Peribiliary Portal System in the Monkey Liver as Evidenced by the Injection Replica Scanning Electron Microscope Method

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Summary. Scanning electron microscope study was carried out on the methyl methacrylate cast of the intrahepatic blood vessels of the monkey and it was unequivocally demonstrated that the peribiliary blood vascular plexus received the afferent vessels from the hepatic artery and emitted the efferent vessels directly draining into the hepatic sinusoids. The possible significance of this vascular route, which is isolated from the portal vein and referred to as the peribiliary portal system, is discussed. The efferent vessels connecting the plexus and the sinusoids may reveal some constrictions suggesting occurrence of a sphincter.

It is generally accepted that the peribiliary or periductal blood vascular plexus in the liver is supplied by the hepatic artery. Drainage of this plexus, however, has been a subject of continuing controversy for over two centuries.

Ferrein (1749, cited by Andrews et al., 1949) suggested that the peribiliary plexus drained into the hepatic sinusoids. Although this view of the “radicular portal veins” was supported in man and cat by some authors (Olds and Stafford, 1930), many investigators using man, cat, rat and other animals including the monkey strengthened the view of the “internal hepatic radicles” or “internal roots” of Kiernan (1833, cited by Andrews et al., 1949) that the peribiliary plexus poured into the portal vein (Elias and Petty, 1953; Mitra, 1966). Furthermore, some conflicting or mixed views were added. Hase and Brim (1966) using rats reported that the peribiliary plexus rich in capillaries continued as the radicular portal veins into the sinusoids in contrast to the usual pattern of the internal roots. Andrews and his associates (Andres et al., 1949; Lozano and Andrews, 1966) contended in man, dog, rat and other animals the occurrence of both connections throughout the plexus, the radicular portal veins and the internal roots, and regarded the latter roots as the afferent.

The conventional light microscope methods of the previous authors, using injected sections (Olds and Stafford, 1930; Andrews et al., 1949; Elias and Petty, 1953; Mitra, 1966), cast samples (Andrews et al., 1949; Lozano and Andrews, 1966; Hase and Brim, 1966) and other specimens including living tissue, are insufficient for persuasible demonstration of the exact three-dimensional distributions and connections of the complicated networks of the hepatic vessels. This technical difficulty seems to have caused that controversy.

A useful method for the study of microcirculation was recently established, which consisted of plastic casting and scanning electron microscopy combined with
microdissection and enabled accurate analysis of the entire blood vascular beds in various organs and tissues including the liver (MURAKAMI, 1971). By this "injection replica scanning electron microscope method," a clear demonstration of the vascular networks, especially the peribiliary plexus and its efferent vessels, in the monkey liver is here attempted.

Fig. 1. Methyl methacrylate blood vascular casts of the liver of a rhesus monkey seen under the scanning electron microscope (a view from the liver surface). CH convergence of the hepatic sinusoids to confluence into the underlying central veins, VH central vein exposed on the liver surface, tA terminal branches of the hepatic artery, t terminal branches of the portal vein, x leakage of resin, arrow (see text). × 75
Fig. 2. Microdissected blood vascular casts of the monkey liver seen under the scanning electron microscope (crab-eating monkey).

A. a block obtained from a deep part, B. a block from a surface area. A hepatic artery branch, B peribiliary plexus, C liver surface, H hepatic sinusoids, P portal vein branch, tA final or terminal branches of the hepatic artery, a afferent vessels of the peribiliary plexus, c cut edges of the portal vein, d collateral branches of the hepatic artery, e efferent vessels of the peribiliary plexus, s side branches of the portal vein, t terminal branches of the portal vein. A ×25, B ×30
Material and Method

The methyl methacrylate blood vascular casts of the monkey liver, which had been obtained in casting the pancreas of a male rhesus monkey (Fujita and Murakami, 1973) and the kidney of a male crab-eating monkey (Murakami et al., 1973), were used. They were microdissected under a binocular, and the parts of interest were isolated (for technical details of casting and dissection see: Murakami, 1971; Fujita and Murakami, 1973; Murakami et al., 1973).

