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The terminal distribution of the hepatic artery

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Abstract

The following conclusions were arrived at on the terminal distribution of the hepatic artery and its microscopical structures in the experiments conducted with the livers from human adult, fetus, dogs and toads, to which were given plastics, Indian ink and Indian-ink shock injections into their hepatic blood vessels. 1. There are arterial anastomotic networks of vasa vasorum in the portal wall. 2. The intralobular arterioles (Elias) and the extralobular arterioles (WEATHERFORD) often arise as direct branches without passing through the periductal arteriolar plexus. In the peripheral zone of the liver, this constitutes the main type of origin. 3. Besides the anastomoses between the intralobular arterioles of the adjacent lobules (Fig. 5), the periductal arteriolar plexus of the bile ducts to the neighboring lobules are interconnected by arterial branches surrounding the interlobular vein ("neighboring arteriolar anastomoses" by the author) (Figs. 2, 5). 4. The terminal arterioles reveal a curve and an isthmus (Figs. 1, 3, 5), where they are supposed to have epithelioid cells in the media. 5. The hepatic vein wall is supplied by the branches of the internal thoracic and phrenic arteries. These anastomose with the interlobular arteries in the interdigitation area of vessels. 6. In the toad the terminal distribution is of a simpler form, in which the arterial capillaries, with an S or a parabolic curve, being constricted by the marginal hepatic cells, join the sinusoid in capillary form. 7. In human fetus of the middle stage (Figs. 6, 7), most of the terminal arterial capillaries open directly to the interlobular hemopoietic tissue, and from there the blood flows into the sinusoid. The precapillaries have an S curve and an isthmus, where they have 3 or 4 primordial epithelioid cells. In other portion, the precapillaries form endothelial canals with little adventitia and open infundibularly to the hemopoietic tissue. These have been proved by the Indian-ink shock injection method. 8. In the fetus of the later stage (Figs. 8-11), with the reduction of interlobular hemopoietic tissue, its arterial branches become fewer, and many branches are connected directly to the hepatic sinusoid. They form a sharper S curve and an isthmus, where 4 or 5 epithelioid cells are differentiated. The arterial terminal branches are precapillaries of endothelial canals having little adventitia and no media muscle. 9. The subcapsular branches of the peripheral interlobular arteries anastomose with one another. Besides these, subcapsular branches come around the hilar region from the hepatic artery, furthermore some are derived from the biliary, inner thoracic, diaphragmatic, intercostal, subcostal, suprarenal and renal arteries. Anastomoses are found between all the subcapsular branches of different origins.

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THE TERMINAL DISTRIBUTION OF THE HEPATIC ARTERY

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There are numerous reports on the intrahepatic vascularization today. As far back as in 1654 GLISSON[18], and later HYRTL[21](1873), REX[39](1888), MELNIKOFF[31] (1924), and ARAI[1,2] (1937—1947) studied it by means of corrosion specimens of plaster, celloidin and celluloid-aceton; BRAUS[6] (1921) with wax reconstruction; while MALL[28](1906), PFUHL[36,37,38] (1921, 1922), ZIMMERMANN[45](1923), LÖFFLER(1927), AUNAP[3](1931), ARAY(1932), and CLARA(1934) with histological specimens. In addition, there are roentgenological studies by KASAHARA[23] (1931), HJORTSJÖ[20] (1951) and FAINSINGER (1950). More recently ELIAS[10—17] *et al.* (1949, 1952, 1953) made reports on subgross anatomy, which they studied histologically by means of wax-reconstruction models, coloring matter injection and vinylite-plastics-injected corrosive specimens, and also on the terminal distribution of the hepatic artery. WAKIM and MANN[42,43](1942, 1953) and KNISELY *et al.*[24,25,26](1939, 1947, 1948) conducted vital observations by the transillumination method. However, opinions on the terminal distribution of the hepatic artery are still divided. Of them WEATHERFORD's[41] (1944) papers on the existence of the periductal arterial capillary network (plexus) and the extralobular arterioles or capillaries, and ELIAS's[10,11,14,15,16,17] (1949—1953) findings that the intralobular arterioles or arterial capillaries arise from the periductal arterial (capillary) plexus, both based on Indian-ink specimens, have particularly advanced the research works in this field. Moreover, there are studies on "Arterienwülste", or "Intimapolster" by PFUHL[36,37,38] (1921, 1922), MÄRK[29,30](1941—1951) and CONTI (1947), studies on "epitheloidzelliges Polster" or "Knospen" by MÄRK[29,30](1941—1951), CORONINI[9] (1956) and BARGMANN[4] (1951).

