A Transmission Electron Microscopic Study on Sinusoidal Cells of Guinea Pig Liver, with Special Reference to the Occurrence of a Canalicular System and “Pored Domes” in the Endothelium

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Summary. Hepatic sinusoidal cells in the guinea pig were examined by transmission electron microscopy (TEM). A meandering canalicular system was detected in the sinusoidal endothelial cell both in thicker portions of cytoplasmic extensions and in small areas of the perikaryon. It consisted of meandering canaliculi with vacuolar expansions and constrictions, which penetrated the endothelial cytoplasm, forming as a whole a network. The canaliculi possessed more than two openings which usually communicated with the sinusoid, but occasionally poured themselves into the Disse’s space. This network of canaliculi seems to permit infiltration of blood plasma.

The “pored domes” recorded by FUJITA and his collaborators on the glomerular endothelium of the rat and rabbit kidney were also revealed on the perikaryonal cytoplasm of the sinusoidal endothelium of guinea pig liver.

Osmium-blackened lipid droplets were found in the sinusoidal endothelium, which suggested the release of lipid into the sinusoid. Short-term administrations of excessive vitamin A exerted no influence on the endothelial lipid droplets.

The guinea pig is a rodent species which stores a very small amount of lipid droplets in its fat-storing cells and the so-called empty fat-storing cells were frequently detected. A single cilium was often found in the fat-storing cells in the guinea pig as in other species.

The majority of recent electron microscope studies on the hepatic sinusoidal cells (non-parenchymal cells) have been carried out in rat or mouse livers. Among rodents, however, hepatic sinusoidal cells have been known to vary ultrastructurally from species to species as recently shown by LEEUW et al. (1982b) in their comparative morphological, peroxidase-cytochemical and experimental (latex-bead endocytosis) studies on the Kupffer and endothelial cells in the rat and mouse. Thus, they strongly precautioned against the careless application of rat liver data to other species. The results in vivo obtained by LEEUW et al. (1982b) have further been confirmed by MONTECINO-RODRIGUEZ et al. (1982) in their peroxidase-cytochemical study of isolated and cultured Kupffer and endothelial cells from rat and mouse liver. Also the fat-storing cell of Ito is known to show considerable species differences. The light microscopic studies by Ito and his collaborators have revealed that the fat-storing cell in...
various rodent species maintained in a natural habitat contains variable numbers of small lipid droplets; it has been proved that the amount of these droplets varies from species to species, being generally largest in the rabbit followed by the rat, mouse and guinea pig in descending order (Satsuki et al., 1956; Ito, 1956, 1978). In the present study, we have performed a transmission electron microscope study on the liver sinusoidal cells in the guinea pig, because, so far as we know, they remain largely uninvestigated in this species and we could fortunately obtain some unknown ultrastructures, especially in the endothelial cell.

MATERIALS AND METHODS

Six guinea pigs of both sexes were used. One female animal received a daily subcutaneous injection of a large dose (150,000 I. U.) of vitamin A (retinyl palmitate; Chocola A, Eisai Co., Ltd.) for 5 days before sacrifice. All the animals were anesthetized with an α-chloralose-urethane mixture. After laparotomy, the liver was fixed by perfusion through the portal vein with a cold fixative containing a 2.5% glutaraldehyde and a 0.1M phosphate buffer at pH 7.4, 0°C. Thereafter, the liver was excised and thin tissue slices were cut, under a drop of the fixative, into minute blocks. After 2 hr fixation, the blocks were rinsed several times in a cold 0.1 M phosphate buffer containing 5% sucrose at pH 7.4, and left overnight in the same buffer at 5°C. They were postfixed at 0°C for 90 min by immersion in a 1% OsO₄ solution in a 0.1 M phosphate buffer (pH 7.4). Following dehydration in graded ethanol, the tissues were embedded in Epon 812 and sectioned on a Porter-Blum Ultra-Microtome MT 2-B. The ultra-thin sections were stained with saturated uranyl acetate and Sato’s lead solution. Micrographs were taken with a JEM-100C electron microscope.

