Department of Anatomy (Prof. T. FUJITA), University of Niigata School of Medicine, Niigata
and Department of Anatomy (Prof. H. OURI), Okayama University School of Medicine,
Okayama, Japan

Microcirculation of Monkey Pancreas with Special Reference to the Insulo-Acinar Portal System. A Scanning Electron Microscope Study of Vascular Casts

Tsuneo FUJITA and Takuro MURAKAMI

Received February 5, 1973

Summary. Methacrylate casts of the pancreatic blood vessels of the monkey were observed under the scanning electron microscope. Microdissection and scanning of the casts were repeated in order to examine the deeper parts of interest successively.

It was demonstrated that a vas afferens, a branch of the intralobular artery, enters deep into the islet which is represented by a three-dimensional net of irregularly swollen capillaries. The termination of the vas afferens at the center of the islet in the monkey was discussed in relation to the central position of A cells in this animal.

From the periphery of the islet numerous vasa efferentia radiate into the exocrine tissue to be connected, at a certain distance, with the capillary network of the latter. They are referred to as insulo-acinar portal vessels as they convey the islet hormones to their first target tissue, the exocrine pancreas.

The capillaries in the exocrine part are gathered into numerous venules whose confluent forms the intralobular vein.

The vas afferens of the islet only occasionally issues a branch directly supplying the exocrine tissue. Otherwise, the latter tissue receives all its blood through the capillaries of the islet.

Using the pancreas of the horse, rabbit and some other animals arterially injected with India ink, one of the authors (T. F.) demonstrated that the pancreatic islet is supplied by a special arteiole, the vas afferens, and the exocrine pancreas receives almost its entire blood supply from the islet via vasa efferentia which comprise a route of hormone transport to be called the insulo-acinar portal system (FUJITA, 1973). This fact which had been reported more or less correctly in some early papers (WHARTON, 1932; THIEL, 1954) but recently has been considered only by occasional authors (HENDERSON, 1969) was evaluated anew under the light of knowledge about the nature of islet hormones acting upon the exocrine function of the pancreas (FUJITA and WATANABE, 1973).

In this paper, a more convincing demonstration and precise analysis of the islet microcirculation was attempted by adopting a new technique recently established by another of the authors (T. M.). It is a combination of plastic casting of blood vessels and scanning electron microscopy and has already been shown incomparably useful for the studies of microcirculation of organs especially in the gut, liver (MURAKAMI, 1971) and kidney (MURAKAMI, MIYOSHI and FUJITA, 1971).

Material and Method

Methyl methacrylate was arterially injected in the pancreas of an adult male

rhesus monkey (3-year-old) and, after polymerization by heat, the tissue was corroded in NaOH (for details of the technique see: MURAKAMI, 1971; MURAKAMI, MIYOSHI and FUJITA, 1971).

The plastic casts of the blood vessels thus obtained were trimmed with a razor blade and dissected under a stereoscopic microscope in order that the parts of interest might be exposed. The specimens were then coated with gold in a vacuum evaporator and observed in a scanning electron microscope, Hitachi SSM-2, with an accelerating voltage of 10 kV.

After observation in the scanning electron microscope, some casts were further dissected with sharp forceps to remove vessels disturbing the view of deeper structures. These specimens were coated with gold and observed in the scanning electron microscope. In some casts, this procedure of microdissection, coating and scanning was repeated several times (Fig. 1).

Fig. 1. Vascular cast of the monkey pancreas seen under the scanning electron microscope. The intralobular arteries (A) and vein (V) in Figure a which hinder the view of the islet of Langerhans (L) were removed one after another by microdissection (Figures b and c). The vas afferens (a) were broken by this dissection leaving a piece entering the islet. Numerous vasa efferentia (e) are seen radiating from the islet. Leakage of methacrylate is indicated by X in Figure a. $\times 200$

Fig. 1.

The pancreas of another adult individual was fixed in Bouin or GPA (SOLCIA, VASSALLO and CAPELLA, 1968) and paraffin sections were stained by aldehyde fuchsin-trichrome or by silver impregnation of HELLMAN and HELLERSTRÖM (1960).

Results and Discussion

The casting substance was judged to have filled every vessel, including capillaries, of the pancreas. The high resolution and large depth of field in scanning electron microscopy afforded much more precise analysis of the three-dimensional extensions and connections of vessels than in the previous method by light microscope observation of dye injected materials. Moreover, microdissection of the plastic casts proved to be highly useful in this kind of study. Figures 1a, b and c, for instance, demonstrate how an islet with its afferent and efferent vessels was exposed by removing the overlying vessels one after another.

