A Histological(Histochemical) Study of the Structural and Functional Unit of the Liver of the Mouse

II. On the Distribution of Succinic Dehydrogenase

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ABSTRACT

The hepatic structural and functional unit of the mouse was demonstrated by the relative enzymatic activity of succinic dehydrogenase in the hepatic parenchyma, employing the method for succinic dehydrogenase of Nachlas et al. (1957), using Nitro- BT to frozen sections of about 10 micra.

In the hepatic structure of the mouse, three different geometrical areas were classified: the perivascular area of the portal stem, which continued into the preterminal portal branch; the area of the preterminal portal vein, and the area of the terminal portal twig, this being considered to be the real functional unit, which extends into the neighbouring hepatic lobule according to the pattern of distribution or activity of succinic dehydrogenase.

The hepatic parenchyma, which showed strong succinic dehydrogenase activity, was considered to correspond with the heavily loaded parenchymal area with mitochondria, according to the previous observations of hepatic mitochondria in the mouse, as presented by the author (1961).

The peripheral areas or zones, including the pericentral area around a central vein, of the real functional hepatic unit, which was described by Rappaport et al. (1954) and others, showed less activity of succinic dehydrogenase, and the perivascular areas of branches of the hepatic vein reacted weakly.

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In regard to the structural unit of hepatic tissue, Wepfer (1664) and Malpighi (1666) termed the parenchymal units attached to the intrahepatic portal venules hepatic acini.

Kiernan (1883) associated the three-dimensional structural unit of the liver with its secretory function.

Brissaud and Sabourin (1888) reported the area of the hepatic parenchymal tissue draining into a bile duct in the portal trigone as the secretory unit of the liver.

Mall (1906) proposed that the columnar structure around the portal field was the portal unit; he was supported by Opie (1944) and Arey (1932).

Rappaport et al. (1954) defined the small irregular morular parenchymal tissue mass attached to the portal terminal venules accompanying the intrahepatic arteries and bile ducts in the livers of dogs and house rabbits as the structural and functional unit of the liver, and called it the simple liver acinus.

Rappaport (1958) termed the hepatic parenchymal tissue consisting of the simple liver acini around the
preterminal portal vessel in man the complex acinus and the larger parenchymal tissue of the simple and complex acini formed around the portal stem the acinar agglomerate. Rappaport proposed that the three kinds of acinar masses described above are the structural and functional units of the liver.

The author (1961) has observed the mitochondria of the liver parenchymal cell of the mouse and their distribution.

As to the distribution of succinic dehydrogenase in the liver, Semenoff (1935) studied the activity of succinic dehydrogenase in the liver of Rana temporaria by the Semenoff method (leucomethylene blue method for succinic dehydrogenase) and reported results opposite to those reported below.

Deane (1944), Seligman and Rutenberg (1951), Padykula (1952), Mustakallio (1954), and Schumacher (1957), studied the distribution of succinic dehydrogenase in livers of the mouse; rat, dog, guinea pig, hamster and rabbit; of the rat, redbit and mice; of the mouse; and of the pig, horse, and cattle, respectively, and they reported that they found a strong reaction mainly in the perportal area.

The author has attempted this present experiment in order to study the structural and functional units of the liver by observing the distribution of succinic dehydrogenase in the liver cell.

MATERIALS AND METHODS

Twenty mature and healthy mice (15 males, 5 females, with average weight of about 25 gm.) were used as experimental animals. They were sacrificed by decapitation. The abdomen was opened immediately, the right lobe of the liver was isolated and frozen sections of about 10 micra were made. After the sections were immersed in physiological saline, they were incubated according to the method of Nachlas et al. (1957) for determining succinic dehydrogenase using Nitro-BT and then they were mounted with glycerol jelly and examined.

For control an incubating medium without sodium succinate was used in order to determine if any endogenous substrate was present in the liver tissue, and such control preparations gave negative reactions.

The degree of enzyme action was recorded according to the Padykula and Pearse methods (1960).

1) In the preparations made by this method after Nachlas et al. (1957) the areas which appeared pink interpreted as areas where the enzyme action was weak, since they were areas where monoformazan was formed or where diformazan was dissolved in lipid.

2) When Nitro-blue tetrazolium chloride was completely reduced and blue diformazan granules appeared or its presence was demonstrated, it was interpreted as evidence of active enzymatic action and the result was recorded according to the amount of the blue granules seen.

OBSERVATIONS

In the preparations for demonstrating the distribution of succinic dehydrogenase, there are areas showing strong activity and areas showing weak enzyme activity in the hepatic parenchymal tissue surrounding the large blood vessel seen in cross-cut. The vessels surrounded by strongly-reacting areas are considered to be part of the portal stem, since branches are observed. Also this perportal area of the portal stem may be recognized as areas corresponding to the acinar agglomerate described by Rappaport. The weak-reacting areas are considered to contain the intercalated veins or the sublobular veins or the collecting veins.

