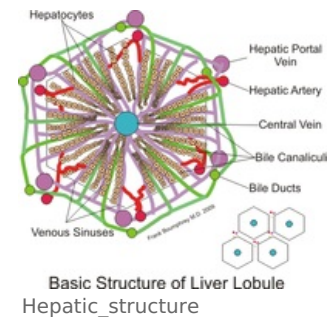


# Toxic liver damage

Liver damage by toxic substances is common because substances enter the liver through the *v. portae* in high concentrations and at the same time detoxification and elimination occurs, thereby protecting other organs. Cells in the centre of the lobules are more susceptible to the effects of toxic substances (less oxygen from the blood reaches them), but some substances preferentially damage periportal areas at the edge of the lobules (e.g. white phosphorus, iron, methotrexate, aflatoxins).

Centrizonal necroses (often occurring in acute lesions) are more favourable prognostically, as new hepatocytes arise periportal and then progress to the centre of the lobe. In contrast, intoxication with substances damaging the periportal cells has a severe prognosis, regeneration is difficult, cells regenerate irregularly in islets, and ligaments form between them → cirrhosis

Professional exposure to hepatotoxic substances is mainly by inhalation and percutaneous routes (e.g. TNT). Non-professional exposure is mainly chronic oral ethyl alcohol intoxication. In acute cases, accidental intoxications (e.g. with mushrooms) or suicide attempts (e.g. with paracetamol) are common.



## hepatotoxicity of substances

### obligatory

It causes damage in all individuals and is dose proportional, so that a minimum dose is not sufficient, but it is necessary to exceed the *hepatotoxic dose* (e.g. for paracetamol 100 mg/kg). The effect occurs after a short time interval and is reproducible in an animal experiment.

### mechanism of action

direct:

- substances acting directly (by themselves or by their metabolites) - they cause damage by denaturing proteins, peroxidation of membranes
- paracetamol', carbon tetrachloride, chloroform', white phosphorus, arsenic, TNT**

indirect:

- interfere with hepatocyte metabolism - e.g. interfere with fatty acid metabolism or block bile secretion
- with a characteristic latency to develop steatosis, necrosis or cholestasis, depending on the dose
- not often found in the work environment
- ethyl alcohol, amatoxin, mercaptopurine, methotrexate**

### facultative

It causes lesion only in vulnerable individuals disproportionate to the dose. It arises unpredictably and sporadically either by **allergic reaction** or **atypical biotransformation** of the substance. In the case of atypical biotransformation, this often involves a different CYP450 isoenzyme. They occur at different time intervals and the damage is not reproducible in the animal. The group mainly includes *drugs* causing viral-like hepatitis, leading to cirrhosis if the drug is not discontinued.

Examples of medications:

- halothane** (anaesthetic) - allergic damage, 50% mortality
- phenytoin'** (antiepileptic) - potent inducer of CYP2D6 isoenzyme
- isoniazid'** (antituberculosis) - rapid acetylators (about half the population) at risk, more toxic metabolite produced with daily alcohol consumption, liver necrosis after combination with rifampicin

## Liver damage

Evaluation according to emergence in time:

### Acute

- professionally rare
- inappetence, nausea, vomiting, icterus, hepatomegaly
- more severe lesions - liver shrinkage, ascites, hemorrhage, coma (typically poisoning with *Amanita phalloides* or paracetamol)
- on the basis of an allergic reaction together with the characteristic manifestations of a hypersensitivity reaction (e.g. exanthema, febrile eosinophilia)

## Chronical

- difficulty in assessing the connection with the profession
- poor prognosis
- cirrhosis, fibrosis or tumour develops
- described after arsenic, carbon tetrachloride, TNT

## References

### Source

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### Bibliography

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