RESULTS

1. Sinusoidal endothelial cells

As is widely known, the sinusoidal endothelial cells are composed of the perikaryon—which slightly bulges into the sinusoid—and a membraneous cytoplasmic extension which lines the major part of the sinusoidal wall (Fig. 1). The membraneous cell extension is composed alternately, though not so regularly of thicker portions of variable shapes and sizes, and thinner portions, which, in their thinnest areas (approximately 60 nm thick), form the so-called sieve plates (Wisse, 1970). These are perforated with a cluster of regularly arranged fenestrae or pores, each ranging from 80 nm to 120 nm in diameter (Fig. 4, 5a, 7). As in other species, the guinea pig hepatic endothelium lacks a continuous basal lamina. The nucleus appears oval, spindle-shaped or rounded in profile (Fig. 1a, b, 2). Large sinusoidal endothelial cells embracing two sinusoids on both sides of the perikaryon as shown in Figure 2 have already been demonstrated by us in the avian and monkey liver (Ohata et al., 1982; Tanuma et al., 1983). The cytoplasm of both the perikaryon and the thicker portions of the cell extension contains considerable amounts of flat cisternae of the rough endoplasmic reticulum and has free polysomes widely distributed in it (Fig. 1–3). The Golgi complex is restricted to the perikaryonal cytoplasm on one side of the nucleus (Fig. 2). Fairly numerous and large lysosomes are distributed both in the perikaryonal cytoplasm and in the thicker portions of the cytoplasmic extension; they are generally larger than those of the fat-
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storing cells (Fig. 1, 3a, 5a). The few mitochondria are mostly distributed in the perikaryon, but they can also be detected in the thicker portions. They are as small as those in the fat-storing cells (Fig. 1b, 2, 3). As seen in Figure 4, the so-called smooth-surfaced curved tubules (about 44 nm in thickness), mostly containing an electron dense material, are also revealed both in the perikaryon and in the thicker portions, though not in any remarkable number (Fig. 3, 4, 5a). Occasionally, a considerable number of microtubules are demonstrated running in random directions (Fig. 4), while microfilaments are hardly recognized, probably due to the low magnifications of the microphotographs. Along the sinusoidal surface of the cytoplasm both of the perikaryon and the thicker portions, many coated micropinocytotic caveolae and vesicles are found, ranging in diameter from 90 to 130 nm, while smooth-surfaced ones are conversely lacking.
The perikaryonal cytoplasm sometimes reveals, besides the micropinocytotic structures, the so-called macropinocytotic vesicles (vacuoles) (Wisse, 1972) measuring 500-1,200 nm in diameter, to which we paid close attention in recent studies on the avian (Ohata et al., 1982) and monkey livers (Tanuma et al., 1983). They contain irregularly shaped masses of moderate to high electron density (Fig. 2, 3b, 4).

In four of the six adult guinea pigs examined, the following were revealed in the sinusoidal endothelial cell of the liver: 1) the occurrence of lipid droplets and 2) of the tortuous canalicular system in the cytoplasm as well as 3) the so-called “pored domes” (Fujita et al., 1976; Yoshinari and Fujita, 1982). In TEM preparations, lipid droplets are preserved, moderately blackened by osmic acid. They measure about 700 nm in diameter on an average and appear sporadically both in the perikaryon and in the thicker portions of the cytoplasmic extension (Fig. 1a, 2, 3a, 4, 5, 9). In an exceptional case, a number have been demonstrated in a perikaryonal cytoplasm (Fig. 3a). The lipid droplets appear without any limiting membrane, but elongated cisternae of rough endoplasmic reticulum have been found to closely abut on their surface. The lipid droplets are thought to move or develop gradually in the cytoplasm toward the sinusoidal lumen to eventually bulge into it, making a small dome-like eminence covered with a thin interrupted or fenestrated cytoplasmic sheet (Fig. 5a, b); upon the breakdown of the fenestrated sheet, the lipid droplet opens into the sinusoidal lumen to release lipid into it (Fig. 2).

