

# Clinical Aspects of Liver Diseases

## 28 Alcohol-induced liver damage

	Page:		Page:		
1	<i>The “alcohol” factor</i>	520	4.6	Chemical additives in alcoholic drinks	528
1.1	Use of alcohol	520	4.7	Coexistent hepatotoxic agents	529
1.2	Abuse of alcohol	520	4.8	Malnutrition and undernourishment	529
1.3	Addiction to alcohol	520	5	<i>Clinical features of alcoholic liver damage</i>	529
1.4	Alcohol as a cause of disease	521	5.1	Types of disease	529
1.5	Costs for the economy	521	5.1.1	Alcoholic fatty liver	529
2	<i>Biochemical effects of alcohol</i>	522	5.1.2	Alcoholic hepatitis	531
2.1	Alcoholic hypoglycaemia	522	5.1.3	Alcoholic cirrhosis	532
2.2	Alcoholic hyperglycaemia	522	6	<i>Complications</i>	532
2.3	Alcoholic hyperlipidaemia	522	6.1	Alcoholic ketoacidosis	532
2.4	Alcoholic hyperuricaemia	523	6.2	Zieve’s syndrome	533
2.5	Alcoholic porphyria	523	6.3	Cholestasis	533
2.6	Haematological disturbances	523	6.4	Fat embolism	533
2.7	Formation of addictive substances	523	6.5	Portal hypertension	533
2.8	Effects of disulfiram	523	6.6	Primary liver cell carcinoma	534
2.9	Alcohol-related interactions	523	7	<i>Diagnostic alcohol markers</i>	534
2.10	Lipid peroxidation	524	7.1	Questionnaire	534
2.11	Immune reactions	524	7.2	Laboratory findings as markers	534
3	<i>Morphological effects of alcohol</i>	524	8	<i>Prognosis</i>	535
3.1	Adaptation	524	9	<i>Therapy</i>	536
3.2	Types of damage	524	9.1	Alcohol abstinence	536
3.3	Steatosis hepatis and fatty liver	526	9.2	Nutrition	536
3.4	Hepatic fibrosis	526	9.3	Substitution	536
3.5	Liver cirrhosis	527	9.4	Physical exercise	536
4	<i>Pathogenesis</i>	527	9.5	Drug therapy	536
4.1	Genetic predisposition	527	9.6	Liver support system	537
4.2	Gender	528	9.7	Liver transplantation	537
4.3	Age	528		• References (1–148)	537
4.4	Previous liver damage	528		(Figures 28.1–28.16; tables 28.1–28.6)	
4.5	Alcohol consumption	528			

### 1 The “alcohol” factor

#### 1.1 Use of alcohol

*We do not know when and where drinkable grape-juice was originally pressed from wild vines, nor when and where wine was produced and enjoyed for the first time following fermentation and purification.* • The oldest find is probably a grape-squeezer containing grape seeds found in the region south of Damascus, dating back to the time around 6000 BC. • Wine consumption and drunkenness are described in the EPIC OF GILGAMESH, which goes back to 4000–3000 BC. God told Noah, who is called Utnapishtim in the epic, to grow grapevines following the Flood (around 4000 BC). This he did: “*And he drank of the wine, and was drunken*” (Genesis, 9.21). • About 2700 BC, Chinese writings mention the benefits as well as the dangers of consuming wine. • Many descriptions pertaining to the consumption of wine (and also beer) as well as to drunkenness can be found in the rock tombs at El Kab in Upper Egypt (around 2500 BC), in the EBER’S Papyrus (around 1550 BC) and in various other discoveries. • A Babylonian clay tablet from the year 2230 BC shows a prescription written by a Sumerian physician regarding the use of wine for medical purposes. The TALMUD defines the correct way to drink wine and praises its medical applications. However, in the Old Testament, ISAIAH (5.11) expresses his anger saying: “*Woe unto them that rise up early in the morning, that they may follow strong drink; that continue until night, till wine inflame them!*” HOMER was aware of the early onset of drunkenness due to a rapid intake of alcohol and complained: “*Often times did you wet my garment, in front, at my bosom, spilling wine from your mouth, in clumsy childishness*” (s. p. 60), “*The wine must have been doing you a mischief, as it does with all those who drink immoderately*” (Odyssey, 21.293). OVID also admonished: “*When drinking, I will set you a limit: Head and feet must never fail.*” The wild drunken orgies of the unleashed bacchantes, priestesses of Dionysus, were dreaded events. PLUTARCH, however, wrote on the moderate consumption of wine: “*The most exquisite amongst all beverages, the most pleasant amongst all food-stuffs, the most appetizing amongst all remedies.*” • In the 11<sup>th</sup> century, pure alcohol was made from strong old wine for the first time in Southern Italy. From ca. 1250, this new substance was offered in Italian chemist’s shops as a panacea and acclaimed as **aqua vitae** (“water of life”), **aqua ardens** (“burning water”), **spiritus vini** (“spirit of wine”) or **quinta essentia** (“fifth essence” = filling the space between the cosmic bodies). The term “**alcohol**” was most probably introduced by PARACELSUS about 1530, from the Arabic word al-kuhl, meaning “the finest part of something”.

