsal serosal surface of the stomach and the stabilizing ring against its mucosal surface.

The animal preparation on its plexiglass plate was attached to the stage drives on a Leitz Dialux microscope which was fitted with saline immersion and long working distance objective lenses. The stomach preparation was transilluminated using a Schott KL 150B fibre optic light source coupled to the image conduit via a flexible light guide; a Ploemopak incident light fluorescent illuminator plus 150 W Xenon light source permitted incident light fluorescence observation. The image was projected to a Cohu 4410 ISIT television camera and observed on an Ikegami television monitor. The preparations were observed initially using transilluminating white light; the illumination was then changed to incident fluorescence and a fluorescent tracer was injected intravenously to observe the flow pattern of the incoming front of intravascular tracer. Brilliant sulfoflavin S (Sigma, St. Louis, Missouri) to a total dose of 20 mg/kg (Hauck & Schroer, 1973) given as 0·1–0·2 ml bolus injections of a 9 mg/ml solution in 0·9 % heparinized saline via a carotid cannula, or FITC bovine serum albumin (Sigma, St. Louis, Missouri) to a total dose of 250 mg/kg given as similar bolus injection of a 50 mg/ml solution were the fluorescent intravascular tracers used.

RESULTS

Scanning electron microscopy of the vascular corrosion casts and acid-digested tissues

The general pattern of the gastric mucosal circulation is illustrated in Figures 1 to 4. The major arteries and veins which supplied/drained the mucosal surface of the stomach lay in a plexus within the submucosa. A view of the base of the mucosa from its submucosal aspect (Fig. 1) showed that, in common with many organs, the larger arteries and veins ran in parallel pairs; the arteries were smaller in diameter than their accompanying veins. Higher magnification of the vascular plexus at the base of the mucosa, as seen from its submucosal aspect (Fig. 2), revealed terminal branching of the submucosal arteries at right angles to the plane of the submucosa.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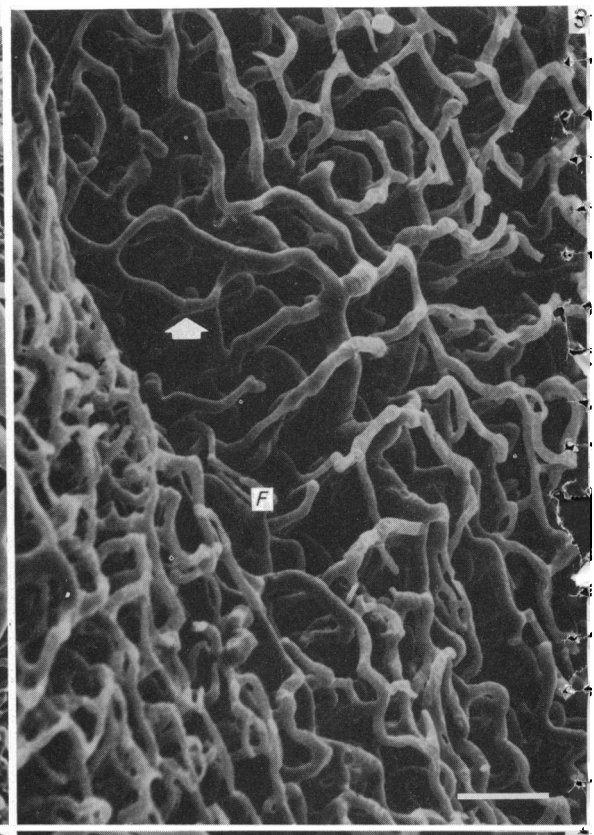
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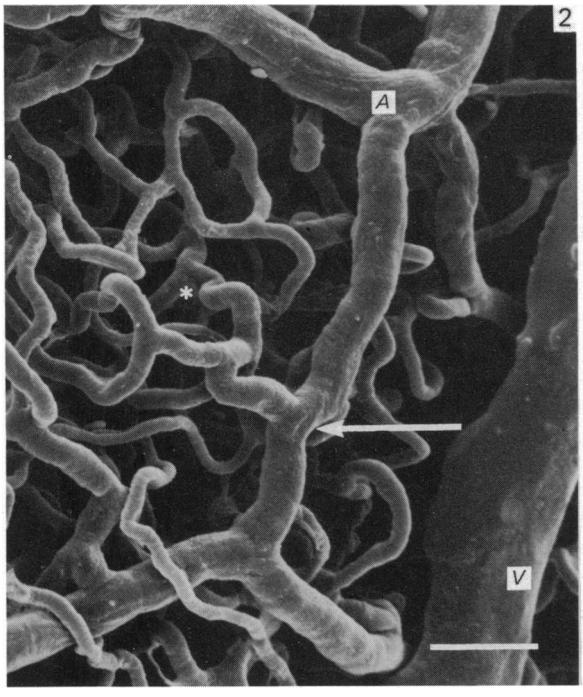
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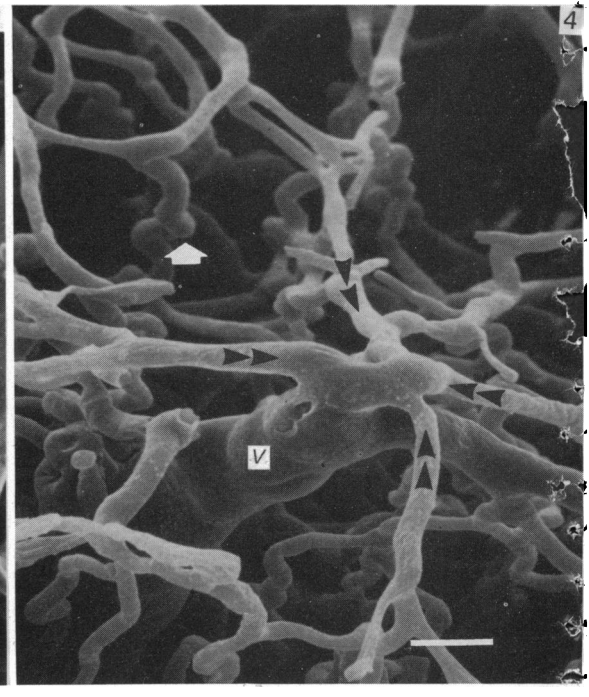
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The luminal aspect was characterized by a honeycomb-like network of capillaries (Fig. 3), an arrangement which presumably reflected the positions of the openings of the gastric pits. Gastric rugae were represented by folds in the vascular casts (Fig. 3). At higher magnification, occasional venules were seen connected to subsurface capillaries (Fig. 4); these venules passed down into the mucosa, perpendicular to the plane of the mucosal surface.

The vascular patterns of the submucosal and luminal aspects of the mucosal circulation have been described previously, for example by Guth & Smith (1975) using intravital microscopy, but are better visualized by the vascular corrosion cast/SEM technique employed here. A more detailed description of the intervening microcirculation follows – little attention had been given to this area previously.

