Nutrition and Health
Series Editor: Adrianne Bendich

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Alcohol, Nutrition, and Health Consequences

Humana Press

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Series Editor Page

The great success of the Nutrition and Health Series is the result of the consistent overriding mission of providing health professionals with texts that are essential because each includes: (1) a synthesis of the state of the science; (2) timely, in-depth reviews by the leading researchers in their respective fields; (3) extensive, up-to-date, and fully annotated reference lists; (4) a detailed index; (5) relevant tables and figures; (6) identification of paradigm shifts and the consequences; (7) virtually no overlap of information between chapters, but targeted, inter-chapter referrals; (8) suggestions of areas for future research; and (9) balanced, data-driven answers to patients' as well as health professionals' questions which are based upon the totality of evidence rather than the findings of any single study.

The series volumes are not the outcome of a symposium. Rather, each editor has the potential to examine a chosen area with a broad perspective, both in subject matter as well as in the choice of chapter authors. The editors, whose training is both research and practice oriented, have the opportunity to develop a primary objective for their book, define the scope and focus, and then invite the leading authorities to be part of their initiative. The authors were encouraged to provide an overview of the field, discuss their own research, and relate the research findings to potential human health consequences. Because each book is developed de novo, the chapters are coordinated so that the resulting volume imparts greater knowledge than the sum of the information contained in the individual chapters.

Alcohol, Nutrition and Health Consequences, edited by Dr. Ronald Ross Watson, Dr. Victor R. Preedy, and Dr. Sherma Zibadi is a very welcome addition to the Nutrition and Health Series. The 43 chapters in this comprehensive volume examine the clinical consequences of alcohol including the beneficial as well as detrimental effects. The book is logically organized into seven sections and begins with an overview section that includes informative chapters on the genetics of alcohol metabolism, laboratory models, and the very earliest effects of alcohol on the embryo and breast-fed neonate. The extensively referenced chapter on alcohol's effects during embryopathy contains excellent tables and figures that describe the consistent detrimental findings of ethanol-induced lipid peroxidation.

The second section contains six chapters that describe both the beneficial as well as the adverse effects of alcohol on the nutritional status of individuals and the nutritional value of certain foods. The chapters review these effects on overall metabolism. The chapter on specific effects on protein contains comprehensive figures and the chapters on lipids and the clinical consequences of alcohol-induced vitamin B12 deficiency contain important, relevant references. Additionally, there are chapters that examine at-risk, culturally specific populations including Native Americans.

The third section contains unique chapters that examine the potential for certain foods and food components to affect alcohol metabolism. Individual chapters review the effects of plant polyphenols, folic acid, zinc, tocotrienols, soy products, oats, and omega 3 fatty acids. Organ systems and disease conditions reviewed include mammary tissue, immune function, HIV infection, maternal to fetal nutrient transfer, gastrointestinal permeability and emptying, liver function including drug detoxification, alcoholic liver disease, cognitive function, and Alzheimer's disease.

Alcohol has been shown to interact with foods and food components to either enhance or depress the food's biological effects. Alcohol can also affect metabolism of foods and food components. Five chapters examine alcohol's interactions with dietary components. One example of the complex interactions involves the consumption of energy drinks especially among young adults who frequently use energy drinks as a mixer with alcohol. The most common active ingredients in energy drinks include caffeine, taurine, guarana, and ginseng. The combination of alcohol and energy drinks appears to increase alcohol absorption as well as the consumption of large volumes of alcohol. The combinations of caffeine and alcohol and cigarette smoking and alcohol are reviewed in the next two chapters that examine the potential benefits and risks of these combinations. The physiological rationale for the frequently seen co-use of cigarettes and alcohol may be due to their stimulation of specific brain areas, as reviewed in the next chapter. The final chapter in this section reviews the complex interactions between alcohol use and its effects on metabolism in individuals at risk for HIV and infected with HIV. The data suggest that there is no safe level of alcohol intake for HIV-infected individuals due to the interactions between alcohol, liver function, HIV drug detoxification, and other factors including the often malnourished state of the patient.

Alcohol consumption can affect the potential to develop certain chronic diseases as well as exacerbate already existing chronic conditions; however, moderate intake may reduce the risk of certain diseases. Section E, containing eight chapters, reviews the association of alcohol with chronic diseases. The chapter on cataracts reviews the role of lifestyle, type 2 diabetes, nutrient status, cigarette smoking, and other factors that are known to increase cataract risk and then examines the data suggesting that alcohol may be an independent risk factor for cataract development. The next chapter reviews the cross-sectional, longitudinal, and intervention trial data and finds consistent reporting of excessive consumption of alcohol and increases in both the level of blood pressure and the subsequent incidence of hypertension. Dyslipidemia is a disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. Dyslipidemia may be manifested by elevated LDL cholesterol or elevated triglycerides or low HDL cholesterol. Excessive alcohol consumption is a major risk factor for dyslipidemia as outlined in the next chapter. Alcohol abuse is also associated with chronic pancreatitis, and symptoms may be reduced with antioxidant nutrient use as reviewed in the next chapter. Also included is an outline of the treatment algorithm. In contrast to the above chronic conditions, epidemiological studies have linked light to moderate alcohol consumption, i.e., 10–30 g alcohol per day, with about a 30 % decreased risk of type 2 diabetes compared to nondrinkers. There appears to be a U-shaped relationship between the amount and frequency of alcohol consumption and type 2 diabetes risk especially in women. The next chapter examines the association between alcohol consumption, adiposity, and obesity. Cross-sectional and prospective studies suggest that long-term, high alcohol intake (>3 drinks/day) is associated with increased abdominal adiposity and weight gain. In contrast to the obese patients, the next chapter describes the etiology of anorexia and it appears that alcohol may play a minor role in this condition whereas bulimics may have alcohol-related psychological dysfunctions. The next unique chapter reviews the influence of alcohol consumption on human cancers known to be caused by viral infections. This chapter includes comprehensive tables that outline those cancers that are associated with viral infections including, but not limited to, Epstein-Barr virus, hepatitis viruses, human papillomavirus, human lymphotrophic virus type 1, human herpesvirus 8, and human immunodeficiency virus (HIV).

