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QUANTITATIVE CHARACTERISATION OF AGEING HEPATOCYTES

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ABSTRACT

Hepatocytes of rats of various ages were investigated morphometrically and qualitatively.

During the postnatal development and ageing

- the volume of hepatocytes increases from 5800 μm^3 to about 10000 μm^3 in 6 months and then decreases to 7300 μm^3 (24th-27th months).
- the number of hepatocytes increases from 41.4×10^6 at birth to 1150×10^6 (6th month).
- the volume of hepatocyte nuclei increases from 410 μm^3 at birth to 840 μm^3 at the 12th month and decreases thereafter to 470 μm^3 at the 27th month.
- the volume density of mitochondria decreases from 0.165 at birth to 0.128 at the 27th month.
- the number of mitochondria increases from 200 at birth to 2200 in the 6th month and decreases thereafter to 1520 at the 27th month.
- the volume of the average mitochondrion decreases from 3.83 μm^3 (at birth) to 0.53 μm^3 (27th month).
- the surface of the hepatocytes increases from 1900 μm^2 to 2780 μm^2.

Due to the fact that the liver is the most important organ of the metabolism it is frequently investigated. Although the organ is made up of various cell types, vessels and an extracellular space of varying width, interest is usually focused on the hepatocytes, which account for 80 to 90 per cent of the liver by volume and are the essential cellular elements. Much qualitative and quantitative data on the

structure and composition of hepatocytes has been obtained especially in the past two decades. A great deal of information about the development, maturation and ageing of the liver and its cells has also been published.

The object of our investigations is to find the common features of hepatocytes and the principles of their changes in various age groups from birth up to advanced age, on the basis of our own systematic studies, and by comparing the results with those of other authors.

The examinations were performed on the livers of male and female Wistar rats at birth, at 1, 2, 3, 4, 5, 6, 7, 14 and 21 days and at 1, 2, 3, 4, 5, 6, 12, 18, 24 and 27 months of age. Thirty liver cells were selected in accordance with certain criteria to maintain uniform conditions. The following characteristics were used for determining the median plane:

- nucleus with clearly visible nuclear membrane
- recognizable sinusoidal cell membrane
- distiguishable bile canaliculi with clearly visible boundary.

The cell was subdivided into four zones for more detailed characterization: sinusoidal (supranuclear) zone, lateral zone, and the zone adjoining the bile canaliculi.

1. Hepatocytes. The volume density of hepatocytes on the 15 th foetal day is 0.60, increasing to 0.85 in the 21st foetal day. After birth till the end of the period of investigation the volume density varies between 0.78 and 0.94.

