Clinical Aspects of Liver Diseases

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► The ***"chemicalization"*** *of the environment* in the course of the last 100 years has proceeded virtually without restraint, partly as a result of ever-advancing technologies and partly because of the continuously rising demands of society and increased industrial productivity. • The liver, however, which is at the centre of the detoxification mechanisms (s. pp 52–56), is not able to adapt to new demands on the detoxification process within three to four generations. Adaptations of this kind by an organ or an organism to harmful or life-threatening influences can only take place over a much longer period of time, if at all (as has been shown in the animal and plant kingdoms).

► The ***"Chemicalization"*** *of the workplace* can be kept almost completely under control by compliance with industrial hygiene regulations. In this way, it is generally possible to avoid toxic liver damage. Specific **exposure** can, however, be expected in *occupational medicine* in the following situations: (*1.*) inadequate protective measures at work, (*2.*) the appearance of new, hitherto unforeseen or (as yet) unknown toxic compounds following a particular incident or due to a change in working techniques, and (*3.*) the combined impact of various toxic substances, especially in conjunction with alcohol and/or drugs. • In *agriculture*, the increasing use of fertilizers, animal feed additives, preservatives and pesticides has become a considerable problem. The occurrence of disulfiram-like effects has also been observed. • Far too little attention is generally paid to the risks of toxic liver damage encountered in *hobbies* or *do-it-yourself activities.* Handling chemical substances – often in small, poorly ventilated rooms over lengthy periods of time – can quite easily increase the danger of liver damage, although under normal circumstances there is nothing to fear if the manufacturer's instructions are strictly adhered to. The risk of damaging one's health is – often unconsciously – suppressed or indeed goes unnoticed.

For every liver disease that cannot be clarified with certainty, each differential diagnosis should always include toxic substances in food, at work, in the house or garden and in those places where people pursue leisure activities. It is extremely difficult to identify the causal noxa. In the individual case, however, identification can be of considerable importance for general assessment purposes and possibly when an expertise is required.

1 Historical review

In the 19th century, cases were observed of workers in the match industry who suffered liver damage due to **phosphorus** contamination leading to acute hepatic dystrophy. • *Since then, the relationship between exogenous noxae and liver disease has been considered unequivocal.*

► **Arsenic:** Liver damage due to arsenic was first described in 1774 by F.L. Bang. In 1888 E. Ziegler et al. reported on damage caused by arsenic to the hepatocytes and sinusoids with subsequent scarring. The occurrence of melanosis, hyperkeratosis and liver fibrosis or cirrhosis was described as *"Reichenstein's disease"* (L. Geyer, 1898). It was observed in Reichenstein (Silesia) and Freiberg (Saxony) and traced back to chronic arsenic poisoning caused by contaminated drinking water (containing up to 25 mg arsenic per litre). Toxic liver damage, even culminating in cirrhosis, due to the presence of arsenic in beer was observed in 1900. Over the following years, there were further reports of arsenic poisoning from drinking water, e.g. in Argentina (A. Ayerza, 1918), Mexico and Taiwan. In 1974 a comprehensive study was published on chronic arsenic poisoning caused by contamination of the river Tononce in Antofagasta (Chile): several hundred people became ill between 1955 and 1972; arsenic was even found in fruit juice, beer and cola as well as in milk and food. (76) • Arsenic was officially introduced as a pesticide in viniculture in 1925 (after it had already been used for this purpose for some time). Since 1942 its use as a pesticide has been banned. Consumption of the so-called *wine-grower's house drink* led to severe liver damage, liver fibrosis with portal hypertension and even oesophageal varix bleeding, carcinoma and haemangioendothelioma of the liver. This homemade wine, which was produced by watering down the wine obtained from a second pressing of the grape skins and which had a low alcohol (3–5 vol. %) but high arsenic content, was consumed in large quantities (3–5 litres per day). • The severe arsenic poisoning of an aircraft pilot who had been spraying arsenic calcium carbonate dust as a pesticide was reported in 1930. • Extensive liver damage was also observed during the long-term treatment of psoriasis with Fowler's solution. • Occurrences of well-water poisoning due to arsenic pesticides were registered as late as 1984 in the USA (2) (s. p. 569) and again in 1998 to an incredible extent in Bangladesh.

► **Thorotrast:** Thorotrast was introduced into radiology by K. Frik et al. in 1928 on the grounds of its excellent opaque properties and good tolerance. As early as 1933, the carcinogenic effect of ThO_2 was pointed out by C. Oberling et al. The occurrence of an angiosarcoma 12 years after the administration of thorotrast was reported by H.E. McMahon et al. in 1947. Production was stopped in 1950, but thorotrast was still occasionally used up to 1958. All in all, about 1 million patients using thorotrast between 1928 and 1958 were examined. $^{232}ThO_2$ is a 90% α-emitter with a half-life of approximately 400 years. It is never excreted from the body. Most of it (70–75 %) is stored in the liver, although the highest relative concentration per gram tissue is found in the spleen. In total, more than 125 thorotrast-induced cases of malignancy have been reported in the literature – even 36, 39 and 44 years after administration. (23, 71) (s. figs. 30.2, 30.3) (s. p. 569)

► **Thioacetamide:** In 1942 thioacetamide was introduced in the USA as a citrus fruit preservative. Shortly after ingestion of this fruit, liver damage (cell necrosis, steatosis) and cirrhosis occurred. There were even reports of fatalities. • Animal experiments showed