The tortuous or meandering canalculi usually with beaded expansions and con-
strictions appear mainly in the thicker portions of the cytoplasmic process but may occasionally occur also in the perikaryonal cytoplasm (arrows); it possesses two openings to pour itself into the sinusoid (SN) or into a wide canaliculus, longitudinally penetrating a thick cytoplasmic extension to finally empty itself into the sinusoid. The thin perisinusoidal and sinusoidal walls of this wide canaliculus appear fenestrated (arrowheads). In a there are found many coated vesicles and pits along the sinusoidal surface. D lysosome, F collagen fiber, H hepatocyte, M mitochondria, MV macropinocytotic vacuoles, N endothelial nucleus, PS Disse’s space, X subendothelial process of a fat-storing cell. a: × 14,300, b: × 18,000

Fig. 3. a and b. Endothelial perikarya of the guinea pig liver showing well-developed rough endoplasmic reticulum and free polysomes. In a, many lipid droplets (LD) are present. Both in a and b, a meandering canalicular system with vacuolar expansions is found in the perikaryonal cytoplasm (arrows); it possesses two openings to pour itself into the sinusoid (SN) or into a wide canaliculus, longitudinally penetrating a thick cytoplasmic extension to finally empty itself into the sinusoid. The thin perisinusoidal and sinusoidal walls of this wide canaliculus appear fenestrated (arrowheads). In a there are found many coated vesicles and pits along the sinusoidal surface. D lysosome, F collagen fiber, H hepatocyte, M mitochondria, MV macropinocytotic vacuoles, N endothelial nucleus, PS Disse’s space, X subendothelial process of a fat-storing cell. a: × 14,300, b: × 18,000

Restrictions appear mainly in the thicker portions of the cytoplasmic process but may occasionally occur also in the perikaryonal cytoplasm (Fig. 3a, b, 6a-c, 9). In general, the meandering canalicular system has more than two openings or orifices to join either the sinusoidal lumen, the Disse’s space or both (Fig. 3, 6), which usually make structures. The canaliculi penetrate the thicker portion either along the long axis of (Fig. 6a, b), or at a right angle to it (Fig. 6c), anastomosing with each other in several places to make a network. As seen in Figure 3a, the meandering canalculus present in the
peripheral portion of the perikaryonal cytoplasm of an endothelial cell not only occasionally has an opening for pouring itself into the Disse’s space but can also communicate with a wide canaliculus running along the long axis of a thicker portion arising from the perikaryon to empty itself into the sinusoid. Thin sinusoidal and perisinusoidal walls of this wide and straight canaliculus show a sieve plate appearance. Similar sieve plate-like structures are also observed in the thin sinusoidal and perisinusoidal walls of the canaliculi as shown in Figure 6b.

The “pored domes” observed in the sinusoidal endothelial cell of the liver in the crab-eating monkey (Tanuma et al., 1983), have occasionally been revealed also in that in the guinea pig. Bulging like domes mainly from the perikaryonal cytoplasm into the sinusoidal lumen, they consist of a lucent vacuole on the surface of the cytoplasm and a convex and pored cytoplasmic sheet covering it (Fig. 1b). In these respects the pored domes resemble the above described lipid droplets bulging into the sinusoidal lumen.

2. Fat-storing cells (liocytes, Ito cells)
Fat-storing cells distributed in the Disse’s space are, as is well known, irregular-shaped cells provided with unknown numbers of cytoplasmic processes extending along the
endothelial lining. Segments of the so-called subendothelial processes are detected everywhere in the Disse’s space. As remarked on in the Introduction, fat-storing cells of the guinea pig contain sparse, small lipid droplets in their cytoplasm as well as in their processes (Fig. 7a, b), but there are occasionally those containing a larger amount of lipid droplets. In agreement with the cells of other species, large amounts of cisternae of the rough endoplasmic reticulum are densely distributed throughout the entire cytoplasm of guinea pig fat-storing cells (Fig. 7a), which are occasionally dilated and filled with a flocculent material (Fig. 7b). Mitochondria and lysosomes are generally small and sparse (Fig. 7a, b). A well-developed large Golgi apparatus is found on one side of the nucleus (Fig. 8). A diplosome can be found within the Golgi area which, however, was only scarcely encountered in the present study. In the guinea pig liver, the so-called empty fat-storing cells can frequently be detected. Along the surface of the fat-storing cells, a few coated micropinocytotic caveolae and vesicles as large as those in the endothelial cell are found, but smooth-surfaced ones are rare. Under high magnifications, microtubules are detected running in random directions in the cytoplasm, especially near the diplosome (Fig. 8a, b).

A relatively large round or elongated nucleus with one or two nucleoli is present at differing locations of the cell body. Deep indentations of the nuclear envelope are frequently visible (Fig. 7).