As far as is known, the time around 6000 BC marks the beginning of a development in which man became more and more familiar with the manifold **use and effect** of wine or other alcoholic beverages, e.g. as roborant, tonic, sedative, narcotic, appetizer, aphrodisiac, disinfectant or an externally applied antiphlogistic. Apart from that, alcohol was an essential part of festive banquets or religious rituals, but was also identified as a cause of drunkenness, physical dysfunction, disease and liver damage when consumed to excess.

#### 1.2 Abuse of alcohol

► Alcohol abuse is defined as overindulgence, i.e. **abnormal** or **pathological drinking behaviour** (according to quantity and modality). However, there are no generally accepted threshold values regarding this definition, since intake and metabolism of alcohol are influenced by many factors varying from individual to individual. Apart from that, alcohol metabolism and tolerance mainly depend on whether the intake is a *singular, intermittent or continuous event*. (s. p. 61) **Lethal alcohol poisoning** generally occurs at blood alcohol concentrations ranging between 3.1 and 5.6‰ (2.0–3.5 g/kg BW). (85) However, there have been reports of isolated cases in which considerably higher concentrations did not lead to death. In this context, reduced tolerance (e.g. caused by coexistent hepatic disease, organopathies, hypothermia, age, drinking speed, drinking habits and type of drink) plays an important role. (4, 69) (s. p. 61) • Excessive alcohol intake to the point of abuse (with the alcohol dose varying from person to person) is characterized by the occurrence of **somatic damage**. • Alcohol abuse bears a certain relationship to the average intake per capita (in litres). In Germany, **annual consumption** increased from 3.1 l (1950) to 12.5 l (1980) and has remained at a level of about 12 l ever since. These statistics, however, do not take into account the large amounts of home-made cider or spirits, which cannot be recorded. Other countries, such as Denmark, Spain, Italy, France and Portugal, also sadly feature in this “top group” with 12–13 l per capita and year. At 7–8 l, consumption is, however, considerably lower in the Netherlands and the U.K., and lowest of all in Norway at 4 l. Worldwide, alcohol consumption has almost tripled since 1970. (67) • Alcohol abuse is found in **all social strata**, with people drinking at social occasions and parties, due to worry or poverty, when doing business and because of stress as well as success. • **Any of these circumstances can pave the way to abuse.** (s. tab. 28.1)

#### 1.3 Addiction to alcohol

► A kind of (low-dose) dependence may also develop when alcohol is consumed daily, albeit in minor quantities. *As a rule of thumb, alcohol always makes people dependent when consumed on a regular basis – no matter what the dose may be.* • Alcohol addiction comprises (1.) **physical dependence** including increased tolerance as well as the withdrawal syndrome and (2.) **psychological dependence** with an uncontrollable desire for permanent or intermittent alcohol consumption, reduced self-control as well as changes in behaviour. (s. tab. 28.1) Alcohol abuse includes addiction without actually being identical to it. • Neither the **brain’s reward system** (A. HERZ et al., 1989) nor the **addiction memory** (J. BÖNING, 1992) are stimulated by *occasional alcohol consumption*. Another explanation for this