

Alcohol – Health Effects, Working Environment and Prevention

Eugenija Žuškin, Jasna Lipozenčić¹, Vlado Jukić², Ana Matošić³, Jadranka Mustajbegović, Nada Turčić⁴, E. Neil Schachter⁵, Milan Milošević

Andrija Štampar School of Public Health, Zagreb University School of Medicine;
¹University Department of Dermatology and Venereology, Zagreb University Hospital Center; ²Vrapče Psychiatric Hospital; ³Alcoholism Referral Center, Sestre milosrdnice University Hospital; ⁴Pension and Disability Insurance Fund, Zagreb, Croatia; ⁵Mount Sinai School of Medicine, New York, NY, USA

Corresponding author:

Professor Eugenija Žuškin, MD, PhD
Andrija Štampar School of Public Health
Rockefellerova 4
HR-10000 Zagreb
Croatia
ezuskin@snz.hr

Received: March 31, 2006

Accepted: May 26, 2006

SUMMARY Alcoholism is a growing medical and public health issue both in adults and in the younger generation. It is a multietiological phenomenon influenced by genetic, psychological, cultural and other factors. Alcoholic beverages have traditionally been prepared from various ingredients such as grapes, hops, rice, honey, etc. Drinking prevalence has varied and is more pronounced in women and the youth. Alcoholism is shown to be of neurophysiological etiology and may lead to impairment of all human body systems. The most frequent cause of death in alcoholics are diseases of the cardiovascular system. The problem of alcoholism at workplace is very important since by affecting health and reducing work productivity it leads to accidents, injuries and decreased working capacity. Efficient solving of alcoholism and related problems includes early detection, so it is necessary to orient the health care services towards primary prevention and early interventions.

KEY WORDS: alcoholism; health effects; workplace; prevention

Alcoholism is a progressive lethal disease characterized by the loss of alcohol consumption control, obsession with alcohol, and denial of relationship between alcohol consumption and deterioration in health and living conditions.

Alcohol addiction, alcoholism, is one of the major public health issues seen from the social and economic perspective (1-3). Recognized as a multietiological phenomenon, alcoholism is primarily

a disorder, and not a symptom of other diseases or emotional problems (4). Relationship between alcohol consumption and health is complex and multidimensional: alcohol is the cause of around 60 different medical conditions, and over 4% of diseases are directly related to alcohol consumption. The severity of alcoholism as a disease depends on a number of genetic, psychological and cultural factors. Social problems usually appear before physical health becomes impaired.

Alcoholism may lead to physical and psychological problems in persons of any age. Older alcoholics very frequently have problems as a consequence of interaction between alcohol consumption and physiological changes developing with age. Chemical composition of alcohol affects almost all body cells, and in high concentrations can lead to coma or death. Among the most common effects, often stated are: impairments of the immune system, frequent infections, high blood pressure, heart rhythm disorders, impairments of the heart muscle, stroke, higher prevalence of malignant conditions, cirrhosis and other impairments of the liver, and malnutrition (5). Alcoholism is also shown to be related to increased mortality, and the most frequently stated causes are accidents, injuries, poisonings, diseases of the cardiovascular system, lung tuberculosis, liver cirrhosis, malignant diseases and suicide (6). Alcohol consumption in pregnant women may cause severe impairments in children, the most severe being fetal alcohol syndrome (FAS). It is characterized by irregularities in the structure and development of the head and face, along with disorders in brain development.

HISTORICAL DEVELOPMENT

Alcohol as a beverage is as old as the human beings themselves, and the history of wine is as old as the mankind. Figure 1 shows the ancient God of wine Bacchus by the Italian baroque painter Michelangelo Merisi da Caravaggio.



Figure 1. Ancient God of wine Bacchus by Italian baroque painter Michelangelo Merisi da Caravaggio, c. 1597.

Prehistorical man knew exactly how to make wine, and the paleontologists have found fossils that most probably are residues of wine or pressed grapes (7). Chemical analyses of 9000-year-old utensils have confirmed that they contained fermented mixtures of rice, fruits (grapes or hawthorn berries), and honey. Analysis of utensils from the Neolithic period (7000-6600 B.C.) in China, in the province of Jiahu and Henan, has revealed the residues of rice wine ingredients. Figure 2 shows a black-figured wine amphora (wine jar) from Greece by Exekias about 540-530 B.C.



Figure 2. Black-figured amphora (wine jar) signed by Exekias, made in Athens, Greece, about 540-530 B.C.

Neolithic tribes drank wine made of broad beans in 6400 B.C. (8). Wine production started in China in 3000 B.C. One of the best known wines of the pharaonic age was *Kankomet*, drunk at the times of Ramses III (1198-1167 B.C.) (9). Archeologists argue that hop beer was produced in the Middle East in 7000 B.C. Grain had been fermented and used for production of beer 2000 years before it was used for making bread. Babylonians were producing beer from barley and wheat malt as early as 7000 B.C. In the old times, beer was called *hqt*, and the Greeks called it *zythus*. It was seen as an important Egyptian drink for the rich and the poor, so it was often placed in the tombs (10). Figure 3 shows Hojo-drinking sake by Koshin (20th century).

Alcohol production of wine and beer is obtained from fermentation of grapes, fruits, grain, hop, honey, and other herbal substances that could be found in all parts of the world. The discovery of the distillation process in the 12th century opened the way to the production of drinks with a high concentration of alcohol, i.e. the spirits. The concentration of alcohol, especially of ethyl alcohol, varies, e.g., beer usually contains around 5%, wine 12%-15% and spirits usually around 45% of alcohol.



Figure 3. Antique Ivory Netsuke Shojō Drinking Sake by Koshim, 20th century.

Numerous are the reasons for drinking alcohol: social customs (celebrations, funerals), in stressful situations when coping with daily problems (most often with interpersonal relationships), and availability of alcoholic drinks. Figure 4 shows *The Drinker* by Adriaen Jansz van Ostade.



Figure 4. *The Drinker* by Adriaen Jansz van Ostade, native of Harlem, c. 1510.

However, much before man became familiar with it, the primates used alcohol (accidentally and passively) to get drunk (11). Such a behavior can still be seen in Africa today, when elephants and monkeys go from tree to tree at the time their fruits are falling to the ground (in fermented state) being highly rich in sugars and water.

The term “drinking disease” (Jiu Bing) was first described in China in an old document *Wang Shuhe’s Canon of Pulsology*, and abnormal drinking (Jiu Bo) in the book *The Spiritual Pivot (Ling Shu)* around 2600 B.C. (12,13). Wan et al. (12) were the first to describe a comatose state as a consequence of alcohol drinking (Jiu Jue). Descriptions of pathogenic manifestations of all diseases (Zhu Bing Yuan Hou Lun) cover the pathology and etiology of illnesses, including alcoholism (14). The first anti-alcoholic medicine was recorded in China in the book *Shen Nong’s Classic of Herbology*. The most commonly applied medicine against drinking contained *Flos Puerariae*, *Fructus Hovenariae*, and the well known prescription for those already drunk was anti-tipsy decoction of *Flos Puerariae* (12).