One of the 6 guinea pigs examined received one subcutaneous injection of a large dose (150,000 I. U.) of the retinyl palmitate daily for five days. In this animal the lipid droplet bulges into the sinusoid (SN), making a dome-like eminence, which is covered with fenestrated cytoplasmic sheet. D lysosomes, EL endothelial lining, H hepatocyte, PS Disse’s space, T electron dense curved tubules; the arrow indicates a meandering canalicular system in the thicker portion; the arrowhead indicates a sieve plate. a and b: ×28,000.
droplets in the fat-storing cells increased in number and size. The enlargement of the cell bodies themselves was not conspicuous, but extraordinarily enlarged cells containing numerous lipid droplets of variable sizes were occasionally encountered. In general, the lipid droplets-containing cells appeared to be fairly increased, and the empty ones were conversely decreased. Dilated cisternae of the endoplasmic reticulum filled with a flocculent material were observed. The relationship between the administration of a large dose of vitamin A and the dilation of the cisternae was obscure, since untreated animals showed similar structures.

Here we must notice that the administration of a large dose of vitamin A for a short period appears to exert no influence on the lipid droplets of the sinusoidal endothelial cell.

In the guinea pig liver, fat-storing cells are occasionally provided with a single cilium which develops from the distal centriole of the diplosome into the Disse’s space (SN), and in special cases, also into an indentation induced on the perisinusoidal surface of the hepatocyte (Fig. 8b). In the longitudinal section of the distal centriole, a conical electron-dense basal foot protrudes at the right angle from the midst of the lateral wall of the centriolar tube. In the vicinity of the centriole, many microtubules are found running in random directions (Fig. 8a, b). In the cross section of the centriole, nine sets of triplet fibers are circularly arranged around the centriolar tube. Subfibers C of the nine triplet sets may be preserved insufficiently (Fig. 8a inset).
Kupffer cells

As in other vertebrates, Kupffer cells of the guinea pig are characterized by a striking bulge into the sinusoidal lumen, protruding pseudopodia, large mitochondria, many lysosomes of variable sizes (some found in large phagosomes), well-developed rough endoplasmic reticulum, a large Golgi complex on one side of the nucleus, ingested blood cells (Fig. 9), and coated micropinocytotic caveolae and vesicles. In the guinea pig liver lipid droplets are occasionally found in Kupffer as well as endothelial cells. An extraordinarily enlarged Kupffer cell filled with about ten ingested erythrocytes may be encountered.

Kupffer cells of the guinea pig are anchored, as in other species, on the endothelial lining of the sinusoid by means of the so-called “junctional complexes” (Wisse, 1970) (Fig. 9). The fuzzy cell coat (glycocalyx) on the surface of the Kupffer cells has usually been completely destroyed probably by the unsuitable prefixation with the glutaraldehyde (Fig. 9) (Wisse, 1972). Only exceptional cases may this labile structure of cell surface be partly preserved (Fig. 10 inset). Short segments of the “worm-like structure (micropinocytosis vermiformis)” are detected in many Kupffer cells, but complex ones as shown in the inset of Figure 10 are only rarely found. In the present study, a particular junction other than the junctional complex was revealed between a Kupffer cell and a slender finger-shaped process from an endothelial perikaryon (Fig. 10). A similar connection between a short papillary process from an intrasinusoidal...
macrophage and a corresponding indentation on the surface plasma membrane of a sinusoidal endothelium has been demonstrated in avian livers (OHATA et al., 1982).

DISCUSSION

1. Sinusoidal endothelial cell

For the sinusoidal endothelial cells in guinea pigs, three hitherto unknown unique ultrastructures were revealed in four of the six animals, used in this study, this being
the occurrence of lipid droplets and a canalicular system in their cytoplasm as well as the appearance of the “pored domes” on the perikaryon.