The arterial partial casts (Figs. 5, 6) served clearly to define the arterial and capillary vessels, eliminating the possibility of confusion of these with venous vessels. The arterial division (see also Fig. 3) invariably occurred at the base of the mucosa; arterial vessels did not penetrate the mucosa to any extent. Thus the entire blood supply to the gastric mucosal/capillary network originated at the base of the mucosa. Anastomoses were frequently seen (Fig. 9) between the supply areas of different terminal arterioles. The initial portions of the casts of these terminal arterioles usually showed marked constrictions (Fig. 5), strongly suggestive of vascular sphincter location at these sites. No evidence of venous filling in these arterial partial casts was found, nor were any large channel structures, suggestive of arteriovenous anastomoses, observed.

The mucosa contained a dense capillary plexus of vessels oriented predominantly at right angles to the plane of the mucosa (Figs. 6, 7, 8, 9, 10). The vascular casts showed that more laterally orientated connections between these capillaries also occurred fairly frequently. Acid-digested and fractured tissue samples confirmed the general orientation, but, in addition, clearly showed the close proximity of the mucosal capillaries to the abluminal surface of the gastric glands (Figs. 8, 9, 10). These glands showed a large number of prominent protuberances on their abluminal surface (Figs. 8, 9, 10) which, from conventional histological studies, were identified as parietal (acid-secreting) cells. The acid-digested tissues also confirmed the submucosal location of the plexus of large supply/drainage vessels of the mucosa (Fig. 9) and the divergent branching of the arterioles and arterial capillaries at the base of the mucosa (Figs. 8, 10).

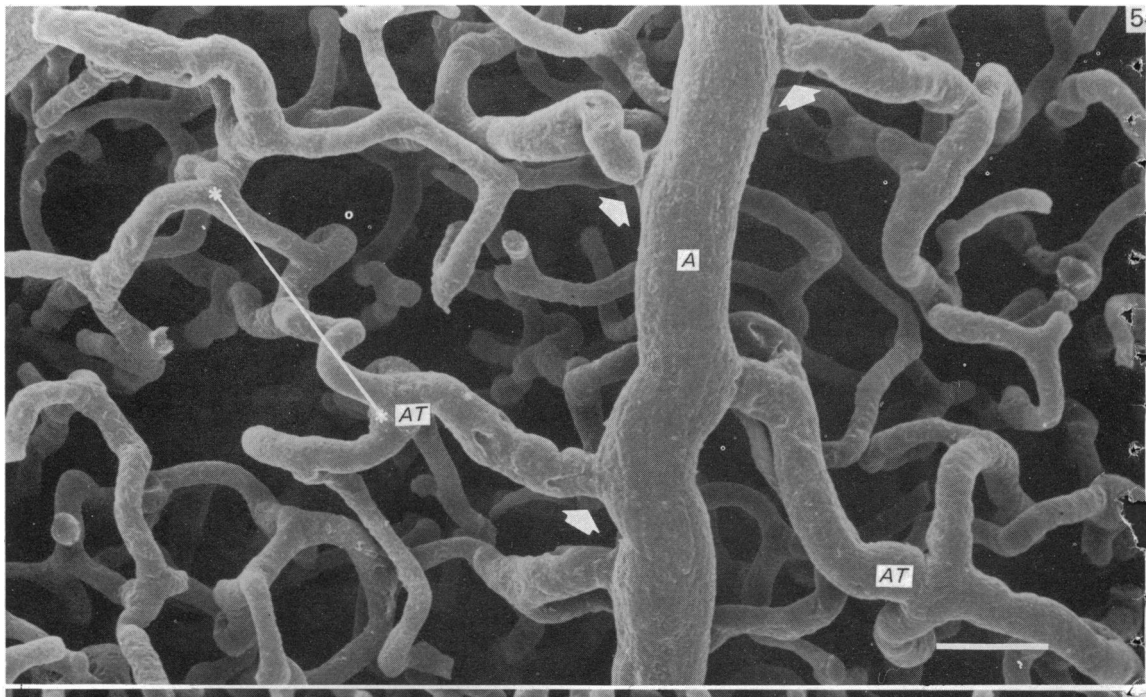
Figs. 1–4. Scanning electron micrographs of vascular corrosion casts of rat gastric mucosa.

Fig. 1. Submucosal aspect of mucosa showing parallel branching pattern of submucous arteries (A) and veins (V). Note occasional fine vessels (arrows) lying in the plane of the submucosa. Bar = 0·3 mm.

Fig. 2. Higher magnification of the submucosal aspect of the mucosa. Note the elongated impressions of endothelial cell nuclei (arrow) on the cast of an arteriole (A) and the arteriolar branching into the capillary plexus surrounding the gastric glands (*). A submucous venule (V) is also seen. Bar = 50 μm.

Fig. 3. Luminal aspect of mucosal cast; note subsurface capillaries (arrowhead) arranged in a honeycomb-like network. A fold (F) in the mucosal surface is evident. Bar = 50 μm.

Fig. 4. Higher magnification of the luminal aspect of a mucosal cast. Note deeper mucosal capillaries (white arrowhead) connecting to subsurface capillaries (black arrowheads) which connect into mucosal venule (V) near the luminal surface of the cast. Bar = 25 μm.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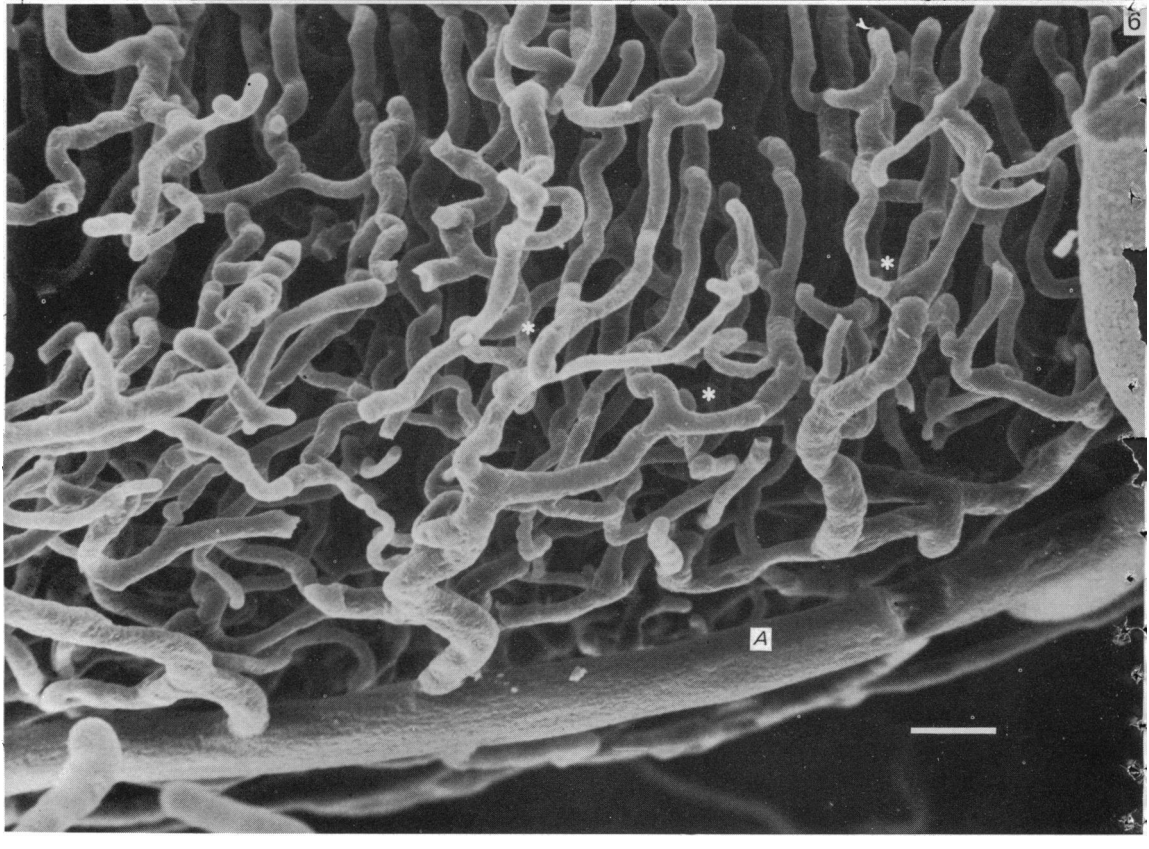
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Retrograde venous partial casts (Figs. 11, 12, 13) clearly showed the mucosal venules, of approximately 20 to 50 μm luminal diameter. They connected with the mucosal capillary network only at, or very close to, the luminal surface of the cast (Figs. 11, 13), and passed through the mucosa without receiving further tributaries (Figs. 12, 13), i.e. all mucosal capillary blood must drain via vessels close to the stomach lumen. The separate drainage areas of individual mucosal venules were clearly demonstrated in the retrograde venous partial casts (Fig. 11).