Fig. 2. Closer view of the cast of the islet shown in Figure 1c. *a* Vas afferens, *e* vasa efferentia. $\times 400$

The description will now be concentrated on the microcirculation through islets of Langerhans which were identified as such by their glomus-like capillary net, either exposed or lying behind the relatively wide meshes of capillaries in the exocrine pancreas (Fig. 2-4).

The intralobular artery branched into arterioles which were each destined to an

islet (Fig. 1a). This corresponds to the previous findings by the dye injection methods in some other animals such as the rabbit (WHARTON, 1932; FUJITA and WATANABE, 1973), horse (THIEL, 1954; FUJITA, 1973) and man (TERBRÜGGEN, 1948).

The end-arteriole or vas afferens of the islet was often considerably long and it usually was straight. In the course of the arteries one may only rarely find a small branch which apparently does not supply an islet but directly supplies the exocrine tissue. A side branch of this category issuing from a vas afferens some distance before the islet is shown in Figure 4. The occurrence of arterial branches directly supplying the exocrine tissue is, however, difficult to judge. In the case of this Figure, one may not exclude the possibility of that side branch passing a small islet tissue before being distributed to the exocrine tissue. Important is the fact, in any case, that the exocrine pancreas receives its blood supply to a great degree, if not exclusively, from the arteriole to the islet and the capillary bed of the latter.

Fig. 3. Islet of Langerhans with its winding and swollen capillaries. Numerous vasa efferentia (*e*) are seen some of which are broken (*x*). Constrictions may be seen at the beginning of the efferent vessels (arrows). $\times 700$

The vas afferens enters, usually more or less deeply, to the core of the islet capillary. In the case of Figure 2 it penetrates the islet with a twisted course. In Figure 4 it follows a straight line to reach the islet core to be divided abruptly into several capillaries. The termination of the vas afferens at the islet center is considered to be correlated to the islet cell distribution within the islet in this animal. In the monkey the A cells tend to occupy the core of the islet, whereas the B cells, the periphery of

it (Fig. 5a). The D cells which are clearly detected by silver impregnation (FUJITA, 1968) are distributed more randomly but never gather on the border of the islet (Fig. 5b). A similar central termination of the islet arteriole occurs in the horse whose islet is characterized by a central position of the A cells (THIEL, 1954; FUJITA, 1973), whereas its peripheral termination is common in the rabbit islet whose A cells are gathered in the periphery of the islet.

Fig. 4. A smaller islet (*L*) supplied by a vas afferens (*a*) and emitting numerous vasa efferentia (*e*). A branch marked *x* apparently is destined directly to the exocrine tissue. $\times 350$

The above description in the monkey seems to support the hypothesis proposed by FUJITA (1973) that the arteriole ends at the site of the A cells in order to take up and convey their hormone, glucagon, to the B cells whose insulin release has recently been known to be stimulated by glucagon. The correlation of vascular pattern and A cell distribution in the islet of different animals had been noticed by THIEL (1954), but she could not suggest its physiological significance.

The sinusoidal capillaries of the islet were twisted and branched to form a complicated three-dimensional network. They are irregularly swollen in many portions. The previous method of dye injection has not been useful for the analysis of the capillary connections within the islet and the descriptions of authors diverge especially on the occurrence or non-occurrence of capillary blind ends. WHARTON (1932), for instance, described blind capillaries in the rabbit, whereas THIEL (1954) recognized

them often in the guinea pig but few of them in other animals. The present scanning electron micrographs indicate no blind ends in the capillary network of the monkey islet (Fig. 2, 3).

The peripheral capillaries of the islet issue a corona-like radiation of numerous thin vessels, vasa efferentia. One or a few constriction on the cast may occur at the beginning of the radiations (Fig. 3). The significance of these constrictions is unknown. It seems that a sphincter has never been described as occurring there. The efferent vessels run a relatively straight course for a certain distance (50–150 μ) and, except for occasional dichotomical divisions, are not anastomosed with each other.

Fig. 5. Paraffin sections of monkey pancreas stained by aldehyde fuchsin-trichrome (**a**) and by Hellman-Hellerström's silver impregnation (**b**). Figure **a** indicates that the dark B cells of the islet surround the light core mainly composed of A cells. Figure **b** shows that the dark D cells are distributed relatively randomly in the islet. $\times 500$

THIEL (1954), who described the vasa efferentia of the horse, rabbit and some other mammals in detail, counted 12–15 efferent vessels in islets of moderate size and up to 35 in especially large islets. In the monkey islets of moderate size shown in Figure 2 one may count no less than 25 efferent vessels and if one takes into account the removed vessels in the front and the hidden ones in the back of the islet, the vessels will exceed 50 in total. The significance of the efferent vessels comprising the hormone transport route called the insulo-acinar portal system has been discussed elsewhere (FUJITA, 1973; FUJITA and WATANABE, 1973) and will not be repeated here.