The most important and interesting finding seems to be the canalicular system which appeared both in the thicker portions of the cytoplasmic extension and in small restricted areas of the perikaryonal cytoplasm, usually facing the sinusoidal lumen, though rarely facing the perisinusoidal space. It consisted of tortuous or meandering canaliculi with beaded expansions and constrictions. The tortuous canaliculi penetrate the endothelial cytoplasm in several directions and anastomose with each other to form a whole complex network. This canalicular network is usually provided with more than two openings into the sinusoid and also, less frequently, into the Disse’s space, both of which usually show at their respective orifices a more or less conspicuous structure. As is well known, in the ordinary capillary endothelium many small smooth-surfaced pinocytotic caveolae and vesicles have been revealed in the cytoplasm, the latter of which may be formed by the pinching off of the former. In view of these pinocytotic structures, PALADE (1953) proposed an original hypothesis of “vesicular transport” of colloidal substance across the capillary endothelial cytoplasm (transport in quanta, PALADE, 1960; cytopempsis, MOORE and RUSKA, 1957). Recently, KOBAYASHI
(1970a–c) has reexamined the transport mechanism across the endothelial cytoplasm by observing the capillary endothelial cell of the snake and the ferritin labeled muscle capillary endothelium of the rat and mouse. On the basis of the results, he proposed a hypothesis of "transport in continuum." According to this, caveolae or invaginations of the plasma membrane engulf substance and form, by its pinching-off vesicles, which, being linked by two or more, make channels through the endothelial cytoplasm, which transport and discharge engulfed substances in the capillary lumen into the periendothelial space. In these channels, diaphragms are observed both at the orifices of caveolae and at the constricted portions corresponding to the sites of fusion of the vesicles; they are presumed to serve for filtration of materials passing through the channels (Kobayashi, 1970a–c). In the TEM preparations, the channels penetrating through the ordinary capillary endothelial cytoplasm may simulate vesicles according to the direction of the section plane. Recently Simionescu et al. (1975) performed an experimental study on the capillary permeability in the rat diaphragm and showed evidence for the existence of patent transendothelial channels, thus supporting the hypothesis by Kobayashi. The meandering canaliculi found in the sinusoidal endothelium of the guinea pig may possibly be different from the channels in the ordinary capillary endo-

Fig. 10. Peculiar junction between the swollen terminal portion of a thin cytoplasmic process protruded from the endothelial perikaryon (EC) and a corresponding indentation induced on the sinusoidal surface of a Kupffer cell (KU); between the plasma membranes limiting these two structures an electron dense junction is seen. D lysosome, E erythrocyte, G Golgi complex, H hepatocyte, M mitochondria, PS Disse's space, RER rough endoplasmic reticulum, SN sinusoid. ×16,800. Inset. A large, complicated worm-like structure occupying a part of the cytoplasm of a Kupffer cell. On the sinusoidal surface of the upper part of this cell, faint remnants of cell coat are preserved. ×12,400
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theleum elsewhere, with regard to their indefinite calibers (90-180 nm in diameter), being unrelated to the coated caveolae and vesicles, which are the exclusive pinocytotic structures of the hepatic sinusoidal endothelial cells devoid of ordinary smooth surfaced ones (WisE, 1970). They have more than two openings into the sinusoidal lumen and occasionally also into the Disse’s space. Further, they are provided with no diaphragms at their somewhat narrowed openings and constricted portions. The tortuous canaliculi forming complex networks in the sinusoidal endothelial cytoplasm may possibly serve as bypaths or diverticuli of the hepatic sinusoid, permitting only a slow passage or retention of the blood plasma. For example, in the case of hypertension of the sinusoidal blood; some amount of the blood plasma may be discharged directly into the Disse’s space.

It is unknown whether the meandering canaliculi in the sinusoidal endothelium might be a steady and unchangeable structure or disappear owing to physiological conditions, and then reappear in response to need, as does the worm-like structure in Kupffer cells.

The above mentioned tortuous canaliculi in the thicker portions of the guinea pig sinusoidal endothelium seem to have already been detected also in corresponding portions of the rat’s liver, as indicated in the following description by WisE (1970): “The sieve plates are not always of a simple single-layered type, but sometimes, a sponge-like network with no resemblance to the single-layered sieve plates (Fig. 4 of WisE).” His sponge-like network might correspond, in profile, to the meandering canaliculi running tortuously through the thicker portion of the endothelial extension of the guinea pig.