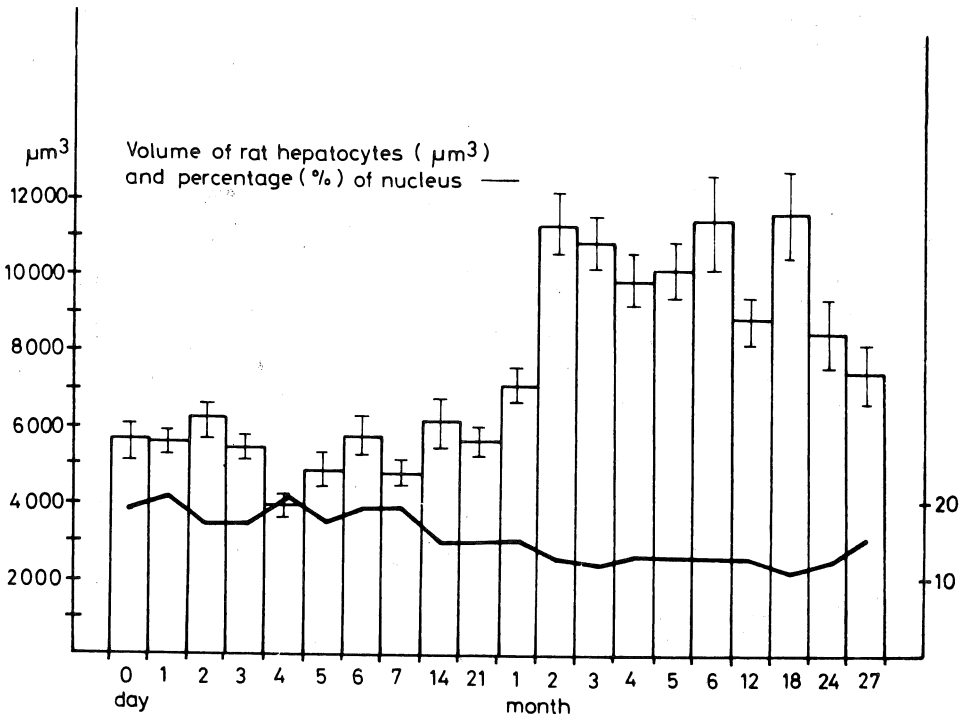

Fig. 1

According to our investigations the liver cell of male rats has a volume of 5776 μm^3 at birth (Fig. 1). The volume drops to 3992 μm^3 about the 4th day following birth, and it is again equal to the volume at birth on the 21st day.

From the 2nd month onwards the volume reaches values in the order of 10,000 μm^3, with a distinct drop on the 24th and 27th months. Our investigations show that the maximum value of the hepatocyte volume of 11539 μm^3 is reached on the 18th month.

2. Nuclei. The volume of hepatocyte nuclei is 413 μm^3 at birth. It increases to 550 μm^3 by the 6th month, reaching 842 μm^3 at the end of the 12th month, after which it drops again to 475 μm^3. The values are substantially higher in old female rats i.e. 622 μm^3 at the end of the 12th month and 852 μm^3 at the end of the 27th month.

3. Mitochondria. The volume density of mitochondria is 0.165 at birth (Fig. 2). It increases to 0.236 till the 14th day, after which it diminishes continuously until it reaches 0.138 at the end of the 12th month. After that there is a slight increase followed by a decrease in density, which reaches its lowest value of 0.128 at the end of the 27th month.

At birth, the absolute volume of the mitochondria per cells is about 780 μm^3. By the end of the 6th month it rises to about 1420 μm^3. By the end of the 12th month the value drops to about 1060 μm^3 and at the end of the 27th month (after an increase in the 18th month) it reaches 803 μm^3,