Alcohol and harmful effects of excessive drinking were well recognized and documented in the old times, particularly in the Bible. The Christian civilization has transferred the symbolic concept of wine consumption. There are a number of different thoughts and facts about the meaning and place of wine. Namely, Jesus and his Apostles were invited to a wedding, and at some point there was no juice of grapes left. So, Jesus turned some 600 liters of water into a fresh juice of grapes. At the Last Supper, Jesus used nonalcoholic juice of grapes as a symbol of his blood and contact with us, and not the wine. The Jewish and Greek word for wine means a fermented juice of grapes, but also intoxication by wine. The original Greek word is *onios*, meaning both alcohol and fresh juice of grapes. However, that word did not indicate directly the possible alcohol contents. The English word *wine* originally had two meanings – nonfermented juice and alcoholic drink. Figure 5 demonstrates recreating old drinks providing an enjoyable form of time-traveling.



Figure 5. Recreating old drinks provides an enjoyable form of time-traveling.

PREVALENCE OF ALCOHOL CONSUMPTION

In general, men drink more often than women. However, the habit, the type of alcoholic drink and the intensity of alcohol drinking show different geographical distribution worldwide, and a series of factors such as sex, age and different social and economic factors have their impact as well. Alcoholism in Islamic countries shows a very low incidence, so it is still not seen as a great issue there. In Islamic world, alcohol addiction has been reduced since addiction in general is seen as a social evil (15). Researches in the United States and Europe indicate that Protestants drink less alcohol than Catholics. Besides, the European drinking culture in the northern countries is different from that in the Mediterranean, which could be the result of numerous factors, including variations in the ecosystem, climate, and social and political structures.

According to studies in the USA, men drink twice as much (21%) as women (10%) (16). Dawson and Archer (17) found a ten-fold difference between men (13.63%) and women (1.33%), and in a study by Emslie *et al.* (18) a significantly higher prevalence of alcohol drinking was observed in men than in women. In Croatia, 81.3% of men and 51.2% of women are the drinking population (19). Alcoholism is somewhat more frequent in those of middle age, lower income and lower education. As to educational level, a great difference has been observed between rural and urban areas: in urban areas, alcoholism is more prevalent in persons with higher educational level, whereas in rural areas it is associated with those with lower education (20). The drinking image has been changing worldwide – with growing numbers of women and younger people as drinkers nowadays.

Higher percentages of symptomatic alcoholism have been observed in women, and the most frequent reasons are family disorders (21). Relationships in the primary family are very important: alcoholics come into contact with alcohol earlier, they start drinking more often earlier, and there is a tolerance to alcohol drinking in their primary family (22).

Painters frequently paint the motifs related to drinking alcohol. Figure 6 shows *Le Bar aux Folies-Bergere* by Edouard Manet.



Figure 6. *Le Bar aux Folies-Bergere* by Edouard Manet, 1881-1882.

PATHOPHYSIOLOGICAL CHANGES IN THE BODY

Alcoholism as a disease of neurophysiological origin and is diagnosed only when changes in the character and personality have developed; normal emotions are neurologically intensified to the abnormal extent, leading to development of chronic conditions, fear, bitterness, guilt and depression. As described by Hagnell and Tunving (23), alcoholism is defined as a state with active signs and symptoms of excessive drinking of alcoholic drinks, including increased tolerance to alcohol and changes in behavior: a pathological desire for alcohol after drinking small quantities; a need to drink the following day; and amnesia after alcohol drinking. Persons who drink and suffer from depressive disorders represent a greater danger both at home and at workplace: untreated alcoholism intensifies the state of depression, reduces reactions to standard medication, increases the prevalence of suicide and murder, criminal offences and traffic accidents (24,25).

Dangerous drinking is mainly associated with harmful effects on health, and there is no clear line between controlled and excessive drinking. Namely, drinking-related problems appear in both groups. This leads to reduced concentration and visual functions, the ability to differentiate light stimuli is impaired, vigility and attention are decreased, and behavior disorders develop (reduced self-control and self-criticism) (26). Research results show that even the lowest concentrations of alcohol cause a certain degree of risk at workplace and in traffic.

The term alcoholic refers to a person not being able to control his or her drinking over a longer period of time. Alcoholics drink alcohol so as to

hide the negative emotions of anger, guilt or depression. Besides, they may develop a feeling that they are stronger than they really are. Alcohol affects cognitive functions as well. Alcoholism as a disease shows three characteristic stages: social consumption, alcoholism, and irreversible impairments.

Acute drunkenness is the result of acute effects of alcohol on a man. **Slight drunkenness** develops with alcohol concentrations of 0.5 to 1.5, drunkenness at 1.5 to 2.5, **heavy drunkenness** at 2.5 to 3.5, and **deep unconscious state** above 3.5 *per* thousand of alcohol in the blood. Depending on alcohol concentration in the blood, such states may lead to disorders of clearness of mind, reduced visual acuity, balance disorders, lower blood pressure, accelerated pulse, vomiting, uncontrolled urination and bowel discharge. Alcohol concentration above 3.5 *per* thousand leads to unconsciousness, coma and possible death. Alcohol concentration in the blood – alcoholemia – determines which psychopharmacological procedure will be taken for the treatment of acute drunkenness (27).

An **alcoholic** is a person who drinks alcohol excessively, and in whom alcohol addiction has led to psychological, physical and social disorders. The consequences of long-lasting alcohol consumption are manifested by impairments of a number of body systems such as digestive, nervous, cardiovascular, and reproductive systems, including mental disorders.

The signs of early alcoholism are unfavorable physical reactions to drinking cessation, appearing even after a short-lasting abstinence. Such persons are preoccupied with drinking; they deny their own addiction and continue drinking despite the knowledge of its harmful effects. Over the course of time, some persons become tolerant to drinking effects and require growing quantities of alcohol to obtain the desired effects. Some alcoholics drink alone, they start early in the morning, and continually turn from the spirits to beer and wine. Gradually, the alcohol starts dominating their thoughts, emotions and actions, and becomes the primary way in which the person interacts with people, at work and in private life.

Laboratory tests done on alcoholics show elevated values of carbohydrate-deficient transferrin (CDT), middle volume erythrocytes (MCV), and gamma glutamine transpeptidase (gamma GT); so, these parameters have shown to be useful criteria for identification of excessive alcohol

consumption, beside medical history and physical examination (28,29). In heavy alcohol addicts with severe destruction of hepatic tissue, glucoenergetic capacity is reduced, so they show a 45%-70% probability of hypoglycemia and reduced tolerance to carbohydrates (30). Breitenfeld *et al.* (31) have described the importance of biological markers in alcohol-related diseases. As regards the prevalence of secondary diseases, a three-fold prevalence of diabetes has been found in alcoholics in Croatia (32).

DERMATOLOGIC REACTIONS

Alcohol abuse is associated with many health problems, especially skin changes (33). As a small, water- and lipid-soluble molecule, alcohol reaches all tissues of the body and affects most vital functions. Cutaneous diseases are now emerging as useful markers of alcoholism detectable at an early and possibly reversible stage of the disease. Similarly, Wegrzynek and Budzanowska (34) suggest that skin disorders may be markers of alcohol misuse. Jacobi *et al.* (35) indicate that ethanol evaporation occurs *via* skin lipid layers but without significant effects on the penetration of a topically applied substance. Pragst *et al.* (36) conclude in their study that fatty acid ethyl ester in skin surface lipids can be used for medium-term retrospective detection of heavy drinking. Excessive alcohol consumption is also manifested by disorder of the porphyrin metabolism (37,38).