Drochmans et al. (1977) observed for the first time, by TEM and SEM, isolated and cultured rat liver sinusoidal endothelial and Kupffer cells, and in the cytoplasm of the former, found an “extensive tortuous vacuolar system,” which showed many pores on the outside through which tracers might penetrate into the vacuolar system. Since the publication of this observation, many investigators have electron microscopically examined isolated and cultured hepatic sinusoidal endothelial cells from rat and mouse liver and found, in the endoplasm of usually round cell bodies, an “extensive network of fenestrations” or a “well-preserved group of fenestrae,” which might correspond to the extensive tortuous vacuolar system reported by Drochmans et al. (1977) (Garvey and Caperna, 1982; Leeuw, et al., 1982a; Montecino-Rodriguez et al., 1982; Nagelkerke et al., 1982; Roos et al., 1982). As can obviously be deduced from the microphotographs of the isolated endothelial cells by these authors, the designations “extensive network of fenestrations” or “extensive tortuous vacuolar system” or “group of the fenestrae” might not sufficiently visualize the structures contained in the endoplasm of the isolated endothelial cells, because the images of the fenestrations of the endothelial sieve plates have almost completely been lost. Rather, it seems more suitable to designate them as “networks of tortuous or meandering canaliculi with vacuolar expansions.” The meandering canalicular components might correspond to the tortuous canaliculi penetrating the thicker portions of the endothelial extension and also those penetrating the endothelial perikaryon of the guinea pig liver. The isolated endothelial cells might be contracted to make a cell rounded and in consequence, a canalicular system would be concentrated to a narrow endoplasm of the rounded cell bodies, making an extensive network together with the fenestrations of the sieve plates, with many openings on the outside of the cell. In the rodent and other mammalian species, the endothelial cell might have the ability to produce canaliculi in the cytoplasm from unknown stimuli such as isolation just as the Kupffer cells produce, under unknown
stimuli, a fairly complex tortuous canalicular system called a "worm-like structure" with many openings on the outside facing the sinusoid.

The occurrence of lipid droplets both in the perikaryonal cytoplasm and in the thicker portions of the cytoplasmic extension of the sinusoidal endothelial cells might also be an exceptional finding as it has been scarcely reported on in existing literature. They were preserved as osmium-blackened droplets, different from vacuolar lipid droplets in the fat-storing cell. Short-term administration of large doses of vitamin A did not exert any influence on them. They showed, however, morphological signs suggestive of the release of lipid into the sinusoid by developing towards it and by bulging therein as a dome-like eminence usually enclosed by a fine interrupted or pored cytoplasmic sheet which could occasionally rupture in the sinusoid to release lipid in the latter.

Tanuma and Ito (1978) were the first to notice the so-called "smooth-surfaced, curved tubules," mostly containing an electron dense material in the bat liver endothelial cytoplasm, and thereafter confirmed them again in the kitten, bird and monkey (Tanuma et al., 1981; Ohata et al., 1982; Tanuma et al., 1983) though any speculation as to their function. Recent experimental studies by Praaning-Van Dalen et al. (1982) and Yokota and Fahimi (cited by Fahimi, 1982) have examined the ultrastructural characterization of endocytotic mechanisms in rat liver Kupffer and endothelial cells, and revealed that horseradish peroxidase is taken up into both Kupffer and endothelial cells by bristle-coated micropinocytosis, and that coated pits might be involved in the selective uptake of the molecules by absorptive (receptor-mediated) pinocytosis. In these instances, the ingested horseradish peroxidase was transported to the macropinocytotic vesicles (Wisse, 1972). The tubular structures possibly identical with our smooth-surfaced curved tubules were involved in transporting ingested material to the macropinocytotic vesicles. Thus, these questionable tubular structures of the hepatic endothelial cells in the bat, kitten, bird and monkey have been shown to be identical with the "transfer tubules" observed by the above authors.