With the purpose to elucidate the characteristic terminal distribution of the hepatic artery, the author conducted a series of experiments with livers from human adults and fetuses, dogs and toads and studied embryological differentiation and fine structures of the hepatic arterial system.

MATERIALS AND METHODS

Two human adults, 131 fetuses, 46 dogs and 27 toads were used.

Livers of one human adult and the greater part of the dogs were injected *in situ* with acrylic resin, according to the method by TANIGUCHI *et al.*[40,41] (1952, 1955). Injection masses, each different in color, were injected into, in the order of the hepatic vein, the portal vein, the hepatic artery or the coeliac axis and the hepatic duct. In the case of the dog materials the injection of the minute vessels was not always successful, because of the technical difficulties.

One human adult and some dog materials were injected with Indian ink containing 10% gelatine. Sections were cut at 50—200 μ. In many fetuses the author tried to obtain adequate specimens for the study of the terminal arterial distribution, but in vain. The Indian-ink masses filling the hepatic sinusoid and diffused in the hemopoietic tissue made the observation of the minute vessels entirely impossible. At last, the author employed a short time injection ("shock-injection method" devised by himself). In this procedure the injection must be finished in a very short time (ordinarily several seconds), i. e. within the period where the subcapsular vessels begin to stain slightly. Sections were cut at 8—10 μ, and counterstained with hematoxylin and eosin. Then the Indian-ink particles were seen attached chiefly to the inner surface of the endothelium, and thus it facilitated the tracing of pattern and fine structures of the minute vessels. Even this method, however, rather rarely offered good results. Therefore, the author had to inject a large number of materials and to section them at random. Besides, hematoxylin-eosin specimens from each embryonal stages were used for the general histological observation. Indian-ink shock injection was also applied to a few dog materials.

Toads were intra-peritoneally injected with lithion-carmine solution, 2 cc daily. After 7—10 days, when the cornea and the skin were stained sufficiently with the dye, the animals were sacrificed. These were counterstained with hematoxylin.

RESULTS AND DISCUSSION

Arterial vascularization of the portal veins and the bile ducts

The portal wall is supplied by branches of the hepatic artery. In the adventitia every two or three arterial branches running along the vein anastomose in the forms of the letters N, H, and A. This was observed in the corrosion specimens of human adult as well as in those of human fetus and dog. In the hilar region the arterial branches of the media are well developed and form a fine network, as REX[39] (1888) reported long ago.

On the wall of larger and medium biliary ducts, the arterial branches of

the interlobular artery are distributed in two layers: the periductal arterial plexus in the submucous tissue and the sub-epithelial periductal arterial capillary plexus. Whereas on the wall of minute ducts, they are consisted of a single layer. These findings, nearly identical with those of WEATHERFORD and ELIAS, were obtained in the observations of corrosion and Indian-ink specimens.

In the hilar region the portal wall, the periductal plexus and the interlobular connective tissue are supplied by common branches arising from the hepatic artery. Nevertheless, the periductal plexus and the arterial network of the portal wall are rather independent, except some interconnections in between. In the intermediate and peripheral zones of the liver, however, the periductal plexuses surrounding two or three bile ducts to the neighboring lobules, which run together in the interlobular tissue, are interconnected by arterial branches surrounding the interlobular vein. The author designates it as the "neighboring arteriolar anastomosis" (Fig. 2). The connection between neighboring periductal plexuses appears as a two- or three-link chain, holding the duct or the vein within each link (Fig. 4).