Alcohol consumption and abuse can have a variety of cutaneous manifestations. Becker (39) reports an increased incidence of dermatoses and alcohol abuse. Marusic *et al.* (40) have demonstrated the presence of skin changes in 31% of patients treated for alcohol addiction. Certain skin disorders have now been demonstrated to be affected by alcohol misuse, in particular psoriasis and discoid eczema (38). Discoid eczema appears to be specifically related to alcohol excess and is associated with deranged liver function. Even early abuse can result in distinctive skin changes or exacerbate existing cutaneous disorders (41). For instance, psoriasis as a chronic skin disease can be triggered by alcohol and was found to be much more prevalent in alcoholics than in control group (42). The same authors found an association between alcohol and HLA-DQA1*0201 in patients with psoriasis. Association between alcohol and psoriasis was also described by Zimmerman (43). Poikolainen *et al.* (44) and Naldi *et al.* (45) report on excess mortality among patients with psoriasis due to alcohol consumption and suggest that

alcohol is a major cause of this excess mortality. Heavy drinking was found to be significantly more common in those with severe psoriasis (46).

Table 1 shows the most common changes on the skin developing as a consequence of alcohol consumption.

Rosacea, post-adolescence acne, superficial infections and porphyria cutanea tarda may also be markers of alcohol misuse. Alcohol drinking has been particularly associated with rosacea and psoriasis (47). Lee *et al.* (48) demonstrated a statistically significant association between leukoplakia and oral submucous fibrosis with alcohol drinking. Freedman *et al.* (49) describe a possible association risk of melanoma with alcohol intake.

Karvonen *et al.* (50) report that alcohol intake and smoking appear to be risk factors for infectious eczematoid dermatitis. Alcohol intake and smoking have also been reported as risk factors in some inflammatory skin disorders.

The study of Yoda *et al.* (51) on the effect of alcohol on thermoregulation during mild heat in humans suggested that decreases in body temperature after alcohol drinking were not secondary to skin vasodilatation, but rather of a decrease in the regulated body temperature evidenced by the coordinated modulation of various effectors of thermoregulation and sensation.

Cutaneous lesions such as vascular spiders, telangiectasias, palmar erythema, nail changes (white nails), changes on mucous membranes (shining tongue), proneness to various infections (fungal and bacterial) as well as Dupuytren's contracture have more frequently been described in patients with alcoholic cirrhosis (52). Petter and Haustein (53) describe severe bullous exanthema and enanthema combined with hepatitis after alcohol consumption.

Alcohol intolerance and facial flushing in patients treated with topical tacrolimus has been reported by Milingou *et al.* (54). Alcohol interactions

Table 1. Skin changes in alcoholics

<p>Changes on blood vessels</p> <ul style="list-style-type: none"> Sudden flushing Petechiae and ecchymoses Nevus araneus Palmar erythema 	<p>Skin tumors</p> <ul style="list-style-type: none"> Malignant melanoma (probable) Basalioma (less) Carcinoma of the respiratory and digestive tract (induced by smoking)
<p>Changes on nails</p> <ul style="list-style-type: none"> Terry nail Koilonychia Clubbed fingers 	<p>Changes due to nutrition imbalance</p> <ul style="list-style-type: none"> Xerosis Delayed wound healing Pellagra Scurvy Zinc deficiency
<p>Changes due to liver impairments</p> <ul style="list-style-type: none"> Icterus Pruritus Porphyria cutanea tarda 	<p>Interactions with existing diseases</p> <ul style="list-style-type: none"> Psoriasis Rosacea Acne vulgaris Seborrheic dermatitis Nummular eczema
<p>Endocrine disorders</p> <ul style="list-style-type: none"> Baldness Hypogonadism Gynecomasty Hyperestrogenism Pseudo-Cushing 	<p>Other</p> <ul style="list-style-type: none"> Facies aethylica Skin atrophy Urticaria and anaphylactic reactions Dupuytren's disease Fetal alcoholic syndrome Bureau-Barriere syndrome (acquired ulcerative mutilating acropathy) Launois-Bensaude syndrome (benign symmetric lipomatosis) Eruptive xanthoma Zieve syndrome
<p>Immune disorders</p> <ul style="list-style-type: none"> Viral infections Bacterial infections Dermatomycoses 	

with drugs and its effects on the treatment of skin diseases have been reported by Zachariae (55). Similarly, Bader *et al.* (56) report on patients with chronic alcohol abuse and ichthyosiform erythroderma with dry skin (i.e. xerosis cutis) as a striking common feature. The authors suggest that this disease be added to the known skin disease caused by chronic alcohol abuse.

ALLERGIC/IMMUNE RESPONSES

Alcoholic drinks are involved in a variety of hypersensitivity reactions (57). These include flushing syndrome, anaphylactoid reactions (urticaria, angioedema) as well as triggering of asthma, food allergy or exercise-induced anaphylaxis in susceptible subjects. Smith *et al.* (58) report on the development of delayed-type hypersensitivity skin responses in alcoholics, indicating that moderate alcohol consumption independently affected delayed skin reaction. Alcohol shows significant impact on immune function causing changes in the form of vasculitis (59).

Among the physiological effects associated with excessive alcohol consumption are alterations in the immune function (60). Alcohol intake may play a role as a promoter of the development of immunoglobulin E (IgE) mediated hypersensitivity to different allergens. Ethanol consumption inhibits Th1-associated interleukin-12 and interferon-gamma cytokine production and delayed-type hypersensitivity. Acetaldehyde, a product of alcoholism metabolism, is known to bind covalently to plasma and red cell protein, which is recognized as foreign by the immune system.

Gonzalez-Quintela *et al.* (61) demonstrated alcoholism consumption above a certain threshold to be associated with an increased total serum IgE level. Similarly, Linneberg *et al.* (62) report a positive association between alcohol consumption and serum total IgE. In an epidemiological study the same authors also demonstrated a positive association between alcohol consumption and the prevalence of positive skin prick test. The risk of developing positive skin prick test tended to increase with the increasing consumption of alcohol. Total and specific serum IgE to common allergens is increased in heavy drinkers (47). The authors suggest that endotoxin mediates most of the immune alterations associated with heavy drinking. Mujagic *et al.* (63) demonstrated that alcoholic liver disease plays an important role in the development of type I allergic skin manifestations. Alcohol in liver disease and not liver disease causes im-

mune abnormalities and accounts significantly for the increased occurrence of allergic skin reactions. Alcohol consumption of more than 14 units/week was associated with an increased prevalence of pollen sensitization (64). The same authors suggest that alcohol consumption above a certain threshold is also associated with an increase in total serum IgE levels.

GASTROINTESTINAL SYSTEM

Having been consumed and passing through different parts of the gastrointestinal (GI) system, alcoholic drinks may damage the esophagus mucosa, interfere with gastric secretion, and stimulate small and large intestine muscles leading to diarrhea (65-67). They also damage the functions of the liver and pancreas, act on the muscles separating esophagus from the stomach, and cause the feeling of heartburn (68). Occult bleeding in alcoholics has been described by Zwas and Lyon (69). Alcohol drinking and cigarette smoking are about equally responsible for the development of peptic ulcer (70). Alcohol inhibits absorption of nutrients in small intestine and enlarges the passage of toxins through intestinal walls, which are then responsible, along with metabolites, mainly acetaldehydes and free radicals, for the impairments. Diseases of the GI system are often associated with deadly outcome.

The risk of developing cancer in alcoholics has been described by Yokoyama *et al.* (70,71). As the most frequent cancers considered to be the consequence of chronic alcohol consumption, the following have been described: cancers of the tongue, tonsils, pharynx, larynx, and esophagus (72).

