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Postnatal changes in the distribution of lipid droplets within the liver lobule of the mouse

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INTRODUCTION

Hepatocytes of adult animals usually contain small numbers of lipid droplets in their cytoplasm. In the liver of growing animals lipid droplets are relatively numerous in the early postnatal period, decreasing thereafter gradually to adult levels (Deane, 1944; Leeson & Cutts, 1972; Cutts, Leeson & Krause, 1973). Recently we have shown that, in the adult mouse, lipid droplets are more numerous in the centrilobular than in the periportal hepatocytes (Asada & Kanamura, 1978). However, in growing animals, although a centrilobular localization of lipid droplets has been mentioned (Leeson & Cutts, 1972; Cutts *et al.* 1973), systematic and detailed observations on the distribution of lipid droplets within the liver lobule are lacking. In this paper we report that in newborn mice the number of lipid droplets is similar in centrilobular and periportal hepatocytes, differences arising only gradually during postnatal development.

MATERIALS AND METHODS

DDD mice of various ages were used. Newborn mice were less than 2 hours old, while adult animals were 3–6 months old. Animals were fed a standard laboratory chow (Oriental NMF) *ad libitum* and were killed by cervical dislocation in the afternoon (3–5 p.m).

Whole livers, or small blocks from the left lobe in adult animals, were fixed in cold 10 % formalin for 12 hours to a few days, then cut at 40 μm with a freezing microtome and stained with oil red O (Lillie, 1944). The sections were mounted in glycerin jelly.

OBSERVATIONS

The 'liver lobule' of this paper is the classical liver lobule. Lipid droplets were observed in the livers of mice of all the age groups studied. In adult animals the staining intensity for lipid droplets was generally weak, but was more evident in centrilobular than periportal areas (Fig. 7). At birth and 1 day after birth, however, lipid droplets were evenly distributed throughout the lobule (Fig. 1). The lipid staining was always more intense at birth and up to about 20 days of age than it was in adult animals. A slightly uneven distribution of the staining, with greater intensity in centrilobular areas, appeared at 2 days (Fig. 2). After this the difference in staining intensity between centrilobular and periportal areas became progressively more marked with age up to 15 days (Figs. 3–5), and then the difference, together with the

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overall staining intensity, gradually decreased to reach the adult level between 21 and 24 days after birth (Fig. 6).

DISCUSSION

We have recently observed that, in the liver of the adult mouse, lipid droplets are more numerous in the centrilobular than in the periportal hepatocytes (1978). The present study has shown, however, that hepatocytes show no heterogeneity in the first 24 hours after birth.

However, a difference in the number of droplets between centrilobular and periportal cells appeared at 2 days after birth: this difference increased between 5 and 15 days after birth, and then fell to reach the adult level between 21 and 24 days.

Similar postnatal changes have been reported in the distribution of glucose 6–phosphatase activity in the mouse liver (Kanamura, 1975), the uniformity between 1 day before birth and 2 days after birth gradually changing between 3 and 10 days to the adult type with higher activity in periportal areas. However, the distribution of lipid droplets only attained the adult state after 21–24 days of age and after a period when the difference between periportal and centrilobular cells had reached a maximum.

Postnatal changes in intralobular arrangement and distribution of [^{3}H]thymidine have been reported in other species. In the rat the hepatic cell plates, arranging irregularly and thickly throughout the lobule from birth to 3 days of age, approach the adult type of configuration, with irregularity and thickness in periportal areas but straightness and thinness in centrilobular areas, some 10 days after birth (LeBouton, 1974). Likewise the cell plates become of adult type at 20 days after birth in the opossum (Cutts *et al.* 1973) and 15 days after birth in the rabbit (Leeson & Cutts, 1972). Labelled cells after injection of [^{3}H] thymidine in the rat are distributed nearly equally throughout the lobule at birth, but are to be found more in the periportal areas after 2 days (LeBouton & Marchard, 1970; LeBouton, 1974). It is clear therefore that functional and structural heterogeneity among hepatocytes is not present in newborn mice, and only develops gradually during the postnatal development.

In the present study 40 μm thick sections were used for the demonstration of lipid droplets. It is known that the lipid demonstrable in histological sections is only a part of the lipid reserves held in the liver. The thicker sections were used in order

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All Figures show sections of livers of mice of various ages and demonstrate the distribution of lipid droplets within the liver lobule. Tissues were fixed with 10% formalin, stained with oil red O. The red-stained lipid appears black.

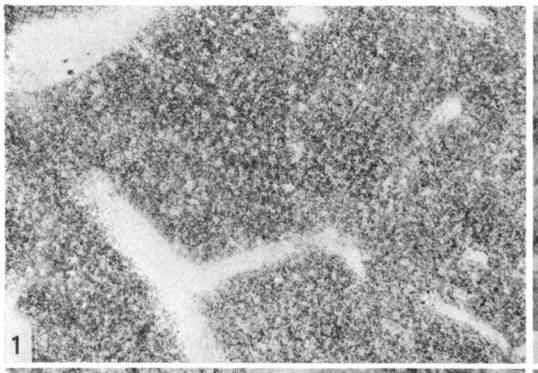
Fig. 1. Section from newborn animal. The staining for lipid droplets is evenly distributed throughout the lobule.

Fig. 2. Section from 2 days old animal. The staining appears slightly uneven in the lobule, being less intense in periportal areas (*p*).

Figs. 3–5. Sections from 5, 10 and 15 days old animals, respectively. The staining is more intense in centrilobular areas, with a marked difference in intensity between centrilobular and periportal areas. Arrows, interlobular vein containing an aggregate of erythrocytes.