The author observed that just as Deane, etc., have reported, the enzyme action of the hepatic lobules was strong in the perportal area and showed lesser reaction toward the pericentral area around the central vein. However, the author also observed that there were both a strong-reacting part and a weak-reacting part in the peripheral area of the simple liver acinus. It was also observed that when the terminal portal vessel was cut across in the perportal area, the above phenomenon appeared stronger around the terminal vessel and weaker toward the periphery.

An enzyme action similar to that appearing in the parenchymal tissues surrounding the terminal portal vessels was observed in the liver parenchymal tissue surrounding the preterminal portal vessels running longitudinally parallel to the long axis of the lobule.
in the portal area after branching off from the portal stem, and this reaction became weaker and weaker as the adjacent central vein area was approached. Because of these observations this area may be considered to be an area corresponding to the complex acini of the liver.

**DISCUSSION**

Rappaport et al. (1954) defined the small irregular morular parenchymal tissue or simple liver acinus around the terminal branches of the portal vein, hepatic artery, and the bile duct as the structural and functional unit of the liver, substituting it for the older concept of the lobular structural unit. His experiment was done by injecting Ranvier’s carmine gelatin and India ink into the portal veins of rabbit and dog. Rappaport (1958), applying by the same method to the human liver the complex acinus and acinar agglomerates around the portal preterminal vessel and the portal stem respectively, dentified the structural and functional units of the liver as the simple liver acinus, the complex acinus, and the acinar agglomerates.

The author (1961) has studied the Rappaport’s proposal in regard with the function of the liver cells, which is based on the amount of mitochondria distributed in them, and he has reported that the structural unit of Rappaport contains an abundant amount of mitochondria, thus supporting his proposal.

Semenoff (1935) determined the distribution of succinic dehydrogenase in the liver of Rana temporaria and reported that he observed strong enzymatic action in the pericentral area, while the periportal area showed weak enzyme action. These observations by Semenoff failed to receive support afterwards.

Deane (1944) has studied the distribution of succinic dehydrogenase in the mice liver and has observed that the cells in the periphery of the lobule show stronger enzyme action than in the cells of the pericentral area.

Seligman and Rutenberg (1951) conducted extensive research on the Blue tetrazolium chloride method and have reported that a strong reaction was observed in the periportal areas in the livers of dogs, rabbits, rats, guinea pigs and hamsters.

Padykula (1952) has studied the succinic dehydrogenase activity in various organs of the rats by the dieterazolium chloride method and has reported that the succinic dehydrogenase distribution in the rat liver corresponds with the reports of Deane, Seligman, and Rutenberg. But Padykula has also pointed out that the distribution of mitochondria, the amount of glycogen, Golgi material, and the amount of bile secretion are related to the quantitative distribution of succinic dehydrogenase.

Mustakalio (1954) obtained the same result as those above in his study of succinic dehydrogenase activity in the normal mouse liver by the method used by Seligman and Rutenberg (1951), using neotetrazolium.

Schumacher (1957) studied the action of 4 respiratory enzymes, succinic dehydrogenase, cytochrome oxidase, TPN-diaphorase and DPN-diaphorase in the livers of the horse, pig, and cattle, and observed that the distribution was identical with the earlier reports on the former 2 enzymes, but that it was in direct contrast to the former 2 enzymes in that the latter 2 enzymes were generally distributed to the pericentral area around the central vein. He also pointed out the fact that these are in close relationship with the blood stream of the lobules and deduced that the oxygen tension is high in the periportal area and lower in the pericentral area, reporting that the enzyme distribution corresponded to this fact. He also added that the former 2 enzymes showed weak reactions in the areas corresponding to the nodal point described by Mall (1905).

The results of the author’s observations are similar to those of other workers except that of Semenoff. The author has attempted to define the functional and structural unit of the mouse liver by the distribution of this enzyme. This unit is nearly identical with the structural unit of Rappaport. The author has found little succinic dehydrogenase action in the endothelium of the vessels or in the epithelium of bile duct.

**REFERENCES**


Brissaud and Sabourin: *Compt. Rend. Soc. de Biol.*
Fig. 1. The pericentral area of the hepatic lobule reacted weakly in succinic dehydrogenase activity in the center and periportal areas reacted strongly at the right lower and the left upper corners (× 100).

Fig. 2. The periportal area of a probable portal stem accompanying with a bile duct, and reacting strongly in succinic dehydrogenase, showed many distinct diformazan granules in the hepatic cells (× 400).

Fig. 3. The weakly reactive perivascular area of a probable sublobular vein contains a little amount of distinct diformazan granules in liver cells (× 400).