CENTRAL NERVOUS SYSTEM

Excessive alcohol consumption, either short- or long-lasting, has adverse effects on the brain. Even in alcoholics without specific neurological or hepatic problems, signs of regional brain damages with cognitive changes have been observed (73,74). Alcohol acts on the brain in different ways and there are a number of factors that may intensify these effects such as age, sex, personal sensitivity to alcohol, duration of drinking, nutrition, and sensitivity of certain brain areas (75). Chronic alcohol consumption reduces certain specific functions related to structural and functional disorders in specific areas of the central nervous system (76,77). Hommer (78) showed that women were more sensitive than men to the consequences of alcohol consumption. In this study, he argues that

men alcoholics have a smaller brain volume compared to nonalcoholics. Degeneration of neurons develops by various mechanisms and in various brain areas during alcohol intoxication.

Toxic effects of ethanol, dietary deficiency, electrolyte disorders, and liver impairments could be important in the etiopathogenesis of brain damage. Form-Frians and Sanchis-Segura (79) indicate that acetaldehydes, the first oxidative metabolites of ethanol, have their role in brain damage related to chronic alcohol consumption. They act on several systems of neurotransmitters in the brain, and inhibit the receptors for glutamates, for which Dodd *et al.* (80) have shown that may be involved in numerous adaptive brain changes manifested after alcohol consumption.

Chronic cigarette smoking deteriorates alcohol-induced neurological impairments, leading to damages of the frontal lobe cell membrane and the cerebellum (81). Upon cessation of alcohol consumption, the central nervous system in chronic alcoholics reacts by developing an alcoholic syndrome, which is more pronounced in those with shorter periods of excessive drinking. Brain excitation in chronic drinking may lead to cell death and degeneration, Wernicke-Korsakoff syndrome and withdrawal disorders.

CARDIOVASCULAR SYSTEM

A high prevalence of cardiovascular diseases (high blood pressure, coronary heart diseases, heart muscle diseases, heart attack) in alcoholics has been described, among others, by Cipriani *et al.* (82) and Lucas *et al.* (83). Studies by some authors have shown that coronary heart diseases are the most common causes of death in alcoholics (around 50%) (84-86). There is a clear correlation between excessive alcohol consumption and the risk of sudden heart death. The authors have shown that alcohol may be responsible for heart arrhythmias and sudden deaths in alcoholics with diseases of the heart muscle but also in those with a healthy heart. Nishida *et al.* (87) argue that alcohol drinking may be one of the direct factors responsible for the development of arrhythmias and asymptomatic disease of the heart valve. Frost and Vestergaard (88) have confirmed that excessive alcohol drinking also increases the risk of atrial fibrillation.

A number of researchers have described a direct impact of chronic excessive alcohol drinking on the heart muscle itself; Fernandez-Sola *et al.* (89) and Dettmeyer *et al.* (90) determined diastolic impairment of the left ventricle with concurrent

systolic impairment. It seems that there is a correlation between systolic and diastolic dysfunction, and the dose of alcohol consumed, as has been confirmed by the results obtained by Rajzer *et al.* (91). Kajander *et al.* (92) found enlargement of the left and right ventricles including thickening of the lining as the result of excessive alcohol drinking.

Changes in blood vessels are the consequence of a number of biochemical changes directly affected by alcohol. Drinking of alcohol >40g/day increases all lipid values. Lipid values, except for LDL, correlate positively with alcohol drinking (93). Aysarouglu *et al.* (94) have described decreased concentrations of magnesium and zinc, and increased concentrations of copper in alcoholics indicating that such persons have already developed the disease of the heart muscle. Some authors point to the impact of alcohol on platelet activity inhibition. Ethanol has also been shown to reduce fibrinogen, factor VII, and vWF. Alcohol may increase fibrinolysis by increasing the activity of tissue plasminogen activator (95). Epidemiological studies have shown that chronic alcohol consumption in high doses increases the risk of stroke (96).

RESPIRATORY SYSTEM

Results of research on the effects of alcohol on lung function show that excessive drinking of alcoholic drinks may have harmful effects on the respiratory lung function (97-103). Measurements of the lung function in healthy subjects after inhalation of ethyl alcohol have shown significant reduction in air flow in large and small airways (FEV₁, MEF₅₀, and MEF₂₅), indicating that in some people alcohol may act by releasing mediators with bronchoconstrictive activity (98). Alcohol consumption significantly increases both inspiratory and expiratory resistance in nasal airways (99). Also, experimental studies have shown that alcohol may cause constriction of the smooth muscle isolated trachea (103).

Researchers have shown that alcohol consumption may have even more harmful impact on lung function than smoking. Drinking of 350 g alcohol a week has the impact on air flow in large airways (FEV₁) comparable to the impact of smoking 15 g tobacco a day (104,105). Garshick *et al.* (106) have described the interaction of alcohol drinking and smoking on reduced air flow in large airways. Šarić *et al.* (107) have described the impact of alcohol drinking on the development of chronic obstructive pulmonary disease in industrial workers. Lebowitz (108) describes alcohol as

a factor responsible for the development of respiratory symptoms. Zellweger (109) and Ayres and Clark (110) describe asthma and rhinitis caused by ingestion and after inhalation of alcoholic vapors of pure ethanol.

Dawson *et al.* (111) point to the instability of respiratory tracts and higher inspiratory force during sleep. Mild intoxication after excessive alcohol consumption may act on sleep in persons with chronic obstructive pulmonary disease, and these persons should reduce their alcohol intake before going to bed (112). Taasan *et al.* (113), Block *et al.* (114), and Isa and Sullivan (115) have reported that alcohol causes an increased number of apnea episodes during alcohol drinking.

Infections observed in alcoholics in the form of pneumonia, peritonitis and bacteremia have been described by Sternbach (116), Thomsen (117), and Ginzburg *et al.* (118), pointing to body hypersensitivity caused by changes in the immune function and defense mechanisms, especially of the liver.

ALCOHOLISM AND WORKING PLACE

The proportion of alcoholics ranges from 8% to 13.9% of the working population (119). Alcoholism represents an important problem at the workplace because of its unfavorable impact on health and working capacity of the employees. By modifying the employee's behavior (impaired reasoning, decreased attention and poorer reflexes), alcohol leads to incomplete and inappropriate working performance, mistakes, accidents and injuries, resulting in health derangement and working disability. Alcoholics cannot have important and responsible jobs, and they are not able of keeping a job for a long time, so the job turnover, absenteeism and job loss is much more frequent in alcoholics than in nonalcoholics (120). Alcohol-related absenteeism is by 40% greater than in nonalcoholics (121).

A number of factors interfering with drinking at workplace are related to work type and interpersonal relations. Older literature often stated a general opinion that hard manual work cannot be performed without the help of alcoholic drinks. A boring job, isolated or demanding, with a low level of autonomy at work, the lack of work complexity as well as insufficient control of working conditions could contribute to the employee's alcohol consumption (122,123). Increased alcohol consumption may be the consequence of exposure to occupational stress at workplace. In certain groups of occupations, alcoholism is seen more frequently,

such as in waiters, hotel employees, sailors, merchants, journalists, doctors, lawyers, and policemen – which are at a high risk of the development of alcoholism (124-126). Data on whether a higher risk of the development of alcoholism could be found in manual workers or office clerks vary from study to study. However, results show that although some studies confirmed a higher prevalence of alcohol drinking in office clerks than in manual workers, the latter take greater quantities of alcohol.

