3 Biochemistry and Functions of the Liver

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1 Metabolic functions of the liver

► The morphological and functional integrity of the liver is vital to the health of the human organism. This essentially depends upon constant maintenance of the numerous biochemical functions of the liver and the diverse metabolic processes occurring in the hepatocytes and sinusoidal cells.

The liver ensures that approximately 70 partial functions within 12 major metabolic areas proceed either continuously or in biological (e.g. circadian) rhythms, or vary according to specific requirements. (s. tab. 3.1)

1. Bilirubin metabolism
2. Porphyrin metabolism
3. Bile acid metabolism
4. Amino acid and protein metabolism
5. Carbohydrate metabolism
6. Lipid and lipoprotein metabolism
7. Hormone metabolism
8. Vitamin metabolism
9. Trace elements and the liver
10. Biotransformation and detoxification function
11. Alcohol degradation
12. Acid-base balance

► *About 500 separate biochemical processes occur in one single liver cell!*

Tab. 3.1: Essential biochemical metabolic functions of the liver

Metabolic processes utilize a variety of differing and contrasting biochemical routes to enable synthesis of degradation and activation or deactivation of substances; in addition, they facilitate cellular uptake and excretory mechanisms. Moreover, there are various links between different metabolic pathways and functional processes. Intermediate chemical products generated in the course of metabolic reactions may be taken up by other pathways or cycles. Substrates are shifted between subcellular structures, and the metabolic end-products of one process are often used as the original substrate for new syntheses.

A general picture of the intricate complexity of various cycles, biochemical pathways and metabolic reactions within the liver has been excellently presented in **two posters.** (27)*

*) 1. *Holldorf, A. W., Krahl-Mateblowski, U., Mateblowski, M., Wütherich, S.*: Pathways of metabolism in liver. (9th Ed., 1992)
2. *Reutter, W., Geilen, Ch., Baum, O.*: Metabolic pathways in the liver cell. (6th Ed., 1998)

2 Regulatory metabolic mechanisms

The intricate network of biochemical reactions occurring within the restricted volume of the liver cell requires subtly controlled metabolic regulatory mechanisms. (28) These occur on **four levels:** (*1.*) at the molecular level, (*2.*) within the organelles, (*3.*) at the cellular level, and (*4.*) at the organ level.

(*1.*) *Regulation* may occur at the **molecular level** for example:
- through negative feedback, whereby the end-product of a metabolic reaction inhibits the activity of the enzyme which determines the speed of reaction. This affords a rapid adaptation of specific chemical reactions in response to alterations in metabolic conditions;
- through changes in the actions of activators and inhibitors;
- through modulation of enzyme activities;
- through changes in the rate of enzyme synthesis or degradation.

(*2.*) *Regulation* can take place within the **organelles** for example:
- Protein synthesis occurs in the ribosomes of the rough endoplasmic reticulum – by contrast, the process of protein degradation occurs in the lysosomes.
- Fatty acids are synthesized in the smooth endoplasmic reticulum, but they are broken down in the mitochondria.

(*3.*) *Regulation* may be effected at the **cellular level** for example:
- Hepatocytes display *metabolic heterogeneity* according to their zonal location within the acinus. (42) (s. p. 24) Specific chemical processes thus proceed exclusively or predominantly in the hepatocytes of the periportal or the perivenous zones. The zonally segregated reactions may also be regulated separately. It seems that, under certain conditions, metabolic processes are also "shifted" from one zone of the acinus to another.
- Hepatocytes interact closely with the sinusoidal cells and Kupffer cells (e. g. in the breakdown of erythrocytes and the degradation of pyrimidine nucleotides).
- Hepatocytes and sinusoidal cells are influenced by vegetative nerve fibre endings in Disse's space.

(*4.*) *Regulation* of metabolic processes may be achieved through biochemical interactions at the **organ level** for example:
- between the liver and the musculature
- between the liver and the kidneys