The infrequency of the mucosal venules passing through the mucosa, compared to the numbers of mucosal capillaries, is obviously suggested by a comparison of Figures 7 and 12. This contrast is also clearly illustrated in Figure 14, which shows an arterial partial cast viewed from the submucosal aspect; the very many capillaries can be compared with the gaps in this cast which were previously occupied by mucosal venules (deliberately left uncast in this preparation).

Transmission electron microscopy

Capillaries around the base of the mucosal glands possessed a continuous and vesiculated endothelium (Fig. 15). The vessels were embedded in a connective tissue matrix which contained collagen fibres and occasional fibroblasts. Progressing towards the gastric lumen, the endothelial cells of the capillaries became increasingly fenestrated, and there was a notable decrease in the amount of connective tissue between the basal lamina of the endothelium and that of the adjacent gastric gland cells (Fig. 16). The capillaries situated immediately below the surface mucous cells were similarly fenestrated and in close proximity to the basal laminae of these cells (Fig. 17). Minimum interstitial diffusion distances were typically between 0·5 and 1·0 μm. Diffusion distances between capillaries and adjacent parietal (oxyntic) cells of the gastric glands were usually even smaller, commonly less than 0·3 μm (Fig. 18). Present observations on the ultrastructure of the capillaries in the mucosal tissues agreed substantially with the brief report by Pellegrini (1968); no other relevant studies are known.

Mucosal venules were infrequently encountered; their endothelial cells contained few vesicles, and were not fenestrated. The venules were embedded in a substantial connective tissue sheath which typically isolated the venular lumen from adjacent gastric gland cells by a minimum distance of 10–30 μm.

In vivo microscopy of gastric mucosa

Submucous aspect

In the experiments where the stomach was prepared for viewing the submucosal aspect of the mucosa, the arterioles and venules of the submucosal vascular plexus could be readily identified; the arterioles and venules generally ran in pairs, with the

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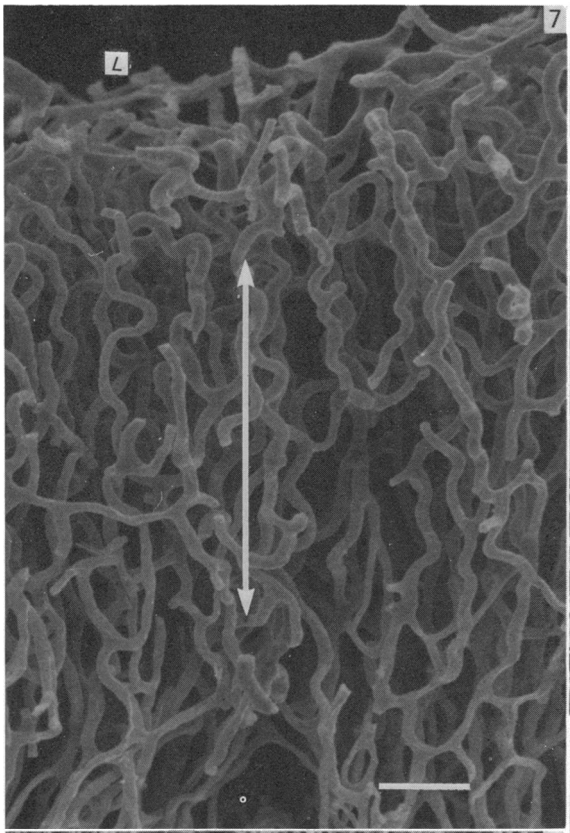
Figs. 5–6. Scanning electron micrographs of arterial partial vascular corrosion casts.

Fig. 5. Submucosal aspect of an arterial partial cast. A submucosal arteriole (A) gives off terminal arteriolar (AT) branches at right angles, which break up to supply the capillary plexus at the base of the mucosa. Note the sphincter-like constrictions at the origins (arrowheads) of the terminal arterioles, and the anastomosis between the territories of the two terminal arterioles (*–*). Bar = 25 μm.