The walls of the sublobular and collecting veins are supplied with arterial branches of the internal thoracic and phrenic arteries, which descend along the hepatic veins as vasa vasorum. They anastomose with the interlobular arteries, in the interdigitation area where the branches of the portal vein, the interlobular arteries and the bile ducts are interwoven with the branches of the hepatic veins.

Terminal branches in the perilobular portion are of two kinds, as described by previous workers (Figs. 1—4).

a) *Extralobular arteriole or arterial capillary* (*WEATHERFORD*) opens to the sinusoid directly on the surface of the hepatic lobule.

b) *Intralobular arteriole or arterial capillary* (*ELIAS*) penetrates into the lobule and opens to the inner part of the sinusoid.

WEATHERFORD and ELIAS state that the extralobular and intralobular arterioles and arterial capillaries arise from the periductal arterial plexus. However this is true only in part, according to the author's own observation with corrosion specimens. Thus, the arterioles and arterial capillaries may arise directly from the main arterial stem (Figs. 1 and 3). Moreover, their pattern shows regional differences. In the intermediate zone of the liver, they arise mainly from the periductal plexus, which is the standard pattern of their origin (Fig. 1). While in the peripheral zone where the periductal plexus is not conspicuous, direct origin from the interlobular artery predominates. In the hilar region, also, main source of the arterioles and arterial capillaries is the periductal plexus, but not a few come directly from the common branches supplying the ducts and vessels.

The intralobular and extralobular arterioles have an S curve (20 μ in dia-

meter with) isthmus (7—10 μ) where they pass the interlobular connective tissue (Figs. 1, 3, 5). The intralobular arterioles are distinguished into two, the superficial and deep ones, by the portion of the sinusoid they open to (Fig. 5). The superficial intralobular arterioles join the outer zone of the sinusoid, while the deep ones open to the deeper zone. These arterioles or arterial capillaries anastomose with those of the neighboring lobules, where the interlobular connective tissue is missing (Fig. 5).

MÄRK[29,30] (1941, 1951), CORONINI[9] (1956) and BARGMANN[4] (1951) found epithelioid cells in the wall of the terminal arterial branches. WAKIM[42,43] and BAGGENSTOSS (1953) and MONTAGNANI[33] (1953) state that the arterio-portal anastomoses, i. e. connections between the terminal branches and the sinusoid, possess in substance the qualities of the arterio-venous anastomosis, and that histologically they are precapillaries consisted of an endothelial canal, which has little adventitia and no media muscle. The above-mentioned S curve and isthmus presumably correspond to the locus, where epithelioid cells are situated. The condition in the fetus, where epithelioid cells are found just at the curve and isthmus, strongly suggests this view (see below).

In the toad (*lithion-carmine vital staining*) the terminal distribution of the hepatic artery is much simpler. The terminal arterial branches are constricted by the outermost hepatic cell cords, just before they open to the sinusoid. Here they are precapillaries or capillaries and describe an S curve or a parabola.

Terminal arterial branches in the fetus were studied with the use of Indian-ink shock injection specimens. It was in the middle fetal stage (5—7 months) that the typical form of the terminal distribution of the hepatic artery is observed for the first time. At this stage the interlobular hemopoietic tissue becomes narrower than that of 3 to 4 months old fetus due to the proliferation and development of hepatic cells. In the perilobular regions are found ink-spotted precapillaries, which mainly open into the interlobular hemopoietic tissue between the hepatic lobules and the interlobular artery, vein and bile ducts. They are consisted of an endothelial canal, possessing little adventitia and no media muscle. The precapillaries to the interlobular hemopoietic tissue form an easy S curve and an isthmus before reaching an infundibular opening. At the curve and isthmus, 3 or 4 primordial epithelioid cells are seen in the layer corresponding to the media. On the inner surface of the endothelial cells are seen Indian-ink particles, which are further spread through the infundibular opening into the interlobular hemopoietic tissue, and from there reach the hepatic sinusoid (Figs. 6, 7).