The isolated blocks were mounted on metal-stubs, coated with gold (Murakami, 1971) or impregnated with osmium (Murakami et al., 1973), and observed in a scanning electron microscope (JSM-U3) with an accelerating voltage of 5 kV. After the observation, the blocks were further microdissected and again observed in the scanning electron microscope. This procedure of dissection and scanning was repeated until the structures were sufficiently exposed (Murakami, 1972; Fujita and Murakami, 1973). When necessary, stereoscopic pairs of electron micrographs were observed (Murakami, 1972).

Results

Though injected only through the thoracic aorta, the blood vessels of the liver were filled with resin (Fig. 1). It would be needless to say that resin reached the liver via the tracts of the hepatic artery and the portal vein. By repeating scanning electron microscopy and microdissection of the casts alternately, the vascular distributions and connections were studied, which will be described below.

No difference in the pattern of intrahepatic vasculature was noticed between the rhesus monkey and the crab-eating monkey.

The blood vascular beds of the monkey liver were formed by the meshwork of the hepatic sinusoids, which was partitioned, by the portal canal conducting the portal vein, into inseparable lobules and was confluenced toward the hepatic canal containing the tributary of the hepatic vein (Fig. 1, 2).

The hepatic sinusoids were mainly supplied by the portal vein. The sinusoids around the final segments of the portal canal were supplied by the terminal branches of the portal vein (Fig. 1, 2, 12), while those bordering more proximal segments received the side branches of the portal vein (Fig. 2, 9). Most of the side branches arose in common trunks with the terminal branches or much larger branches and ran some distance along the parent vessels of these branches (Fig. 2, 9), while others originated independently and were immediately divided into the sinusoids (Fig. 2, 10, 11). The former type of the side branches was exclusively observed in the larger portal canal and the latter type in the rather smaller portal canal. As the portal canal was traced more proximally toward the hilus of the liver, the system of the portal side branches was less developed. Thus, as described in the rat and other mammals including man by Elias and Popper (1955), Hase and Brim (1966) and other authors, the hepatic sinusoids around the large portal canal were poorly supplied by the portal vein.

The hepatic sinusoids also received capillaries from the hepatic artery. The hepatic artery ran in the portal canal together with the portal vein (Fig. 2) and its final branches went along the terminal branches of the portal vein to pour into the
hepatic sinusoids at the ends of the portal canal (Fig. 12). In its course, the hepatic artery gave off collateral branches which ran into the portal canal to empty on or beneath the surface of the lobules into the hepatic sinusoids (Fig. 8, 10). Elias and his associates (Elias, 1949; Elias and Petty, 1953) described in man, rat and other animals the so-called intralobular arterioles that passed deep into the lobules to end near the central veins. We failed, as Hase and Brim (1966) and Mitra (1966) did in the rat, to demonstrate such deep arterioles, except in the liver surface where the

Fig. 3. Peribiliary plexus of large caliber. A. crab-eating monkey, B. rhesus monkey. a Outermost layer of the peribiliary plexus, v venous network of the outer layer of the peribiliary plexus; e and H (see the legends in Figure 2). Thick arrow inserted at the corner of the Figure is directed distally. Note the connections of the outermost layer with the hepatic sinusoids (white g in Figure B). A ×75, B ×90.
Fig. 4. Peribiliary plexus cut longitudinally and viewed from the inner side (crab-eating monkey). A, before dissection, B after dissection; the boxed area in Figure A. I inner layer of the peribiliary plexus, O outer layer of the peribiliary plexus; a, e, v and thick arrow (see the legends in Figure 2 and 3). Identification of each vessel may be facilitated by r and f.

A ×100, B ×200
arterial capillaries occasionally ended near the area of the hepatic vein (arrow in Fig. 1). An arterial capillary labelled *aa* in our Figure 9 crept between the final twigs of the portal vein, but it ended just superficially (white arrow).

The peribiliary plexus, the blood vascular beds supplying and enveloping the bile duct, appeared as a basket-like column, which ran in close association with the portal vein and the hepatic artery (Fig. 2). It gradually tapered and ended in the final segments of the portal canal by sending off a few faint vessels, the efferent vessels (Fig. 10–12).

