

## INTRAHEPATIC LYMPHATICS IN THE HUMAN FETUS

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### ABSTRACT

*Graphic reconstruction of dilated intrahepatic lymphatics in a 36 week old fetus displayed an anastomosing network of channels with intraluminal valves. Examination of the liver in 42 fetuses between the gestational age of 15 to 40 weeks showed that lymph vessels were visible as early as the 15th week. The detection of intrahepatic lymphatics was not related to the weight of the liver, the underlying cause of death, gender, or congenital anomalies.*

This study was prompted by the finding of dilated lymph vessels with intraluminal valves in the portal tracts of a fetus of 36 weeks gestational age who displayed Marfan's syndrome and cardiomegaly at birth, and who died from cardiac insufficiency 20 hours after delivery. The lymphatics were initially thought to be ectatic or possibly part of a generalized lymphangiomatosis syndrome.

### MATERIALS AND METHODS

From the liver of a 36 week old fetus with Marfan's syndrome, serial sections 10 $\mu$  thick, stained with Sirius Red Hematoxylin were submitted to the graphic reconstruction technique of Staubesand (1). In brief, serial sections were projected on transparent paper sheets from which drawings were made. Because the sheets can be superposed, the shape of structures can be determined through hundreds of sections or more. To display the shape spatially, each drawing was

projected on a perpendicular plane to that of the drawing. The direction of this plane was chosen to best depict the anatomic structure. From the post-mortem files, 42 sufficiently well-preserved livers of fetuses with gestational ages from 15 to 40 weeks were also examined. In the sections stained with hematoxylin and eosin, each portal tract was carefully scanned for the presence of lymphatic vessels. Identification of a lymphatic was based on the combination of at least 3 of the following criteria: a) absence of red blood cells; b) presence of flattened cells lying on very thin collagen fibers; c) an irregular vessel circumference; d) very thin vascular wall in proportion to the diameter of the lumen. Venules of comparable size uniformly have several smooth muscles cells; e) localization next to arteries, veins or bile ducts or a grouping of several adjacent channels; f) presence of intraluminal valves.

Where findings were in doubt, the lymphatics were taken as absent. In addition 6 livers of infants between the age of 2 days to 6 months were examined. In order to know whether the presence of lymphatics was related to the size and composition of portal tracts, 5 livers of each gestational age group of 15-20, 21-25, 26-30, 31-35, and 36-40 weeks were examined morphometrically using a semi-automatic Kontron system. The Kontron system consisted of a magnetic X-Y tablet with a cursor for delineating the circumference of the portal tracts, portal veins and lymphatics. The data were registered by computer and statistically analyzed.

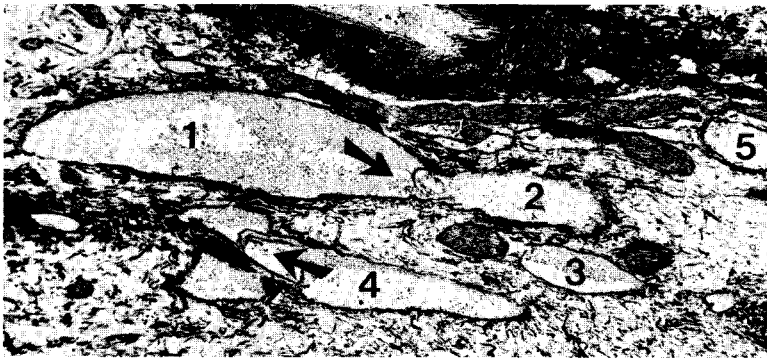


Fig. 1. Photomicrograph of dilated lymphatic vessels in a 36 week old fetus as derived from reconstructed drawings. Arrows point to intraluminal valves. Sirius Red Hematoxylin (x56).

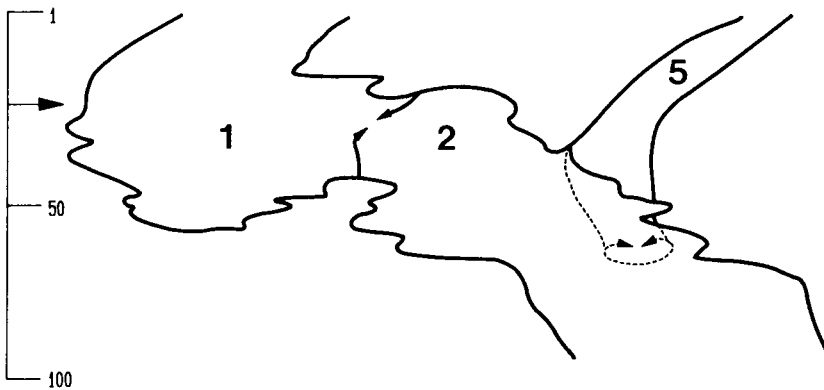


Fig. 2. Reconstructed drawing of channel 1, 2, and 5 (see Fig. 1). Note the valve at the junction of channels 5 and 2 and a valve between channels 1 and 2 which are two segments of the same longitudinally sectioned lymphatic. The arrow on the scale corresponds to the level of the section in Fig. 1.