There are eight factors that might explain why some occupations show a higher prevalence of alcohol addiction: 1) an opportunity of alcohol drinking at workplace; 2) social pressure of alcohol drinking at workplace; 3) separation from normal social or sexual relations (e.g., sailors, frequent travelers); 4) the lack of control; 5) high or low income; 6) conflicts with colleagues; 7) strenuous and/or stressful job; and 8) employment of persons who are already potential alcoholics (127).

Administrative disciplinary procedures implemented are based on the Act on Protection at Work (Official Gazette No.114/2003). According to the Health Care Act (Official Gazette No. 12/2003) and Healthcare Measures Program (Official Gazette No. 30/2002), preventive medical examinations of workers are done with special emphasis on risk factors including alcoholism and smoking.

ASSESSMENT OF WORKING CAPACITY AND DISABILITY

Working capacity could be significantly disturbed in persons who engage in excessive alcohol consumption, so that timely assessment of their remaining working capacity and assessment of adequate workplace are essential for the prevention of consequences within the working environment and the community at large. If the working capacity is reduced by more than 50% compared to a healthy insuree of the same or similar educational attainment, i.e. there is a remaining working capacity – an occupational working disability is determined. If the changes in health state are so overwhelming that there is no working capacity left, a general working disability is determined.

Assessment of **working incapacity, disability, and remaining working capacity** of alcoholics is affected by physical, mental and social consequences of excessive alcohol drinking. In the assessment of permanent working incapacity of an alcoholic, the degree of incapacity is based on the findings of gastroenterologic, cardiologic,

neurologic and psychiatric tests as well as on medical records on the course and outcomes of the provided treatments. For the assessment of mental disability, it is important to determine the pathological deviations before the onset of alcohol addiction such as abnormalities during schooling, employment, in family and interpersonal relations, and possible intellectual deficit. Alcoholism may appear in comorbidity with other mental illnesses, so that assessment of working capacity is influenced by the expected course of these illnesses along with the unfavorable impact of alcohol addiction.

In case of severe consequences of drinking with advanced stage of decompensated liver cirrhosis, coagulopathy, encephalopathy, and varicose esophagus as well as in case of decompensated alcoholic cardiomyopathy, a general working disability is determined.

Polyneuropathic impairments dominant in lower extremities represent a limitation to work associated with standing, walking, walking under pressure, working at heights, etc. Because of this consequence related to alcohol drinking, many employees are put at an occupational risk, including unskilled workers, construction workers, forestry and industry workers, workers in agriculture, etc. Tremor of hands makes impossible performance of work tasks that require skilfulness and precision with hands. The stated symptoms, along with coordination dysfunction, most often occur together, thus significantly compromising working capacity.

A patient with alcohol-related epilepsy is limited in the types of work that might endanger his or her own life or life of others in case of loss of consciousness. In case the epilepsy is caused either genuinely or posttraumatically, alcohol drinking strongly affects the course of treatment and prognosis.

Changes in mental health affect the working capacity already at an early stage of alcohol drinking, especially in work comprising well differentiated and responsible tasks. Due to alcohol consumption, intellectual and mnemonic functions are reduced, thus interfering with the planning, creativity and responsibility at work.

In practice, assessment of working capacity of persons addicted to alcohol often comprises the state after the treatment of a malignant disease. Most common malignant diseases found in this population group are malignant diseases of the tongue, pharynx, larynx and lungs, and also of the GI tract. In such cases, most often a general

working disability is determined. In case of comorbidity, lung tuberculosis of diverse intensity and consequence to functional capacity may occur occasionally.

If, apart from certain contraindications, there is a remaining working capacity, assessment of working capacity may determine an occupational working disability. In such patients occupational rehabilitation is almost impossible because the treatment outcome is almost always questionable, and remissions are inadequate, which greatly affects the ability to acquire new skills and knowledge necessary for work at another workplace. When physical, neurological and mental consequences of alcohol drinking permit, and depending on the degree of impairments, contraindications are determined as well as occupational working disability with the right to be relocated to another workplace, thus extending the expected working period.

PREVENTIVE MEASURES

Alcohol-related problems represent a challenge to medicine and public health. Prevention and abstinence are very important. Early therapy in primary care is efficient and a number of interventions are available, such as pharmacological interventions and those related to changes in behavior during the treatment of alcohol addiction. Physicians in primary health care play an important role here, as well as cooperation with alcoholics, physicians, families and therapeutic communities. The most important thing is to motivate an alcoholic for the treatment and for accepting the long-lasting process of recovery. Secondary prevention includes the measures of early detection and treatment of alcohol addicts, which gives better prognostic results. Tertiary prevention includes the measures of discontinuing the process of further development of irreversible alcohol-related consequences and the patient's disability, and this includes medical and sociotherapeutic measures and an appropriate procedure considering the type of workplace and working disability.

Associations of alcoholics anonymous in the clubs of treated alcoholics play an important role in secondary and tertiary but also in primary prevention of alcoholism. Resumed alcohol drinking has been recorded in about 40% of treated alcoholics (128-132). The problem is being solved at the point where it has been mainly manifested: in clubs of treated alcoholics organized in companies, communities, and healthcare institutions. Besides the persons with the alcohol problem, the program also involves those who suffer its con-

sequences and could support the solutions, i.e. family members, coworkers and superiors from workplace (133,134).

Alcohol-related difficulties develop much earlier than the clinical picture of alcoholism, so that it becomes necessary to redirect healthcare services towards early detection. Increased numbers of persons who start drinking at an early age indicate the need of introducing preventive measures at schools. At the workplace, it is necessary to have early detection of alcohol-related problems, which would enable immediate implementation of appropriate measures. This would result in safer workplace, reduced absenteeism, increased working productivity, and less personal and family problems. Since alcohol drinking represents a health problem that affects the entire population, not only the working but also the school population, it is necessary to organize educational measures that would lead to improvement of health of the working and school populations, with the aim of raising the awareness of the problems of alcohol drinking and of the causes that might result in alcoholism.