Fig. 6. Lateral view of a fractured arterial partial cast. Note terminal arterioles arising from a submucosal artery (A), and breaking up (*) into capillaries at the base of the mucosa. Bar = 25 μm.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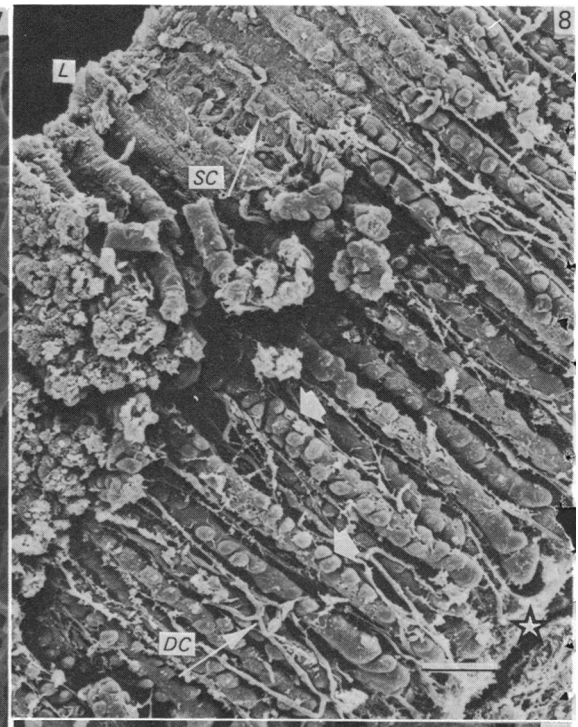
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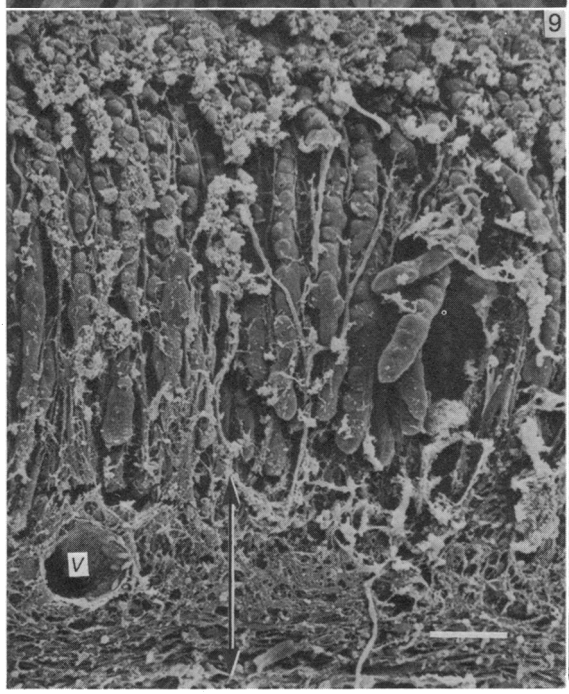
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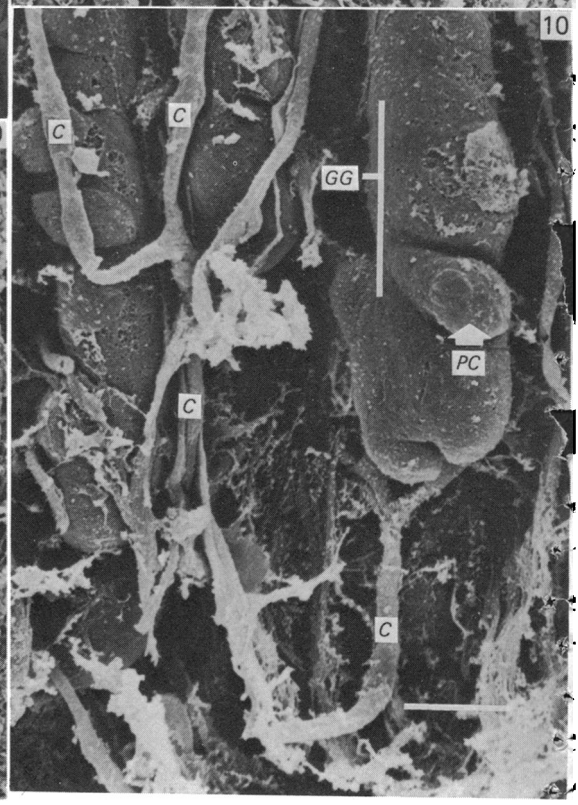
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arterioles exhibiting smaller diameter and a much faster red cell velocity than the corresponding venules. In transmitted light microscopy, flow in the arterioles could be identified breaking up into the capillary plexus surrounding the gastric glands and then flowing into the mucosa (i.e. down and out of the plane of focus); this flow could not be followed for more than 50 μm into the mucosa.

Flow was also observed in larger vessels coming out of the mucosa (towards the observer) and entering the submucosal venules. Occasional segments of the submucosal venous network exhibited very sluggish flow, or no flow, between entering mucosal venules; in these areas haematocrit was very low and often there were no red cells.

In addition to the mucosal vessels, occasional submucosal capillaries were seen. These were supplied as a branch from the submucosal arterioles and then ran for long distances as single vessels in the plane of the submucosa, external to the submucosal vascular plexus of larger vessels, before draining into the submucosal venules; they usually exhibited rapid flow.

Observation after the injection of a bolus of fluorescent tracer confirmed the pattern of flow direction observed with transmitted light; the front of tracer appeared first in the submucosal arterioles, then passed into the mucosal capillaries at the base of the mucosa and finally appeared in larger vessels draining the mucosa into the submucosal venules.

Luminal aspect

The subsurface capillaries, surrounding the gastric pits in a honeycomb-like array, could be readily observed. Flow appeared to come into these subsurface vessels from capillaries deeper in the mucosa, and then travelled in a converging pattern towards infrequently placed draining vessels. Flow then passed down into the mucosa, but could not be followed to the submucosa. Observation of bolus i.v. injections of fluorescent tracer confirmed this pattern of flow. The vessels of the entire drainage field of a particular mucosal venule appeared to exhibit fluorescence at approximately the same time – i.e. there were no markedly early or late filling regions.

In all the *in vivo* preparations, it was important to carefully adjust the gap between the image conduit below, and the stabilizing ring above, the mucosa. If the gap was too small, the mucosa blanched and few red cells and little flow were observed. If

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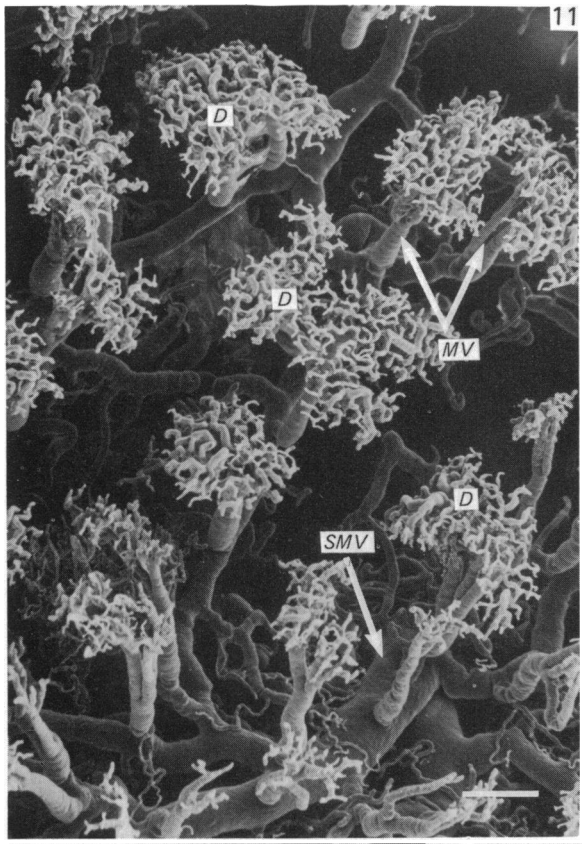
Figs. 7–10. Scanning electron micrographs of gastric mucosal capillaries revealed by vascular casting (Fig. 7) or acid digestion (Figs. 8–10).

Fig. 7. Vascular cast of the mucosal capillaries, fractured and viewed at right angles to the plane of the mucosa. Note that the predominant capillary orientation (double-headed arrow) is perpendicular to the plane of the mucosa; the gastric lumen (L) is at the top of the micrograph. Bar = 50 μm.