The peri-insular zone with its radiation of efferent vessels appears relatively empty because of its looser vascular distribution. This corresponds to the clear peri-insular zone ("heller Hof" or "periinsulare, relativ kapillarmarme Zone") noticed by THIEL (1954) in the India ink injected materials. The peri-insular space tends to be less conspicuous in smaller islets as the radiary vessels are short there.

The vasa efferentia are connected with the capillary net of the exocrine pancreas which forms round or polygonal meshes apparently corresponding to the spaces which should have been filled by individual acini and ductules.

The exocrine capillaries drain into gradually thicker roots of venules which are gathered into a thick intralobular vein. After running a certain distance towards the proximal pole of the lobule, this vein first begins to accompany its arterial partner, the intralobular artery. As correctly pointed out by THIEL (1954), however, the veins of the pancreatic lobules are irregular in their course and they often do not accompany an intralobular artery at all.

サルの膵臓の微小循環、とくに膵島—腺房門脈系について.

走査電子鏡による血管鑄型の研究

藤田 恒夫 と 村上 宅郎

アカゲザル膵臓の血管のメタクリレート鑄型を走査電子鏡で観察した。鑄型の微小解剖と電子鏡観察とをくりかえして、順次深部の構造を観察することができた。

小葉内動脈の枝が1本ずつ膵島にはいる。膵島は不規則に膨隆する毛細血管の三次元的網工から成るが 上記の輸入血管は深く侵入して その中心部に終る。このことは、サルのA細胞が島の中心部を占めることに関連している。

膵島の周縁から多数の輸血管が外分泌部へ放散し、ある距離を走ってのち、その毛細血管網につながる。この血管は島ホルモンを その最初の標的組織である膵外分泌部へ輸送するみちで、膵島—腺房門脈とよぶべきものである。

外分泌部の毛細血管は多数の小静脈に移行し、これは小葉内静脈に集められる。

膵島の輸入血管は時に小枝を直接外分泌部に与えることがある。しかしこれを除外すれば、外分泌部が受ける血液は すべて島の毛細血管から来ることになる。

References

- Fujita, T.: D cell, the third endocrine element of the pancreatic islet. Arch. histol. jap. 29: 1-40 (1968).
———: Insulo-acinar portal system in the horse pancreas. Arch. histol. jap. 35: 161-171 (1973).
Fujita, T. and Y. Watanabe: The effects of islet hormones upon the exocrine pancreas. In: (ed. by) T. Fujita: Gastro-entero-pancreatic endocrine system—A cell-biological approach. Tokyo, Igaku Shoin, 1973. (p. 164-173).
Hellman, B. and C. Hellerström: The islets of Langerhans in ducks and chickens with special reference to the argyrophil reaction. Z. Zellforsch. 52: 278-290 (1960).
Henderson, J. R.: Why are the islets of Langerhans? Lancet 7618: 469-470 (1969).
Murakami, T.: Application of the scanning electron microscope to the study of the fine distribution of the blood vessels. Arch. histol. jap. 32: 445-454 (1971).

- Murakami, T., M. Miyoshi and T. Fujita:** Glomerular vessels of the rat kidney with special reference to double efferent arterioles. A scanning electron microscope study of corrosion casts. *Arch. histol. jap.* 33: 179-198 (1971).
- Solcia, E., G. Vassallo and C. Capella:** Selective staining of endocrine cells by basic dyes after acid hydrolysis. *Stain Technol.* 43: 257-263 (1968).
- Terbrüggen, A.:** Untersuchungen über Inselapparat und Inseladenome des Pankreas, insbesondere über die Zelltypen bei Diabetes mellitus und Spontanhypoglykämie. *Virchows Arch.* 315: 407-460 (1948).
- Thiel, A.:** Untersuchungen über das Gefäß-System des Pankreasläppchens bei verschiedenen Säugern mit besonderer Berücksichtigung der Kapillarknäuel der Langerhansschen Inseln. *Z. Zellforsch.* 39: 339-372 (1954).
- Wharton, G. K.:** The blood supply of the pancreas, with special reference to that of the islands of Langerhans. *Anat. Rec.* 53: 55-81 (1932).
-

藤田 恒夫
〒951 新潟市旭町 1
新潟大学医学部
第三解剖学教室

Dr. Tsuneo FUJITA
Department of Anatomy
Niigata University School of Medicine
Niigata, 951 Japan