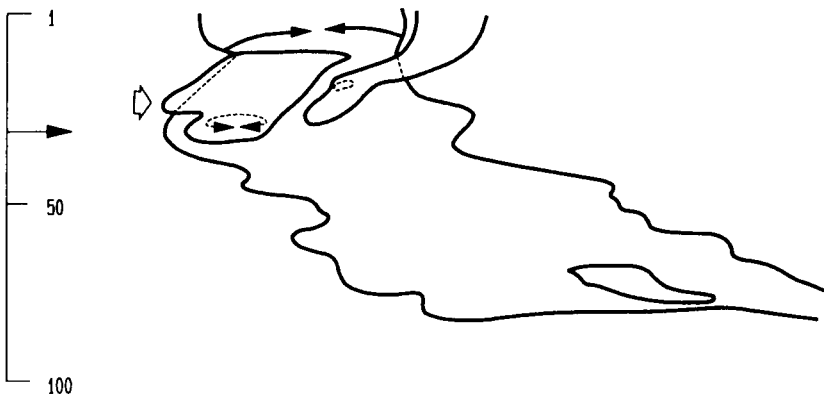


Fig. 3. Reconstructed drawing of channel 4 (see Fig. 1). It cannot be demonstrated whether the blind sac (open arrow) opens into the loose connective tissue or into smaller lymphatics. A valve is present at the junction between the blind sac and the main channel. The arrow on the scale corresponds to the level of the section in Fig. 1.

## RESULTS

The graphic reconstruction of the liver of a 36 week old fetus with Marfan's syndrome is shown in *Figs. 1-3*. The lymphatic vessels formed an anastomosing network with saccular dilatations. Intraluminal valves were seen at the entry of smaller branches into larger ones and also along the course of larger lymphatics. Due to section thickness, the origin of smaller lymphatic branches in the loose connective tissue of the portal tract were not able to be recognized although some branches seemed to "disappear" into the surrounding tissue. From reconstruction it became clear that the structures were normal lymph vessels, although ectatic, and not characteristic of lymphangioma. The findings in the 42 fetal and 6 infantile livers were extremely heterogenous. In the 15-20 week gestational age group, no lymphatic vessels were identifiable in 3 of 7 livers although one fetus at 17 weeks had a discrete lymph vessel with a visible valve. At 26-30 weeks in 2 out of 6 livers no lymphatic vessels were detected. All the other livers showed lymphatic vessels in highly variable numbers. The width of these lymphatics differed substantially in the same liver and among the various fetuses. In general, lymphatic vessels could be seen in portal tracts (diameter greater than 1mm) but in the groups of 15-20 and 21-25 weeks smaller portal tracts (diameter of 250 $\mu$ ) contained lymphatics. The detection of lymphatic vessels was not related to the weight of the liver, the underlying cause of death, the gender or associated congenital anomalies. The morphometric results were highly variable.

## COMMENT

This study demonstrated that in the human liver, intrahepatic lymphatics located in the portal tracts were detected from at least the 15th week of gestation. Because this gestational time was the earliest studied, it is not known whether intrahepatic lymphatic vessels appeared even sooner in fetal life. The lymphatic vessels contained valves suggesting the

presence of unidirectional lymph flow. Pfuhl (2) had noted that hepatic lymphatic vessels were valveless, but intraluminal valves in small lymphatics were found in straight segments although not at the entrance of smaller branches into larger ones. The latter arrangement, however, was seen at the junction of the embryonic lymphatic sacs with the superior cardinal vein (3). Popper and Schaffner (4) have also described the presence of valves within lymphatics in the hepatic hilum. Moreover, a photograph similar in appearance to the dilated lymphatic vessel in the 36 week old fetus shown here was provided by Huth (5) who first ligated portal lymphatics in the hepatic hilum of adult rats and rabbits. Our study, however, did not disclose the basis for variability in lymphatic size. Specifically, there was no correlation with vascular congestion. Although the degree of filling of lymphatics in post-mortem material was especially difficult to judge, it was possible that "normal" lymphatics were collapsed whereas "dilated" ones were functionally active.

## REFERENCES

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