Fig. 8. Acid-digested tissue, fractured to reveal the gastric glands. Parietal cells protrude from the glands (arrowheads). Capillaries are seen both deep (DC) in the mucosa, and near the surface (SC). The lumen of the stomach is indicated (L), as is the opposing submucosal region (★). Bar = 50 μm.

Fig. 9. View of base of the mucosa, showing muscularis mucosa (double-headed arrow) and a submucosal venule (V). Note the rounded base of the gastric glands and the capillaries lying between them. Bar = 50 μm.

Fig. 10. Higher magnification of the base of the gastric glands (GG). Note protruding parietal cells (PC) and capillaries (C) close to the abluminal surface of the gland cells. Bar = 15 μm.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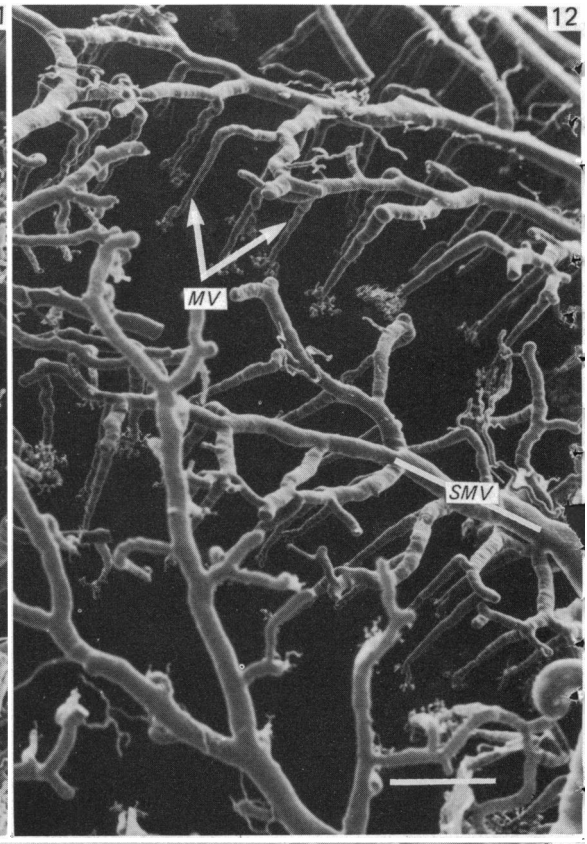
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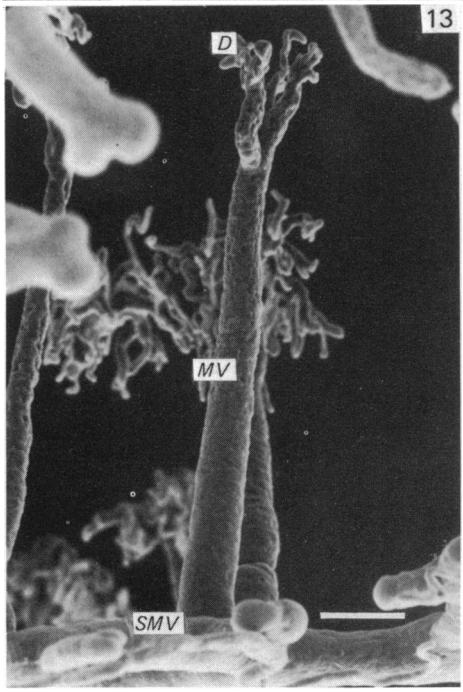
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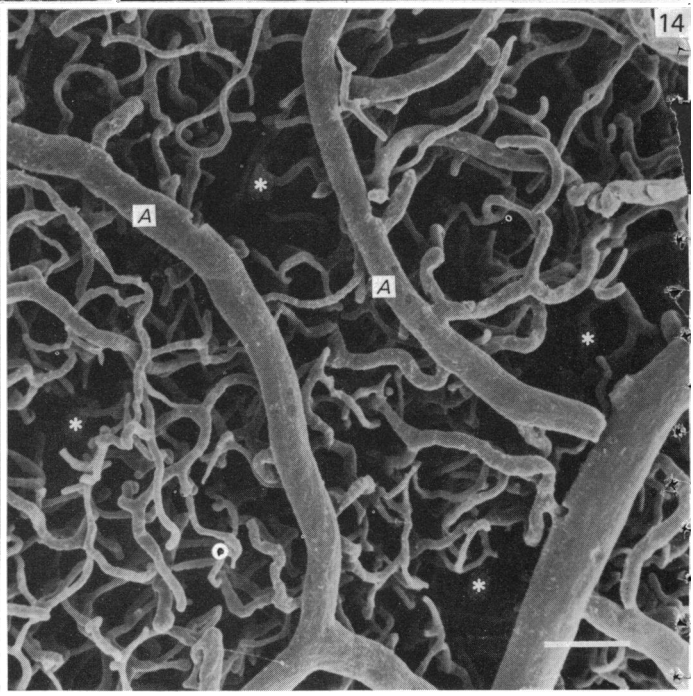
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the gap was too great, the sample was not stabilized sufficiently and the field of view constantly changed with minor gastric and respiratory movements of the animal.

DISCUSSION

The mucosal blood supply of the corpus of the rat stomach is derived from arteries of the submucosal vascular plexus. These vessels branch to form the terminal arterioles, which then break up into a leash of capillaries at the base of the mucosa. In general, these terminal arterioles supply discrete areas of the mucosa, as reported by Hase & Moss (1973).

Occasional anastomoses were, however, observed at the base of the mucosa between the fields of supply of adjacent arterioles, and there were also connections between capillaries of adjacent gastric glands higher up in the mucosa.

The observation of small constrictions in the vascular casts at the commencement of many of the terminal arterioles suggests that these may represent the location of sphincter sites which control local gastric mucosal blood flow. Guth & Smith (1975) reported submucosal arterial diameter reductions of 30% during splanchnic nerve stimulation: however, they appear not to have observed specific sphincter sites in their *in vivo* preparations. Schnitzlein (1957) confirmed earlier reports that constriction of the mucosal arterioles in the rat stomach caused mucosal ischaemia; under these conditions the mucosal capillaries themselves remained patent. In the present study, no casts of arterioles were found in the mucosa above its most basal layer. This is in conflict with Nylander & Olerud's (1961) account of mucosal arterioles high in the mucosa. However, Schnitzlein (1957) found that only those mucosal vessels nearest the muscularis mucosa have smooth muscle, and Hase & Moss (1973) did not find arteriolar vessels within the mucosa proper.

The capillary network of the mucosa consists of the interglandular mucosal capillaries, which in general run perpendicular to the plane of the mucosa, and the honeycomb meshwork of subsurface capillaries which runs in the plane of the mucosa and connects the interglandular capillaries to the mucosal venules. This arrangement had been shown previously, but with less clarity (Oka, 1970; Hase & Moss, 1973; Guth & Rosenberg, 1972; Guth & Smith, 1975). Furthermore, the present work has conclusively established that the venules only drain from the capillary network immediately below the mucosal surface – there are no capillary connections to mucosal venules deeper in the mucosa. In addition, the mucosal venules occur infrequently.