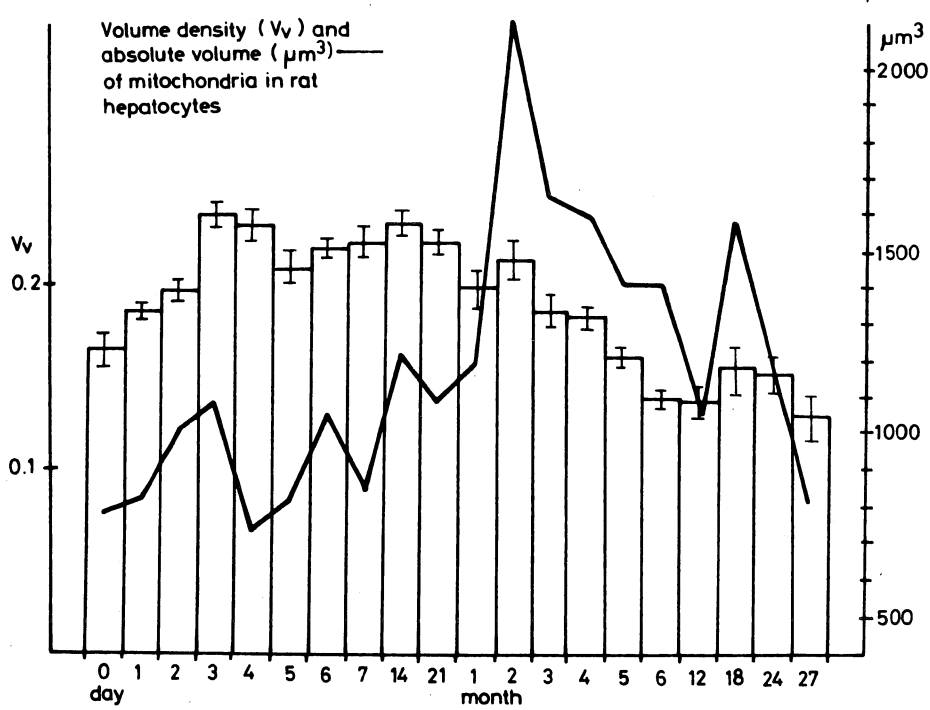

Fig. 2

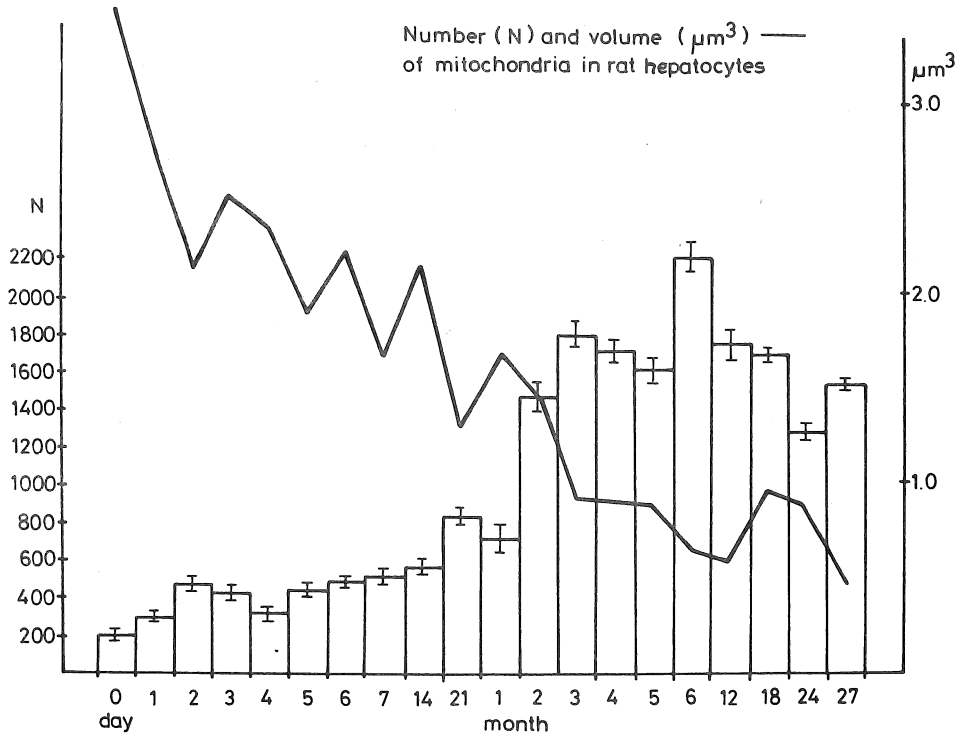

Fig. 3

i.e. approximately the same value as at birth. By comparison, in female rats the absolute volume of the mitochondria increases to 2464 μm^3.

The number of mitochondria per hepatocyte at birth is around 204. By the end of the 6th month their number increases to 2199. After that the number of mitochondria diminishes again, reaching 1516 at the end of the 27th month (Fig. 3).

The volume of an individual mitochondrion is around 3.83 um^3 at birth. In the course of further postnatal development the volume diminishes continuously, reaching 0.64 μm^3 at the end of the 6th month. The smallest mitochondria (0.53 μm^3) are found at the end of the examination period at the 27th month.

However, already at birth degenerative changes may be detected in the mitochondria. They are found as various forms of autophagocytosis. Mitochondria are seen surrounded by myelinic membranes. These changes are induced by focal catabolic changes and possibly by the formation of myelinic membranes from outer and inner membranes.

4. Plasma membrane. The plasma membrane also plays an important role in liver function. It fullfils different functions in the sinusoidal and lateral areas and in areas adjoining the bile canaliculi.Increase in the surface of resorbing areas and of areas adjoining the bile canaliculi is

of essential importance in the adaptation of the cell to the growth and functional demands of the liver.

Formation of microvilli in the sinusoidal areas increases the surface by a factor of 1.8 to 3.7. This means that the superficial area of hepatocytes at birth is 1900 μm^2 and in animals 27 month old 2784 μm^2. At birth, the number of microvilli is 1323 and at the end of the 27th month 5471.

The qualitative and quantitative data obtained by us on the development of hepatocytes from birth up to old age show that quantitative data can be used for characterizing the development of hepatocytes and their organelles. They can also be used for explaining the nature of functional changes in hepatocytes during life. Quantitative data on individual cell organelles also give an explanation to the different responses of male and female livers.