References

1. World Health Organization. Report of a WHO Expert Committee on problems related to alcohol consumption. Geneva: WHO, 1980.
2. World Health Organization. Public health aspects of alcohol availability. Report on working meeting held in Geneva. Geneva: WHO, 1982.
3. World Health Organization. Potential contribution of state monopoly systems to the control of alcohol-related problems. Report on working meeting held in Skarpo, Sweden. WHO Document MNH/PAD/87,15, 1987.
4. Lang B. Drinking and alcoholism in the Republic of Croatia. *Alcoholism* 1999;28:3-15.
5. Smith JW. Medical manifestations of alcoholism in the elderly. *Int J Addict* 1995;30:1749-98.
6. Goldshtein RI. Causes of death of alcoholics. *Zh Nevropatol Psikhiatr Im S S Korsakova* 1985;85:1235.
7. Living out our past through wine. Available at: <http://www.eat-online.net/english/education/wine.htm>
8. Neolithic period. Available at: http://museum.uppen.edu/new/exhibits/pnline_exhibits/wine-neolithic.html
9. The importance of wine through history. Available at: <http://www.eat-online.net/english/education/wine.htm>
10. Ancient Egyptian alcohol. Available at: http://www.thekeep.org/~kunoichi/kunoichi/themes-tream/egypt_alcohol.html
11. Dei Geschichte der Alkoholverwendung. Available at: <http://www.drogenring.org/suff/alkhist.htm>
12. Wan F, Zhong G, Liu L. A textual research on drinking disease and antidrinking remedies. *Zhonghua Yi Shi Za Zhi* 1994;24:203-6.
13. Guo L, Zhao H. Research on original editions of Lei jing (classified canon). *Zhonghua Yi Shi Za Zhi* 2002;32:213-5.
14. Chao YC, Wang SJ, Chu HC, Chang WK, Hsich TY. Investigation of alcohol metabolizing enzyme genes in Chinese alcoholics with avascular necrosis of hip joint, pancreatitis and cirrhosis of the liver. *Alcohol Alcohol* 2003;38:431-6.
15. Keller M. Beer and wine in ancient medicine. *Q J Stud Alcohol* 1958;19:153-4.
16. FYI. Drinking in America. Available at: <http://www.ncadd.org/facts/fyidina.html>
17. Dawson DA, Archer L. Gender differences in alcohol consumption: effects of measurement. *Br J Addict* 1992;87:119-23.
18. Emslie C, Hunt K, Macintyre S. How similar are the smoking and drinking habits of men and women in non-manual jobs? *Eur J Public Health* 2002;12:22-8.
19. Mustajbegovic J, Doko-Jelinić J, Pucarincvetković J, Milošević M, Žuškin E. Hrvatska zdravstvena anketa: potrošnja alkohola. Skup Prostorna distribucija populacijskih kardiovaskularnih rizika u Hrvatskoj. (Vuletić S, Kern J, Heim I, Strnad M, editors). Zagreb: Academy of Medical Sciences of Croatia, 2005; p. 6.
20. World Health Organization, Regional Office for Europe. Drinking practices of specific categories of employees. Report on a WHO consultation. Copenhagen: WHO Europe, 1990.
21. Breitenfeld D, Lang B, Thaller V, Breitenfeld T, De Syo D, Jagetić N. Psycho-social characteristics of female alcoholics. *Coll Antropol* 1998;22:613-8.
22. Thaller V, Buljan D, Breitenfeld D, Marusic S, Breitenfeld T, De Syo D, *et al.* Anthropological aspects of alcohol consumption and alcohol

- related problems. *Coll Antropol* 1998;22:603-11.
23. Hagnell O, Tunving K. Mental and physical complaints among alcoholics. *Q J Stud Alcohol* 1972;33:77-84.
 24. Jukić V, Brataljenović T. Obitelji prisilno liječenje alkoholičara. *Soc Psihijatrija* 1984;12:21-219.
 25. Jukić V. Problemi ovisnika o alkoholu u Prekršajnom pravu. *Soc Psihijatrija* 1985;13:119-33.
 26. Jukić V, Pavlinušić B, Peko-Čović I. Karakteristike paranoidnih stanja kod alkoholičara u tijeku liječenja. *Soc Psihijatrija* 1985;13:99-106.
 27. Brečić P, Jukić V, Skočilić Ž, Vuk S. Psihofarmakološki izbor u akutno opitom stanju. *Soc Psihijatrija* 2000;28:117-20.
 28. Toppich E, Vetter K. Alcohol and various occupational medicine aspects. *Z Gesamte Hyg* 1990;36:560-4.
 29. Thaller V, Buljan D, Marušić S. Biochemical tests in the prognosis of alcoholism. *Eur J Psychiatry* 1999;13:107-19.
 30. Thaller V, Buljan D, Golik-Gruber, Marušić S. Metabolički poremećaji. In: Thaller V. *Alkoholologija*. Zagreb: Naklada CSCAA, 2002; pp. 91-2.
 31. Breitenfeld D, Mikula I, Thaller V, DeSyo D, Breitenfeld T, Zoricic Z. Biological markers of alcohol related disorders. *Coll Antropol* 1998;22:213-6.
 32. Matošić A, Marušić S, Karlović D, Torre R. Komorbiditet ovisnosti o alkoholu i šećerne bolesti. *Soc Psihijatrija* 2003;31:18-21.
 33. Kostović K, Lipozenčić J. Skin diseases in alcoholics. *Acta Dermatovenerol Croat* 2004;12:181-90.
 34. Wegrzynek I, Budzanowska W. Alcohol and the skin. *Przegl Lek* 2001;58:198-203.
 35. Jacobi U, Bartoll J, Sterry W, Lademann J. Orally administered ethanol: transepidermal pathways and effects on the human skin barrier. *Arch Dermatol Res* 2005;296:332-8.
 36. Pragst F, Auwarter V, Kiessling B, Dyes C. Wipe-test and patch-test for alcohol misuse on the concentration ratio of fatty acid ethyl esters and squalene CFAEE/CSQ in skin surface lipids. *Forensic Sci Int* 2004;143:77-86.
 37. Krivosheev BN, Krivosheev AB. Alcohol and its effect on porphyrin metabolism. *Ter Arkh* 1994;66:32-6.
 38. Higin E, duVivier A. Alcohol intake and other skin disorders. *Clin Dermatol* 1999;17:437-41.
 39. Becker J. Increased incidence of dermatoses in nicotine and alcohol abuse. *Hautarzt* 1995;46:735.
 40. Marušić S, Thaller V, Matošić A, Torre R. Dermatological manifestations in alcohol addiction. *Alcoholism* 2004;40:127-37.
 41. Smith KE, Fenske NA. Cutaneous manifestations of alcohol abuse. *J Am Acad Dermatol* 2000;43:1-16.
 42. Zheng GY, Wei SC, Shi TL, Li YX. Association between alcohol, smoking and HLA-DQA1*0201 genotype in psoriasis. *Acta Biochim Biophys Sin (Shanghai)* 2004;36:597-602.
 43. Zimmerman GM. Alcohol and psoriasis: a double burden. *Acta Dermatol* 1999;135:1490-3.
 44. Poikolainen K, Karvonen J, Pukkala E. Excess mortality to alcohol and smoking among hospital-treated patients with psoriasis. *Arch Dermatol* 1999;135:1490-3.
 45. Naldi L, Peli L, Parazzini F. Association of early-stage psoriasis with smoking and male alcohol consumption: evidence from an Italian case-control study. *Arch Dermatol* 1999;135:1479-84.
 46. Monk BE, Neill SM. Alcohol consumption and psoriasis. *Dermatologica* 1986;173:57-69.
 47. Bader U, Hafner J, Burg G. Erythroderma and alcohol abuse. *Schweiz Med Wochenschr* 1999;129:508-13.
 48. Lee CH, Ko YC, Huang HL, Chao YY, Tsai CC, Shich TY, *et al.* The precancer risk of betel quid chewing, tobacco use and alcohol consumption in oral leukoplakia and oral submucous fibrosis in southern Taiwan. *Br J Cancer* 2003;88:366-72.
 49. Freedman DM, Sigurdson A, Doody MM, Mabuchi K, Linet MS. Risk of basal carcinoma in relation to alcohol intake and smoking. *Cancer Epidemiol Biomarkers Prev* 2003;12:1540-3.
 50. Karvonen J, Poikolainen K, Reunala T, Juva-koski T. Alcohol and smoking: risk factors for infectious eczematoid dermatitis? *Acta Derm Venereol* 1992;72:208-10.
 51. Yoda T, Crawshaw LI, Nakamura M, Saito K, Konishi A, Nagashima K, *et al.* Effects of alcohol on thermoregulation during mild heat exposure in humans. *Alcohol* 2005;36:195-200.