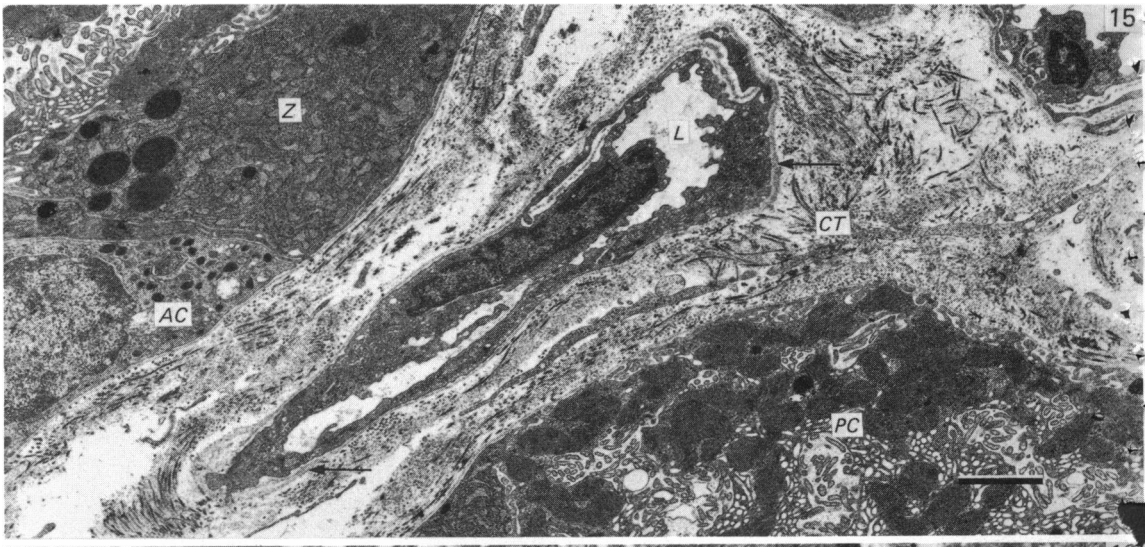
Figs. 11–14. Retrograde venous and orthograde arterial partial vascular casts of the rat gastric mucosa.

Fig. 11. Mucosal aspect of retrograde venous partial cast. Note submucosal veins (SMV), mucosal venules (MV) and drainage areas (D) of subsurface capillaries. Bar = 175 μm.

Fig. 12. Submucosal aspect of retrograde venous partial cast. Note submucosal veins (SMV) and mucosal venules (MV). The absence of capillary connections into the latter vessels, except near the mucosal surface, is evident. Bar = 400 μm.

Fig. 13. Lateral view of a mucosal venule (MV) draining from the subsurface capillaries (D) into the submucosal vein (SMV). Retrograde venous partial cast. Bar = 100 μm.

Fig. 14. Submucosal aspect of an orthograde arterial partial cast. Gaps in the cast network (*) indicate positions normally occupied by mucosal venules. Note submucosal arteries (A) supplying the basal region of the mucosal capillary plexus via terminal arterioles. Bar = 50 μm.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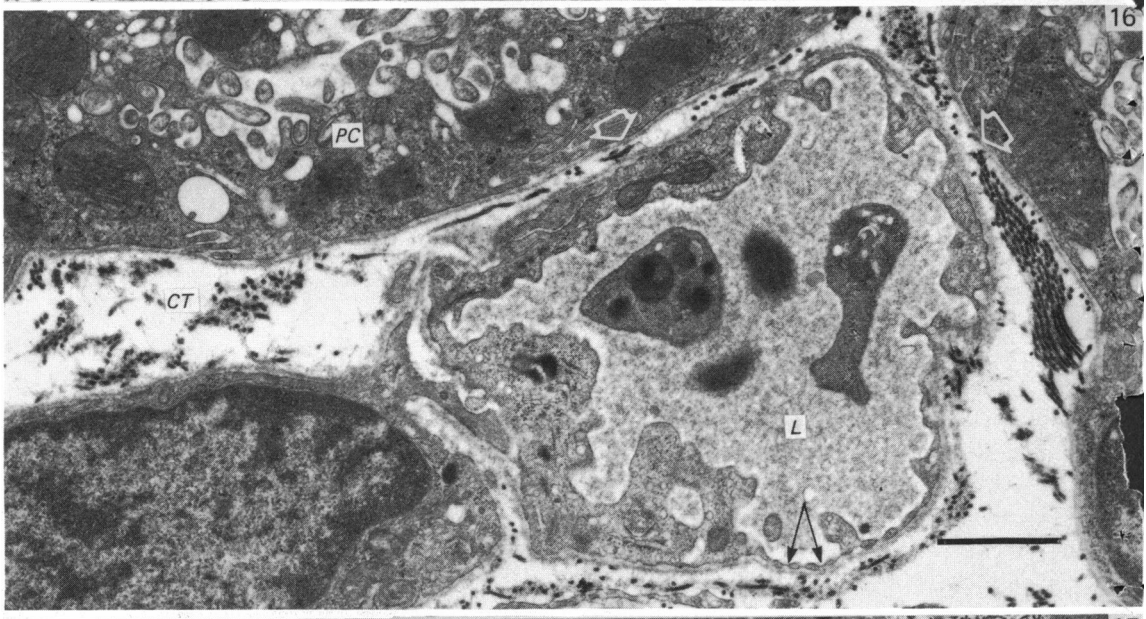
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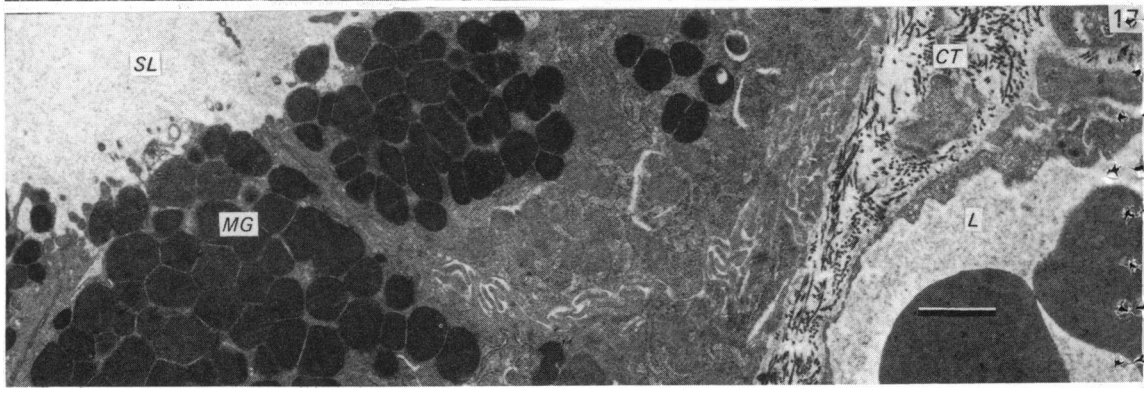
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A preliminary calculation indicated that the surface area of the mucosal capillary endothelium exceeds that of the mucosal venules by more than one order of magnitude. The likely importance of these findings is discussed later.