The peribiliary plexus received at various levels many arterial branches, the afferent vessels, which arose from the hepatic artery in common trunks with the collateral branches to the sinusoids (Fig. 2–5, 8–10). And the plexus consisted of the networks of double layers, an outer layer mainly formed by relatively thick vessels and an inner layer of fine capillaries (Fig. 4).

The afferent vessels, after giving off fine twigs to the outermost layer (Fig. 3, see below), were divided in the outer layer of the plexus (Fig. 2–9) and entered deep to supply the inner layer of fine capillaries (Fig. 4). The capillaries of the inner layer converged and formed a venous network of the outer layer (Fig. 4). This typical pattern observed in the medium-sized and large plexus was broken in the small and distal plexus. Here, weak afferent vessels formed the layer of fine capillaries (Fig. 10–12).

No communication was noticed between the hepatic artery and the portal vein, nor between the latter vein and the peribiliary plexus.

**Fig. 5.** Large peribiliary plexus and its connecting vessels (rhesus monkey). *a, e, s, H* and *thick arrow* (see the legends in Figure 2 and 3). × 60
The peribiliary plexus emitted, at every segment in its intrahepatic course, multiple efferent vessels radiated toward the adjacent hepatic sinusoids. The efferent vessels from the smaller plexus were always weak ones derived from the fine capillaries of a single layer (Fig. 10–12), while those from the larger plexus formed thick trunks into which the venous network of the outer layer converged (Fig. 3–9). The typical thick efferent trunks were exclusively observed in the large plexus with well-developed networks near the hilus of the liver (Fig. 5–7). Each of the efferent vessels, regardless of their thickness, was characterized by an independent.

Fig. 6. Well developed efferent vessel of the peribiliary plexus (crab-eating monkey). x Leakage of resin; a, d, e, g, B, H and thick arrow (see the legends in Figure 2 and 3). Note that the efferent vessel (e) receives a capillary of the outermost layer (g). ×240
Fig. 7. Well developed efferent vessel and its communicating hepatic sinusoids (rhesus monkey). B, H and e (see the legends in Figure 2), double and triple arrows (see text). ×120

Fig. 8. Medium-sized peribiliary plexus and its connecting vessels (rhesus monkey). B, H, a, e, d and thick arrow (see the legends in Figure 2 and 3). ×120
and isolated course without any communication with the portal vein and the hepatic artery.

In the juxtasinusoidal portion of the thicker efferent vessels one often recognized marked constrictions (double arrows in Fig. 7) or circular striations (triple arrows in Fig. 7). This figure was especially conspicuous when the vessel appeared expanded by resin.

The efferent vessels of the peribiliary plexus were divided at the periphery of the portal canal or on the surface of the lobules to supply the hepatic sinusoids. The weak efferent vessels from the smaller plexus drained into only a few sinusoids (Fig. 10, 11), while the efferent trunks from the larger plexus were divided like palms and emptied into a more or less extensive mass of the sinusoids (Fig. 5-7). Except in rare cases where a weak vessel penetrated into a lobule (ee in Fig. 11), the efferent vessels were always connected with the sinusoids on the surface of the lobule. The efferent vessels from the distal end of the plexus ran, together with the final branches of the hepatic artery, a distance along the terminal branches of the portal vein and poured into the sinusoids on the surface of the lobules at the final segments of the portal canal (Fig. 12-14). Even at this terminal portion, the efferent vessels were isolated from the portal vein and also from the hepatic artery.

It was observed that the peribiliary plexus was surrounded by a thin network of fine vessels (Fig. 3). This outermost layer of the plexus, which was indistinct in small plexuses, was supplied by the afferent vessels of the plexus and poured mainly
into the venous network of the outer layer (Fig. 3), though it frequently had direct drainage into the hepatic sinusoids (Fig. 3) and occasionally into the efferent vessels (Fig. 6). No communication was noticed between the outermost layer and the portal vein.