52. Bulfoni A. Vascular spiders, palmar erythema and Dupuytren's contracture in alcoholic hepatic cirrhosis. Clinical-statistical contribution. Arch Sci Med (Torino) 1980;137:355-60.
53. Petter G, Haustein UF. Steven-Johnson syndrome with transition to toxic epidermal necrolysis after carbamazepine administration, heroin and alcohol abuse. Hautarzt 1999;50:884-8.
54. Milingou M, Antille C, Sorg O, Saurat JH, Lubbe J. Alcohol intolerance and facial flushing in patients treated with topical tacrolimus. Arch Dermatol 2004;140:1542-4.
55. Zachariae H. Alcohol interactions with drugs and its effect on the treatment of skin diseases. Clin Dermatol 1999;17:443-5.
56. Beder U, Hafner J, Burg G. Erythroderma and alcohol abuse. Schweiz Med Wochenschr 1999;129:508-13.
57. Gonzalez-Quintela A, Vidal C, Gude F. Alcohol, IgE and allergy. Addict Biol 2004;9:195-204.
58. Smith ES, Riechelmann H. Cumulative lifelong alcohol consumption alters auditory brainstem potentials. Alcohol Clin Exp Res 2004;28:508-15.
59. Bruno A. Cerebrovascular complications of alcohol and sympathomimetic drug abuse. Curr Neurol Neurosci Res 2003;3:40-5.
60. Waltenbaugh C, Vasquez K, Peterson HD. Alcohol consumption alters antigen-specific responses: mechanisms of deficit and repair. Alcohol Clin Exp Res 1998;22(5 Suppl):220S-223S.
61. Gonzalez-Quintela A, Gude F, Boquete O, Rey J, Meijide LM, Suarez F, *et al.* Association of alcohol consumption with total serum immunoglobulin E levels and allergic sensitization in an adult population-based survey. Clin Exp Allergy 2003;33:156-8.
62. Linneberg A, Petersen J, Nielsen NH, Madsen F, Frolund L, Dirksen A, *et al.* The relationship of alcohol consumption to total immunoglobulin E and the development of immunoglobulin E sensitization: the Copenhagen Allergy Study. Clin Exp Allergy 2003;33:192-8.
63. Mujagić H, Prnjavorac B, Mujagić Z, Festa G. Alcohol in alcoholic liver disease is a causative factor for development of allergic skin manifestations. Med Arh 2003;57:273-8.
64. Campos J, Gude F, Quinteiro C, Vidal C, Gonzalez-Quintela A. Gene by environment interaction: the -159C/T polymorphism in the promoter region of the CD14 gene modifies the effect of alcohol consumption on serum IgE levels. Alcohol Clin Exp Res 2006;30:7-14.
65. Wetterling T, Veltrup C, Driessen M, John U. Drinking pattern and alcohol-related medical disorders. Alcohol 1999;34:330-6.
66. Laheij RJ, Verlaen M, Van Oijen MG, De Doelder MS, Dejong CA, Jansen JB. Gastrointestinal symptoms and ethanol metabolism in alcoholics. Dig Dis Sci 2004;49:1007-11.
67. Szalay F. Alcohol-induced gastrointestinal diseases. Orv Hetil 2003;144:1659-66.
68. Bode JC, Bode C. Alcohol, the gastrointestinal tract and pancreas. Ther Umsch 2000;57:212-9.
69. Zwas FR, Lyon DT. Occult GI bleeding in the alcoholic. Am J Gastroenterol 1996;91:551-3.
70. Yokoyama A, Muramatsu T, Ohmori T, Higuchi S, Hayashida M, Ishii H. Esophageal cancer and aldehyde dehydrogenase-2 genotypes in Japanese males. Cancer Epidemiol Biomarkers Prev 1996;5:99-102.
71. Yokoyama A, Ohmori T, Makuuchi H, Maruyama K, Okuyama K, Takahashi H. Successful screening for early esophageal cancer in alcoholics using endoscopy and mucosa iodine staining. Cancer 1995;76:928-34.
72. Castelli E, Hrelia P, Maffei F, Fimognari C, Foschi FG, Caputo F. Indicators of genetic damage in alcoholics: reversibility after alcohol abstinence. Hepatogastroenterology 1999;46:1664-8.
73. Neiman J. Alcohol as a risk factor for brain damage: neurologic aspects. Alcohol Clin Exp Res 1998;22:346S-351S.
74. Harper C, Matsumoto I. Ethanol and brain damage. Curr Opin Pharmacol 2005;5:73-8.
75. Kril JJ, Halliday GM. Brain shrinkage in alcoholics: a decade on and what have we learned? Prog Neurobiol 1999;58:381-7.
76. Oscar-Berman M, Marinkovic K. Alcoholism and the brain: an overview. Alcohol Res Health 2003;27:125-33.
77. Corral-Varela M, Cadaveira F. Neuropsychological aspects of alcohol dependence: the nature of brain damage and its reversibility. Rev Neurol 2002;35:628-7.
78. Hommer DW. Male and female sensitivity to alcohol-induced brain damage. Alcohol Res Health 2003;27:181-5.
79. Forn-Frias C, Sanchis-Segura C. The possible role of acetaldehyde in the brain damage

- caused by the chronic consumption of alcohol. *Rev Neurol* 2003;37:485-93.
80. Dodd PR, Beckmann AM, Davidson MS, Wilce PA. Glutamate-mediated transmission, alcohol, and alcoholism. *Neurochem Int* 2000;37:509-33.
 81. Durazzo TC, Gazdzinski S, Banys P, Meyerhoff DJ. Cigarette smoking exacerbates chronic alcohol-induced brain damage: a preliminary metabolite imaging study. *Alcohol Clin Exp Res* 2004;28:1849-60.
 82. Cipriani F, Cucinelli ML, Dimauro PE, Angioli D, Conte M, Voller F, *et al.* Mortality in a cohort of alcoholics from Arezzo in 1979-1997. *Epidemiol Prev* 2001;25:63-70.
 83. Lucas DL, Brown RA, Wassef M, Giles TD. Alcohol and the cardiovascular system research challenges and opportunities. *J Am Coll Cardiol* 2005;45:1916-24.
 84. Ojesjo L, Hagnell O, Otterbeck L. Mortality in alcoholism among men in the Lundby Community Cohort, Sweden: a forty-year follow-up. *J Stud Alcohol* 1998;59:140-5.
 85. Barboriak JJ, Rimm AA, Anderson AJ, Schmidhoffer M, Tristani FE. Coronary artery occlusion and alcohol intake. *Br Heart J* 1977;39:289-93.
 86. Hein HO, Sorensen H, Suadicani P, Gyntelberg F. Alcohol consumption, Lewis phenotypes, and risk of ischaemic heart disease. *Lancet* 1993;341:392-7.
 87. Nishida N, Ikeda N, Esaki R, Kudo K, Tsuji A. Conduction system abnormalities in alcoholics with asymptomatic valvular disease who suffer sudden death. *Leg Med (Tokyo)* 2003;5:212-9.
 88. Frost L, Vestergaard P. Alcohol and risk of atrial fibrillation or flutter: a cohort study. *Arch Intern Med* 2004;164:1993-8.
 89. Fernandez-Sola J, Nicolas JM, Pare JC, Sacanella E, Fatjo F, Cofan M, Estruch R. Diastolic function impairment in alcoholics. *Alcohol Clin Exp Res* 2000;24:1830-5.
 90. Dettmeyer R, Reith K, Madea B. Alcoholic cardiomyopathy *versus* chronic myocarditis – immunohistological investigations with LCA, CD3, CD68 and tenascin. *Forensic Sci Int* 2002;126:57-62.
 91. Rajzer M, Mertyna P, Betkowska-Korpala B, Kawecka-Jaszcz K. The effect of chronic alcohol consumption on systolic and diastolic left ventricular function. *Przegl Lek* 2004;61:895-901.
 92. Kajander OA, Kupari M, Laippala P, Savolainen V, Pajarinen J, Penttila A, *et al.* Dose dependent but non-linear effects of alcohol on the left and right ventricle. *Heart* 2001;86:417-23.
 93. Sillanaukee P, Koivula T, Jokela H, Pitkajarvi T, Seppa K. Alcohol consumption and its relation to lipid-based cardiovascular risk factors among middle-aged women: the role of HDL(3) cholesterol. *Atherosclerosis* 2000;152:503-10.
 94. Aysaroglu D, Inal TC, Demir M, Attila G, Acarturk E, Emre Evlice Y, *et al.* Biochemical indicators and cardiac tests in chronic alcohol abusers. *Croatian Med J* 2005;46:233-7.
 95. Salem RO, Laposata M. Effects of alcohol on hemostasis. *Am J Clin Pathol* 2005;123:S96-105.
 96. Masoero E, Frattini P, Favalli L, Rozza A, Scelsi R, Govoni S. Effect of acute alcohol on ischemia-induced glutamate release and brain damage. *Alcohol* 2000;22:173-7.
 97. Series F, Cormier FY, Desmeules. Alcohol and the response of upper airway resistance to a changing respiratory drive in normal man. *Respir Physiol* 1990;81:153-6.
 98. Robinson RW, White DP, Zwillich CW. Moderate alcohol ingestion increases upper airway resistance in normal subjects. *Am Rev Respir Dis* 1985;132:1238-41.
 99. Sisson JH, Stoner JA, Romberger DJ, Spurzem JR, Wyatt TA, Owens-Ream J, *et al.* Alcohol intake is associated with altered pulmonary function. *Alchol* 2005;36:19-30.
 100. Lange P, Groth S, Nyboe J, Appleyard M, Mortensen J, Jensen G, *et al.* Chronic obstructive lung disease in Copenhagen: cross-sectional epidemiological aspects. *J Intern Med* 1989;226:25-43.
 101. Žuškin E, Bouhuys A, Šarić M. Lung function changes by ethanol inhalation. *Clin Allergy* 1981;11:243-8.
 102. Eccles R, Tolley NS. The effect of alcohol ingestion upon nasal airway resistance. *Rhinology* 1987;25:245-8.
 103. Jakupi M, Djokić TD, Karahoda-Gjurgjeala D, Žuškin E, Musa A, Haxhiu R. Effect of ethanol on the isolated airway smooth muscle tone. *Acta Med Iug* 1986;40:207-14.
 104. Strom K, Janzon L, Hanson BS, Hedblad B, Rosberg HE, Arborelius M. Alcohol consumption modifies the total lung capacity in smokers. *Respiration* 1996;63:66-72.