While the present findings on the mucosal microvascular architecture of the rat stomach are in general agreement with the account by Hase & Moss (1973), no arteriovenous anastomoses in the submucous vascular plexus have been found. Barlow, Bentley & Walder (1951) described considerable numbers of arteriovenous anastomoses in human stomach, although Barlow (1952) also stated that they were difficult to find. However, in more recent morphological studies, they could not be found by Guth & Smith (1975) and Piasecki (1974, 1975) in rat, dog or human stomachs. Those illustrated by Oka (1970) and by Hase & Moss (1973) cannot be identified as such with confidence without additional evidence from serial sectioning or the preparation of stereo photographs. In the present *in vivo* microscopic studies, occasional fine vessels were seen in the submucosa itself, which connected between the arterioles and venules. These were not arteriovenous anastomoses, however, because they had a long, tortuous course and were of narrow diameter (< 10 μm). No arteriovenous anastomoses were seen high in the mucosa, such as have been described by Nylander & Olerud (1961). As has been pointed out elsewhere (Murakami, 1978; Gannon, 1978), the vascular corrosion cast/SEM technique is a great advance on the previously employed light microscopic and microangiographic techniques, especially if stereo photography is routinely employed. It seems unlikely, therefore, that arteriovenous anastomoses would have been missed in the present study unless they are very rare indeed.

The present *in vivo* microscopic findings indicate that the directions of blood flow in the mucosa, deduced from the connections observed in the vascular casts, are correct. The present observations confirm previous *in vivo* microscopic studies by Guth & Rosenberg (1972) and Guth & Smith (1975), whose techniques we have employed here. The large number of arteriovenous anastomoses reported by Lakhtina & Kozlov (1975) from intravital microscopy were not seen in the present study.

Although a quantitative study has not been made, transmission electron microscopic observations of the present study indicate that the mucosal capillaries are in very close proximity to the gastric glands; the parietal cells protrude from the abluminal surface of the gastric glands and the interstitial diffusion distance from capillary to parietal cell is often less than 0·3 μm. The capillary endothelium here is fenestrated and contains numerous vesicles. Therefore hindrance to the diffusion of small molecules between the capillaries and parietal cells is minimal. While this is impor-

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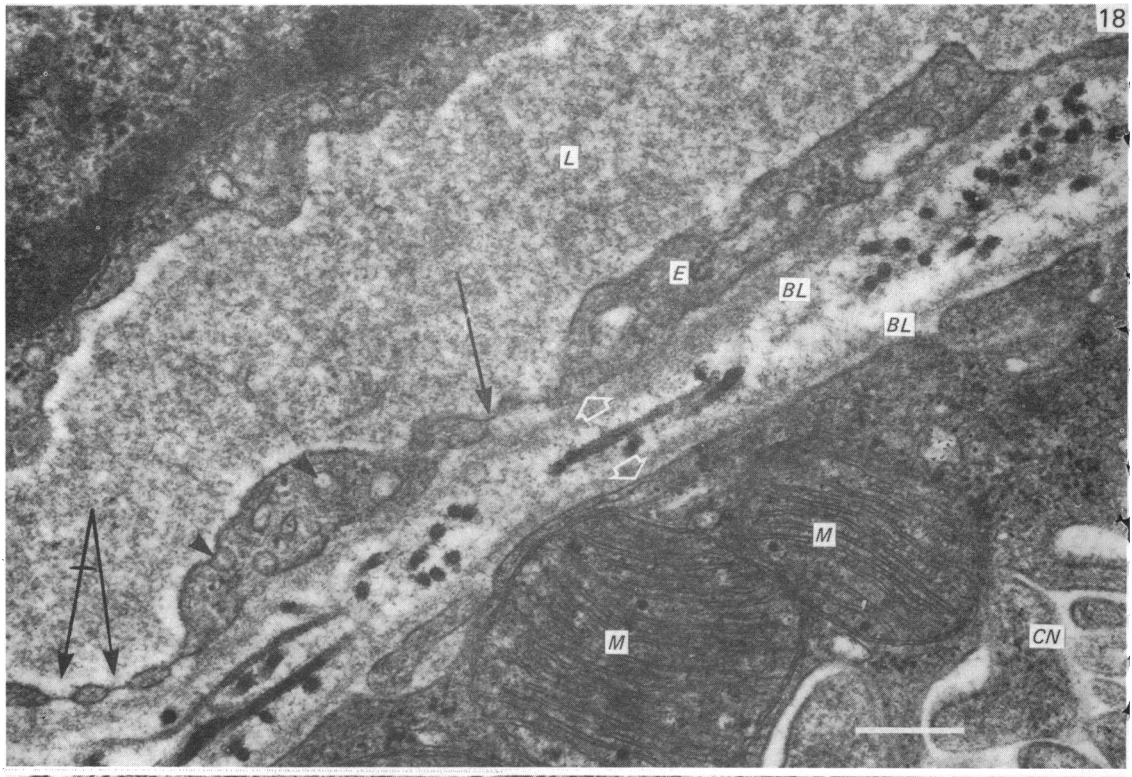
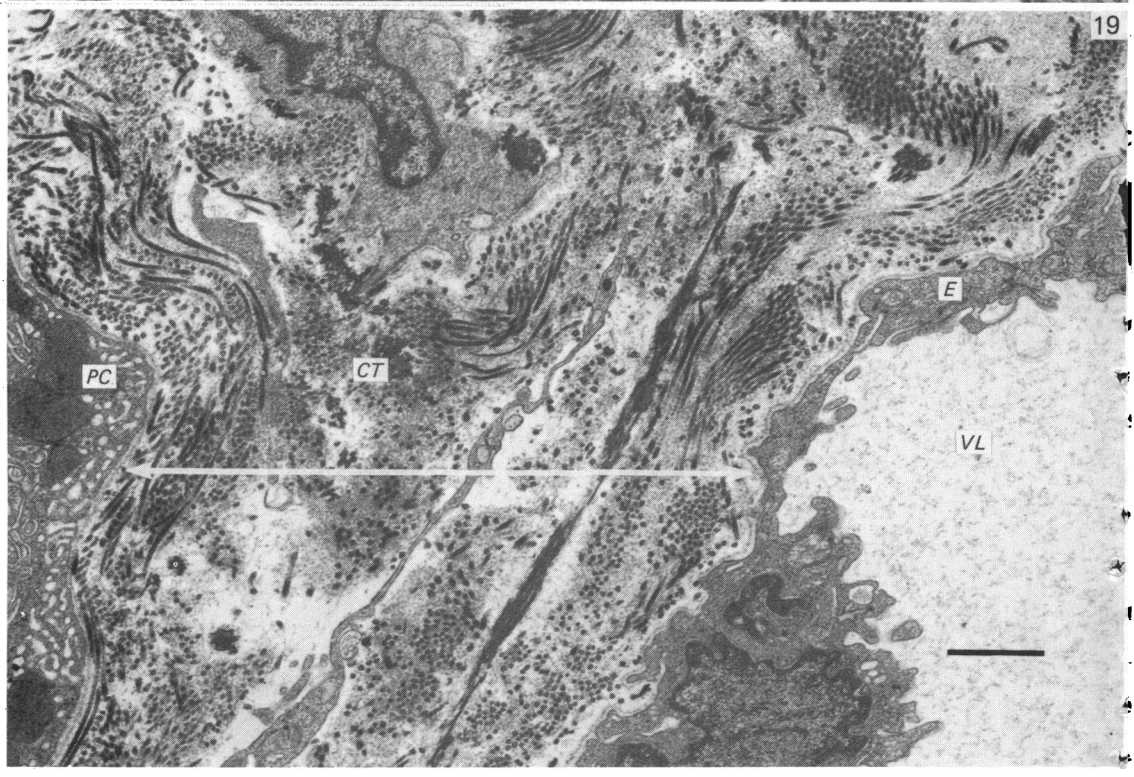
Figs. 15–17. Transmission electron micrographs of sections of rat gastric mucosa.