**Discussion**

The present scanning electron microscope study on the vascular casts unequivocally reveals that the peribiliary plexus in the monkey liver receives its afferent vessels from the hepatic artery and emits its efferent vessels directly draining into the hepatic sinusoids. The present scanning microscopy also confirms that this route to the sinusoids via the peribiliary plexus is completely isolated from the route of the portal vein as well as the arterial pathway to the sinusoids. Such direct connections of the peribiliary plexus with the portal vein as described in man, dog, rabbit, cat, rat, monkey and some other animals by Andrews and his associates (Andrews et al., 1949; Lozano and Andrews, 1966), Elias and Petty (1953), Hase and Brim (1966), Mitra (1966) and many other authors were never noticed throughout the material examined in this study. Also the fine network surrounding the

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**Fig. 10.** Small-sized peribiliary plexus and its connecting vessels (crab-eating monkey). $z$ Micro-dissected fragments of the casts; A, B, H, P, a, c, d, e, s and thick arrow (see the legends in Figure 2 and 3). $\times 240$
Fig. 11. Small-sized peribiliary plexus and its connecting vessels (rhesus monkey). A, B, H, e, s, and thick arrow (see the legends in Figure 2 and 3); ee (see text). ×300
Peribiliary plexus and tentatively called the outermost layer in this paper was entirely isolated from the portal vein. Thus, together with the results of Olds and Stafford (1930) who studied the serial sections of the India ink and prussian blue injected liver of man and cat under the light microscope, our findings strongly strengthen the classical view of the “radicular portal veins” (see above). Our findings never support the view of the “internal hepatic radicles” or “internal roots” of Elias and Petty (1953), Mtra (1966) and other authors, nor the mixed views proposed by Andrews and his associates (Andrews et al., 1949; Lozano and Andrews, 1966) and Hase and Brim (1966) (see also above).

Sinusoidal termination of the hepatic artery through the peribiliary plexus described by Elias and Petty (1953) was not encountered.

The present scanning microscope study, moreover, proves that the efferent vessels of the peribiliary plexus are distributed as if they cover deficiencies of the portal supply to the sinusoids. Especially in the large portal canal where the

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**Fig. 12.** Terminal end of the peribiliary plexus and its connecting vessels (crab-eating monkey). $tB$ terminal end of the peribiliary plexus; $A$, $B$, $H$, $P$, $tA$, $e$, $t$ and thick arrow (see the legends in Figure 2 and 3). $\times 240$

**Fig. 13.** Microdissected form of the boxed area in Figure 12. $n$ (see text); $H$, $tA$, $e$ and $t$ (see the legends in Figure 2); $k$, $l$ and $m$ (see Figure 14). $\times 420$
sinusoidal branches of the portal vein are scarce, the thick efferent vessels from the well-developed peribiliary plexus undertake a major supply to the hepatic sinusoids. This importance in sinusoidal circulation of the peribiliary plexus has already been suggested in the rat by Hase and Brim (1966).

Gemmels and Heath (1972) studied ATPase on the microvilli of the bile and pancreatic ducts of secretin-treated sheep and suggested the reabsorption of some constituents of bile through the intrahepatic bile duct. The peribiliary plexus and its efferent vessels may possibly convey such reabsorbed substances. It is well known in man that in some types of the secondary biliary cirrhosis degeneration of the hepatic cells occurs along the peribiliary area. This localized degeneration seems to be explained by the independence of the peribiliary plexus and its efferent vessels. As far as we know, hormone-releasing cells have not been reported in the intrahepatic bile duct.

Some impressions or surface irregularities were noticed in the efferent vessels. Constrictions and circular striations in the efferent vessels of thicker caliber (Fig. 7) resemble the luminal relief of arteries (Fig. 2, 11, 12) and suggest the occurrence of sphincters or muscle fibers in the efferent vessels (cf. Murakami, 1972). Although not noticed in the efferent vessels, round or spindly impressions (n in Fig. 13) and linear marks, probably representing the nuclear protrusions of the endothelial cells.
and the boundaries of these cells, were sometimes observed in the portal vein and the hepatic artery. Other surface structures of the casts were uncertainly interpreted. Such muddy deposits on the casts as indicated by the black arrow in Figure 9 may be the macerated remains of the tissue.

The morphological features of the vascular route from the peribiliary plexus to the hepatic sinusoids exactly meet the criteria of a portal system, as proposed in the title of this paper. Studies are now in progress to elucidate whether the peribiliary portal system evidenced in the monkey may also be the case in other species of mammals, including man.

References