In the fetus of the later stage (8—9 months) (Figs. 8—11), the interlobular and intralobular hemopoietic tissues as well as their arterial branches are further reduced. Many of the terminal arterial branches are connected to the sinusoid in

the forms of the intralobular and extralobular arterioles (precapillaries) (Figs. 8, 9), but some retain the form opening into the interlobular hemopoietic tissue (Figs. 10 and 11). They are endothelial canals with little adventitia. The precapillaries to the interlobular hemopoietic tissue and the extralobular precapillaries have a sharper curve and a more abrupt isthmus than those of the middle stage. In the media can be recognized 4 or 5 differentiated epithelioid cells (Figs. 10 and 11).

It may seem questionable from the functional viewpoint that the arterial blood should flow directly into the interlobular hemopoietic tissue, but it is not altogether unreasonable, considering the fact that it is in a transitional stage of differentiation of the fetal circulation. In ELIAS's illustration (Pl. 1, Fig. 4) of a fetus specimen, we see irregular black spots suggestive of an Indian-ink mass diffused in the hemopoietic tissue.

Arterial anastomoses under the hepatic capsule

The subcapsular branches of the interlobular arteries (so-called perforating capsular branches), which run between the hepatic lobules and reach the subcapsular layer, anastomose with each other and form arterial networks on the surface of the hepatic parenchyma (corrosion and histological specimens). This virtually substantiates the views of MELNIKOFF[31], ARAI[1,2] and ELIAS[10–17]. The perforating branches also anastomose with branches of the hepatic artery, which come detouring around the hilar region to the subcapsular layer. Besides these, subcapsular branches derived from quite different sources are found in the corrosion specimens, as described by MICHELS[32] on the basis of his observations of dissected upper abdominal viscera: Aa. phrenicae superiores et inferiores, Aa. intercostales XI et XII, Aa. thoracicae internae, A. cystica, Aa. renales and Aa. suprarenales mediae. There are many anastomoses between these subcapsular branches and those of the interlobular and hepatic arteries, in the regions of the round ligament, lig. venosum, the gallbladder wall, the bare area and the fibrous appendix. They serve as important collateral pathways between the hepatic artery and other arterial systems.

CONCLUSIONS

The following conclusions were arrived at on the terminal distribution of the hepatic artery and its microscopical structures in the experiments conducted with the livers from human adult, fetus, dogs and toads, to which were given plastics, Indian ink and Indian-ink shock injections into their hepatic blood vessels.

1. There are arterial anastomotic networks of vasa vasorum in the portal wall.

2. The intralobular arterioles (Elias) and the extralobular arterioles (WEATHERFORD) often arise as direct branches without passing through the periductal arteriolar plexus. In the peripheral zone of the liver, this constitutes the main type of origin.

3. Besides the anastomoses between the intralobular arterioles of the adjacent lobules (Fig. 5), the periductal arteriolar plexus of the bile ducts to the neighboring lobules are interconnected by arterial branches surrounding the interlobular vein ("neighboring arteriolar anastomoses" by the author) (Figs. 2, 5).

4. The terminal arterioles reveal a curve and an isthmus (Figs. 1, 3, 5), where they are supposed to have epithelioid cells in the media.

5. The hepatic vein wall is supplied by the branches of the internal thoracic and phrenic arteries. These anastomose with the interlobular arteries in the interdigitation area of vessels.

6. In the toad the terminal distribution is of a simpler form, in which the arterial capillaries, with an S or a parabolic curve, being constricted by the marginal hepatic cells, join the sinusoid in capillary form.

7. In human fetus of the middle stage (Figs. 6, 7), most of the terminal arterial capillaries open directly to the interlobular hemopoietic tissue, and from there the blood flows into the sinusoid. The precapillaries have an S curve and an isthmus, where they have 3 or 4 primordial epithelioid cells. In other portion, the precapillaries form endothelial canals with little adventitia and open infundibularly to the hemopoietic tissue. These have been proved by the Indian-ink shock injection method.