Fig. 15. Section of a capillary deep in the mucosa, near the submucosa. Note the continuous endothelium bounding the lumen (L), and the capillary basal lamina (arrow). Connective tissue (CT) separates the capillary from a parietal cell (PC), argentaffin cell (AC) and zymogen cell (Z) of adjacent gastric glands. Bar = 1·5 μm.

Fig. 16. Section of a capillary in the mid-region of the mucosa. Note the fenestrations (arrows) in the endothelial cell, and the close proximity (arrowheads) of the capillary basal lamina to that of adjacent parietal cells (PC). Bar = 1·0 μm.

Fig. 17. Section showing lumen (L) of fenestrated capillary closely apposed to the basal membrane of surface mucous cells containing mucous granules (MG). The lumen of the stomach is indicated (SL). CT, connective tissue. Bar = 1·0 μm.


18
L
E
BL
BL
M
M
CN


19
E
PC
CT
VL

tant for the diffusion of metabolites to the highly active parietal cells, diffusion of molecules in the opposite direction may also be of particular importance to the normal functioning of the stomach (see below).

At the luminal surface, the endothelium of the subsurface capillaries is also fenestrated and distances from the capillary wall to the basal lamina of adjacent surface mucus cells is typically less than one micron. Because of the honeycomb-like array of these subsurface capillaries, it seems certain that virtually all surface mucus cells will be in close proximity to this capillary network.

The ultrastructure of the walls of the mucosal venules, and their relationship to the gastric glands, contrasted markedly with that of the mucosal capillaries. The venular endothelium is not fenestrated and these vessels are surrounded by a thick connective tissue sheath; minimum interstitial distances from the venules to the parietal cells of around 10–30 microns were observed. Taken together with the mucosal microvascular architecture and blood flow pattern, these findings provide an important insight into a possible mechanism by which the gastric mucosa is able to resist damage by acid.

It has long been recognised that secretion of H^+ by the parietal (oxyntic) cell is associated with an equivalent extrusion of HCO_3^- into the interstitial fluid (Teorell, 1951). More recent studies have indicated that mucosal protection against acid within the gastric lumen centres on the secretion of HCO_3^- by the surface epithelial cells into an 'unstirred layer' of gastric mucus gel (Flemström, 1977; Allen & Garner, 1980). A pH gradient across the mucus layer is thereby established and acts as a protective barrier between the luminal acid and the gastric epithelium (Williams & Turnberg, 1981). The higher the HCO_3^- concentration in the interstitial fluid, the better able is the mucosa to cope with acid exposure (O'Brien & Bushell, 1980). Moreover, the gastric mucosa, when actively secreting acid into the lumen and therefore passing HCO_3^- into the interstitium, is better able to cope with acid exposure than is the non-secreting mucosa (O'Brien & Silen, 1976; Smith, O'Brien, Fromm & Silen, 1977).

Thus, the possible functional importance of the microvascular arrangement of the mucosa reported here becomes evident. The arterial vessels invariably break up into the capillary network near the base of the mucosa. Because of the proximity of the capillaries to the parietal cells of the gastric glands, interstitial alkalinisation associated with active acid secretion would be expected to lead to rapid alkalinisation of the capillary blood. This alkalinised fluid is then transported to the abluminal aspect of the surface epithelial cells, thereby optimizing the capacity of these cells either to secrete HCO_3^- into the gastric lumen or to neutralize back-diffusing H^+. Blood drains from the interglandular plexus to the mucosal venules only via the subsurface capillary network; the venules occur infrequently and are relatively thick-

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Fig. 18–19. Transmission electron micrographs of sections of rat gastric mucosa.

Fig. 18. Capillary lumen (L) bounded by an endothelium showing fenestrae (arrows) each covered by a diaphragm, and endothelial vesicles (arrowheads). Note close proximity (white arrowheads) of capillary to basal membrane of a parietal cell which shows prominent mitochondria (M) and canaliculi (CN). The two cells are separated by the basal laminae (BL) of each cell and a few collagen fibrils. Section from mid-mucosal level. Bar = 0·25 μm.

Fig. 19. Mucosal venular lumen (VL) bounded by a continuous endothelium (E) showing few endothelial vesicles. Note the dense connective tissue (CT) of collagen and fibroblasts separating the venule from a parietal cell (PC) by 7 μm (white double-headed arrow). Bar = 1·0 μm.

walled. Diffusion distances from gastric gland cells to the venules are far greater than they are to the capillaries. Loss of the alkaline tide from the parietal cell region directly into the venous circulation must therefore be comparatively slight.

It appears that the gastric mucosal microvasculature is so structured that when active acid secretion is occurring, and therefore protection against luminal acid is most required, maximal protective capacity is afforded by the very organization of the mucosal microcirculation.

SUMMARY

The circulatory pattern in the gastric mucosa of the rat and relationships of mucosal capillaries to gastric gland cells were investigated. Techniques used included the vascular corrosion cast/scanning electron microscope method, scanning electron microscopy of acid-digested tissues, conventional transmission electron microscopy and *in vivo* light microscopy.

Arterial break-up into capillaries invariably occurs around the base of the gastric glands. The mucosal capillaries are fenestrated and vesiculated, and pass in close proximity to the abluminal aspects of the cells of the gastric glands, particularly the parietal cells. At the apices of the glands, the capillaries form a honeycomb network closely applied to the abluminal aspect of the surface epithelial cells, before draining into infrequent venules which are embedded in a substantial connective tissue sheath. No capillary drainage occurs into these venules deeper in the mucosa. No evidence of either mucosal or submucosal arteriovenous anastomoses was found.

Because of the close proximity of the fenestrated mucosal capillaries to the parietal cells and surface epithelial cells and the direction of capillary blood flow, the alkaline tide of the actively secreting parietal cell must be transferred to the abluminal aspect of the surface epithelial cells. The capacity of these cells to secrete HCO_3^- or to neutralize back diffusing H^+ ions would thereby be increased.

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