By using a scanning electron microscope (SEM), Fujita et al. (1976) revealed, in a fenestrated glomerular endothelial sheet (lamina fenestra or areolae fenestratae) of the rat kidney, domes and shelves formed of a fenestrated cytoplasmic sheet above the ordinary level of the endothelial lining, and proposed a hypothesis that they might be formed by the anastomosis of microvilli and thus be involved in the replacement of depleted parts of the areolae fenestratae. Thereafter, Yoshinari and Fujita (1982) used SEM to observe the glomerular endothelium in the rabbit kidney, and revealed the domes both on the areolae fenestratae and on the perikaryonal swelling, designating them as the "pored domes." In their TEM studies Wolff (1966) and Wolff and Merker (1966) had earlier demonstrated the "pored domes" of Yoshinari and Fujita (1982) and presumed that they might have been produced by formation of larger vacuoles in the endothelial cytoplasm and by the atypical opening of pores into them. As for the formation mechanism of the pored domes, Yoshinari and Fujita (1982) discarded the anastomosing-microvilli hypothesis, based on the SEM observation of rabbit glomerular endothelium which is characterised by the scantiness of the microvilli, and instead suggested a mechanism similar to that of Wolff (1966) as well as Wolff and Merker (1966), describing them as appearing to consist of a pored cytoplasmic plate covering a cavity in the endothelial cytoplasm. Yoshinari and Fujita (1982) presumed that the superficial cytoplasm of the glomerular endothelium has an ability or tendency to form pored plates. Our previous TEM study demonstrated the pored domes on the perikaryon of the sinusoidal endothelial cell of the monkey liver (Tanuma et al., 1983);
the present TEM study showed the same structures on the sinusoidal endothelial perikaryon of the guinea pig, and confirmed their identical structure and appearance with the pored domes on the glomerular endothelium of the rat. In the hepatic sinusoidal endothelium, however, they rarely appear on the thinner portions of the cytoplasmic extension, which usually form sieve plates corresponding to the areolae fenestratae of the glomerular endothelium.

As assumed by Yoshinari and Fujita (1982), the causes which might induce the formation of the pored domes and their functions remain unknown. One suggested possibility is that they might be hollow structures comparable to the meandering canaliculi found in the cytoplasm of the thicker portions and the perikaryon of the hepatic sinusoidal endothelium, which are often lined with fenestrated cytoplasmic layers.

The pored domes and lipid droplets in the guinea pig sinusoidal endothelium may be different structures although both are covered with a convex pored or fenestrated cytoplasmic sheet. The superficial cytoplasm of the sinusoidal endothelium may also have an ability or tendency to make pored membranes as has been suggested in the glomerular endothelium of the kidney (Yoshinari and Fujita, 1982).

2. Kupffer cells

As in other animal species, Kupffer cells of the guinea pig liver were provided with ultrastructural characteristics of fixed hepatic macrophages, connected to the endothelial lining by means of the so-called junctional complexes of Wisse (1970). But there are opinions contrary to this which claim that Kupffer cells are attached to the endothelium with cytoplasmic processes that pass through the fenestrations or penetrate the cytoplasm of endothelial cell extending into the Disse’s space (Fahimi, 1982). The junctional attachment between the two cell types has been refuted (Jones and Summerfield, 1982). A complex “worm-like structure” was confirmed only in a few cases, although its short segments have often been detected. Recent studies report that the complex worm-like structures have been retained in isolated and cultured Kupffer cells (Brouwer et al., 1982; Leeuw et al., 1982). These results may agree with the maintenance or appearance of a canalicular system in the endothelial cytoplasm in isolated and cultured states, as described above.

3. Fat-storing cells

The most important metabolic activity of the fat-storing cells consists in their involvement in the vitamin A metabolism and storage (Goodman, 1980). The present study has revealed that in one guinea pig, the daily receiving of a subcutaneous injection of large doses of retinyl palmitate for five days increased considerably the number and size of lipid droplets stored in the fat-storing cells on one hand, producing strikingly hypertrophic cells, while on the other, the so-called empty fat-storing cells decreased (Ito, 1978). These findings possibly support the view that the cells might be involved in storing increased amounts of lipid droplets to incorporate the excess vitamin A from the hypervitaminotic blood for the purpose of the defense of the body from toxic substances.

Since Ito and Shibasaki (1968) first revealed, in the fat-storing cells in the normal human liver, the sensory or solitary cilium which developed from the distal centriole of the diplosome located within the Golgi apparatus into the Disse’s space, it has been found in a vast variety of vertebrate species and is now considered to be a non-motile sensory cilium or chemoreceptor (Wake, 1971; Yamamoto, 1975; Yamamoto and
ENZAN, 1975; TANUMA and ITO, 1978, 1980; OHATA et al., 1982; TANUMA et al., 1983). Recently KNOOK and LEEUW (1982) have succeeded in the isolation and purification of fat-storing cells from the rat liver, and have produced a detailed morphological and chemical characterization of them. In their paper, they have described a single cilium’s development from the distal centriole of the diplosome in the isolated fat-storing cell.

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