Fig. 6. Section from 24 days old animal. The intensity and distribution of the staining is similar to those of adult animals (Fig. 7).

Fig. 7. Section from adult animal. The staining intensity is weak, but stronger in centrilobular areas than periportal areas. Arrows, central vein containing aggregate of erythrocytes.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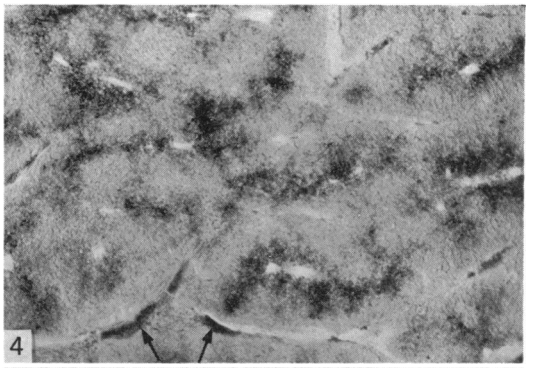
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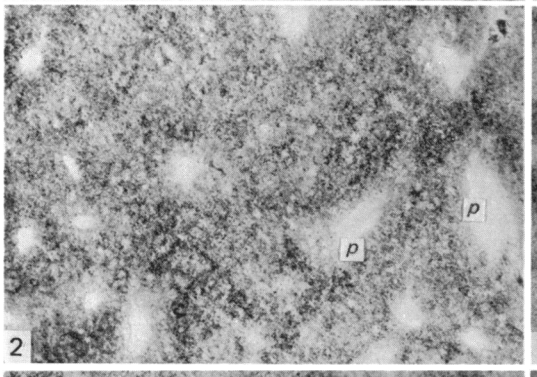
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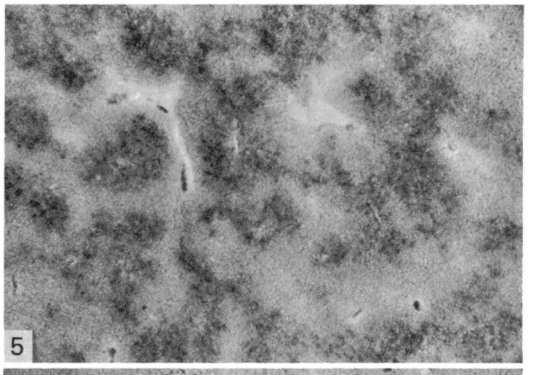
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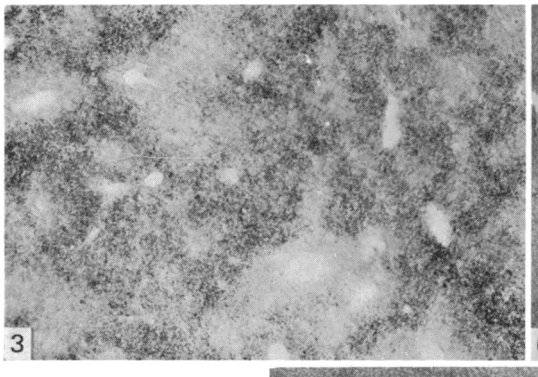
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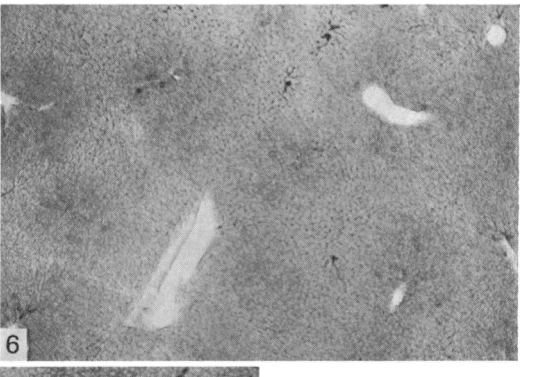
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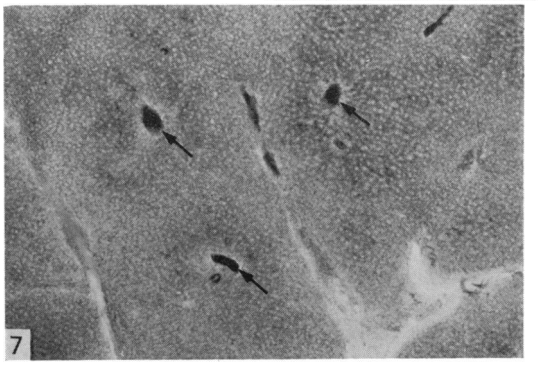
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to decrease loss of the dye and/or lipid droplets during the preparation of the stained sections.

The functional significance of these changes in the lipid droplet distribution in hepatocytes during the postnatal period is unknown. However, the deposition of the droplets seems related to drinking mother's milk, for the stage up to 17 days after birth, when deposition of the droplets is most marked, corresponds with the suckling period.

SUMMARY

The changes in the distribution of lipid droplets in the liver lobule were studied during the postnatal development of the mouse. At birth, and 1 day after birth, lipid droplets were evenly distributed throughout the lobule. A slightly uneven distribution of the droplets, more in centrilobular areas, appeared 2 days after birth. After this the difference in the number of droplets between the cells of the centrilobular and periportal areas became progressively more marked reaching a maximum by 17 days of age, and then decreasing to the adult level between 21 and 24 days. Thus, heterogeneity among hepatocytes with respect to lipid content is not present in newborn mice but develops gradually during the postnatal development.

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