8. In the fetus of the later stage (Figs. 8—11), with the reduction of interlobular hemopoietic tissue, its arterial branches become fewer, and many branches are connected directly to the hepatic sinusoid. They form a sharper S curve and an isthmus, where 4 or 5 epithelioid cells are differentiated. The arterial terminal branches are precapillaries of endothelial canals having little adventitia and no media muscle.

9. The subcapsular branches of the peripheral interlobular arteries anastomose with one another. Besides these, subcapsular branches come around the hilar region from the hepatic artery, furthermore some are derived from the biliary, inner thoracic, diaphragmatic, intercostal, subcostal, suprarenal and renal arteries. Anastomoses are found between all the subcapsular branches of different origins.

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EXPLANATIONS OF FIGURES

Figs. 1—4. The intermediate zone of the liver of a human adult injected with Indian ink through the hepatic artery.

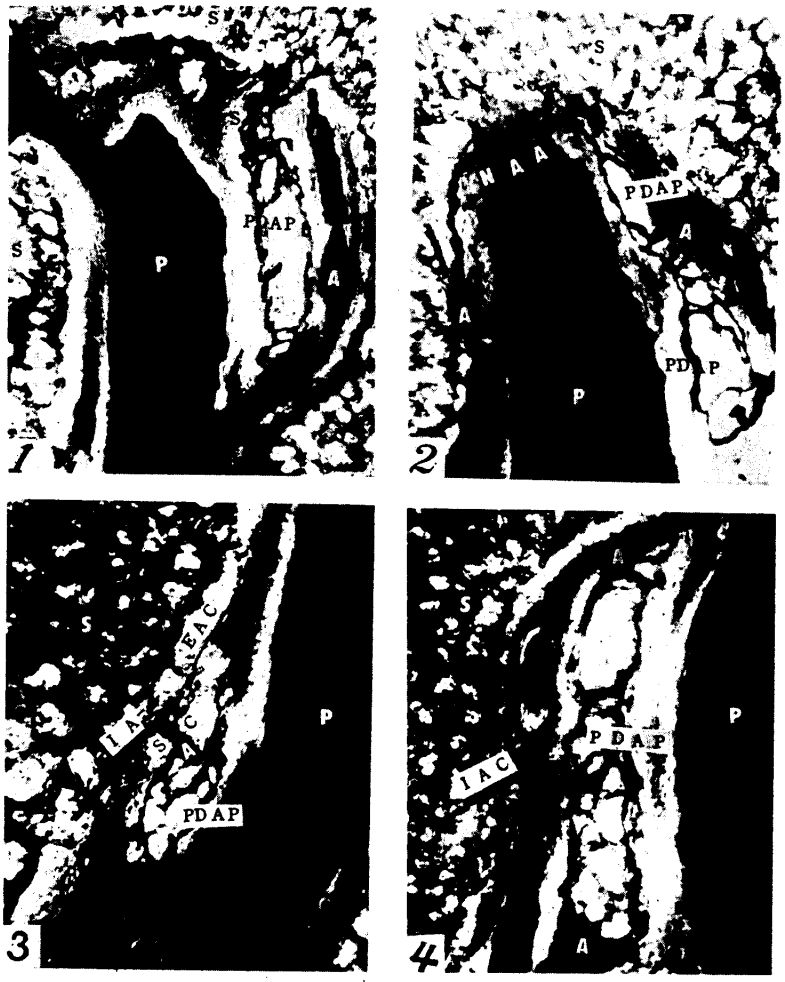
Fig. 1. One of the intralobular arterioles (IA) arises from the periductal arterial capillary plexus (PDAP) and forms an S curve with isthmus (SC). Another in the upper left corner arises directly from the interlobular artery. (×100)

Fig. 2. The periductal arterial plexus on the right side of the interlobular vein is connected with that on the opposite side (not seen in this section), by the "neighboring arteriolar anastomosis" (NAA), which is seen as crossing the interlobular vein. (×100)

Fig. 3. An intralobular arteriole (IA) and an extralobular arterial capillary (EAC) arise directly from the interlobular arteries. (×200)