105. Holma B, Kjaer G. Alcohol, housing, and smoking in relation to respiratory symptoms. *Environ Res* 1980;21:126-42.
106. Garshick E, Segal MR, Worbec TG, Salekin CM, Miller MJ. Alcohol consumption and chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1989;140:373-8.
107. Šarić M, Lučić-Palaić S, Horton RJM. Chronic nonspecific lung disease and alcohol consumption. *Environ Res* 1977;14:14-21.
108. Lebowitz MD. Respiratory symptoms and disease related to alcohol consumption. *Am Rev Respir Dis* 1981;123:16-9.
109. Zellweger JP. Asthma and rhinitis induced by the ingestion of pure ethanol and by the inhalation of alcohol vapors. *Schweiz Med Wochenschr* 1982;112:212-4.
110. Ayres JG, Clark TJ. Alcoholic drinks and asthma: a survey. *Br J Dis Chest* 1983;77:370-5.
111. Dawson A, Bigby BG, Poceta JS, Mittler MM. Effect of bedtime alcohol on inspiratory resistance and respiratory drive in snoring and nonsnoring men. *Alcohol Clin Exp Res* 1997;21:183-90.
112. Easton PA, West R, Meatherall RC, Brewster JF, Lertzman M, Kryger MH. The effect of excessive ethanol ingestion on sleep in severe chronic obstructive pulmonary disease. *Sleep* 1987;10:224-33.
113. Taasan VC, Block AJ, Boysen PG, Wynne JW. Alcohol increases sleep apnea and oxygen desaturation in asymptomatic men. *Am J Med* 1981;71:240-5.
114. Block AJ, Hellard DW, Slayton PC. Effect of alcohol ingestion on breathing and oxygenation during sleep. Analysis of the influence of age and sex. *Am J Med* 1986;80:595-600.
115. Issa FG, Sullivan CE. Alcohol, snoring and sleep apnea. *J Neurol Neurosurg Psychiatry* 1982;45:353-9.
116. Sternbach GL. Infections in alcoholic patients. *Emerg Med Clin North Am* 1990;8:793-803.
117. Thomsen JL. Diseases of the airways and lungs in forensic autopsy material in alcoholics. *Med Sci Law* 1997;37:23-6.
118. Ginzburg MA, Krut'ko VS, Burnusus ZI. Characteristics of the x-ray picture of pulmonary tuberculosis in alcoholics. *Vestn Rentgenol Radiol* 1990;4:30-6.
119. Ojesjo L. The relationship to alcoholism of occupation, class and employment. *J Occup Med* 1980;22:657-66.
120. Olkinuora M. Alcoholism and occupation. *Scand J Work Environ Health* 1984;10:511-5.
121. Jukić V, Čulav-Sumić J. Radno nesposobni duševni bolesnici u kontekstu nekih odredbi Zakona o mirovinskom osiguranju. *Soc Psihijatrija* 1998;26:193-7.
122. Mullahy J, Sinderlar JL. Drinking, problem drinking and productivity. *Recent Dev Alcohol* 1998;14:347-59.
123. San Jose B, Van de Mheen H, van Oers JA, Mackenbach JP, Garretsen HF. Adverse working conditions and alcohol use in men and women. *Alcohol Clin Exp Res* 2000;24:1207-13.
124. Miller NS, Sheppard LM. The role of the physician in addiction prevention and treatment. *Psychiatr Clin North Am* 1999;22:489-505.
125. Mangili A. Alcohol and working. *G Ital Med Lav Ergon* 2004;26:255-8.
126. Violanti JM. Predictors of police suicide ideation. *Suicide Life Threat Behav* 2004;34:277-83.
127. Harford TC, Parker DA, Grant BF, Dawson DA. Alcohol use and dependence among employed men and women in the United States in 1988. *Alcohol Clin Exp Res* 1992;146:8.
128. Rotim K, Jukić V, Rudež I, Čulo A, Ševerdija R. Odnos radne sposobnosti alkoholičara i njihove uključenosti u klubove liječenih alkoholičara. *Soc Psihijatrija* 1995;23:89-95.
129. Alcoholics Anonymous, AA. *World Services Inc.*, New York, 1939.
130. Alcoholics Anonymous, *The Third Edition of the Big Book*, Alcoholics Anonymous World Services Inc., New York, 1976.
131. Alcoholics Anonymous, *Twelve Steps and Twelve Traditions*, AA World Services Inc., New York, 1953.
132. Ojesjo L, Hagnell O, Otterbeck L. The course of alcoholism among men in the Lundby Longitudinal Study, Sweden. *J Stud Alcohol* 2000;61:320-2.
133. Hudolin V. *Alkohološki priručnik*. Zagreb: Medicinska naklada, 1991.
134. Hudolin V. *Klubovi liječenih alkoholičara*. Zagreb: Školska knjiga, 1990.