Fig. 4. Connection of the neighboring periductal arterial plexuses. (×200)

Fig. 5. A half-diagrammatical figure of two hepatic lobules of a human adult (×50), injected with colored resins through the portal vein, the hepatic artery and the bile duct. Note S-formed isthmus of the arterioles (*arrows*) and anastomosis (AA) between the intralobular arterioles of the two lobules.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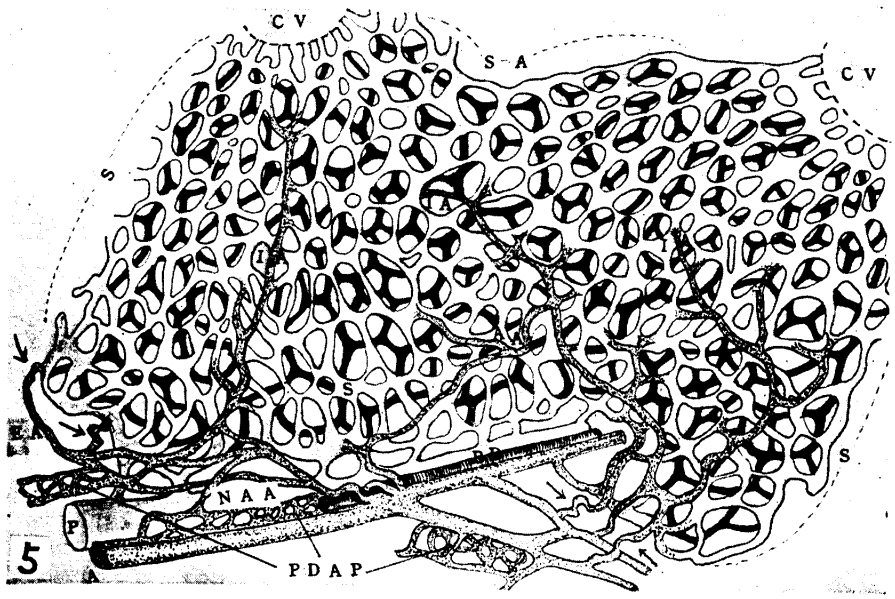
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Figs. 6—11. Indian-ink shock injection specimens of the fetuses, H-E counterstaining (×400). Indian ink is seen as fine granules attached to the epithelium, as indicated in the diagrams. *Arrows* point blood stream.

Figs. 6 and 7. Fetus in the middle stage (5 months old). The terminal arterial branch opens to the interlobular hemopoietic tissue. Note S-formed isthmus, where primordial epithelioid cells (PEC) are seen.

Figs. 8 and 9. Fetus of later stage (8 months old). The intralobular arterial capillary opens directly to the sinusoid.

Figs. 10 and 11. Fetus of later stage (8 months old). The terminal branch to the interlobular hemopoietic tissue has a sharper S curve. DEC : differentiated epithelioid cells.

A : interlobular artery, BD : bile ducts, CV : central vein, EA : extralobular arteriole (WEATHERFORD), EAC : extralobular arterial capillary (WEATHERFORD), IA : intralobular arteriole or capillary (ELIAS), ILHT : interlobular hemopoietic tissue, LC : liver cells, P : portal branches, PDAP : periductal arterial (capillary) plexus, S : sinusoid, SA : sinusoidal anastomosis, SC : S formed curve with isthmus


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LC
S
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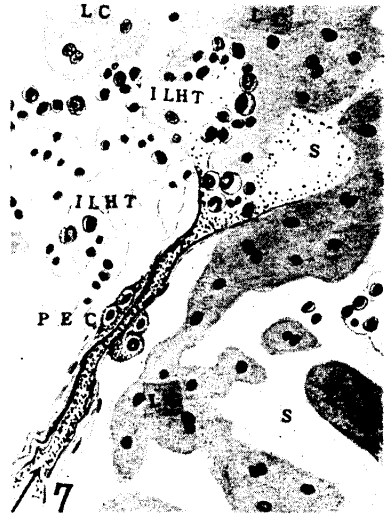
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