Two of the most serious diseases to affect chronic alcohol users are cancers, mainly of the digestive tract, and liver diseases. These two areas are reviewed in depth in the final 12 chapters of this comprehensive volume. Chronic alcohol users have an increased risk of many cancer types and alcohol use can affect the treatment of cancers not directly related to alcohol abuse. The effects of alcohol on the development and treatment of liver, colorectal, urinary tract, esophageal, and other digestive tract cancers are each reviewed in separate chapters. In contrast, chapters include the epidemiological findings that low or moderate intake of wine is associated with reduced risk of development of certain cancers. As indicated in previous chapters, the combination of alcohol use and cigarette smoking is

frequently seen. Their synergism in upper digestive system cancers is described in detail with excellent tables and figures and suggests that acetaldehyde, a human carcinogen derived from both alcohol and cigarettes, is a major factor.

The final section on alcohol and liver diseases contains eight comprehensive chapters. Topics reviewed include nonalcoholic fatty liver disease and nonalcoholic steatohepatitis (NASH); chronic viral infections in the liver; hepatic insulin resistance and other associations with effects of obesity and type 2 diabetes; cholesterol metabolism and its management; adverse effects of ceramide, a lipotoxin, and the use of ceramide-lowering drugs; dietary lipids and the potential for polyunsaturated fatty acids to reduce the chronic inflammation seen in many liver diseases; protein-calorie malnutrition and multiple micronutrient deficiencies associated with chronic liver diseases and the use of enteral and parenteral nutrition therapies; and the role of the liver in assuring adequate vitamin A delivery to the rest of the body once dietary vitamin A has been consumed. This final chapter reminds us of the liver's functions of storing and metabolizing vitamin A and synthesizing vitamin A binding proteins that permit the release of vitamin A from the liver to be distributed to all cells and tissues of the body.

The logical sequence of the sections as well as the chapters within each section enhance the understanding of the latest information on the current standards of practice with regard to chronic alcohol use and its consequences for clinicians, related health professionals including the dietician, nurse, pharmacist, physical therapist, behaviorist, psychologist, and others involved in the team effort required for successful treatment of alcoholism as well as liver diseases that may or may not be directly related to alcoholism. Other relevant diseases as well as conditions that adversely affect the liver's normal metabolic processes are also included. This comprehensive volume has great value for academicians involved in the education of graduate students and postdoctoral fellows, medical students, and allied health professionals who plan to interact with patients with relevant disorders.

The volume contains over 100 detailed tables and figures that assist the reader in comprehending the complexities of the metabolism as well as the potential benefits and risks of alcohol on human health. The over-riding goal of this volume is to provide the health professional with balanced documentation and awareness of the newest research and therapeutic approaches including an appreciation of the complexity of the effects alcohol can have on virtually every organ system within the body. Hallmarks of the 43 chapters include key words and bulleted key points at the beginning of each chapter, complete definitions of terms with the abbreviations fully defined for the reader, and consistent use of terms between chapters. There are over 3,400 up-to-date references; all chapters include a conclusion to highlight major findings. The volume also contains a highly annotated index.

This unique text provides practical, data-driven resources based upon the totality of the evidence to help the reader understand the basics, treatments, and preventive strategies that are involved in the understanding of how alcohol may affect healthy individuals as well as those with chronic alcohol use with or without relevant infectious diseases, obesity, diabetes, and/or neurocognitive declines. With equal importance, critical issues that involve patient concerns, such as malnourishment; potential effects on mental functions; and addiction and withdrawal are included in well-referenced, informative chapters. The overarching goal of the editors is to provide fully referenced information to health professionals so they may have a balanced perspective on the value of various preventive and treatment options that are available today as well as in the foreseeable future.

In conclusion, *Alcohol, Nutrition and Health Consequences*, edited by Ronald Ross Watson, Ph.D.; Victor R. Preedy, Ph.D., D.Sc., FRIPH, FRSH, FIBiol, FRCPath; and Sherma Zibadi, M.D., Ph.D., provides health professionals in many areas of research and practice with the most up-to-date, well-referenced, and comprehensive volume on the current state of the science and medical consequences of alcohol use. This volume will serve the reader as the most authoritative resource in the field to date and is a very welcome addition to the Nutrition and Health Series.

Adrianne Bendich, Ph.D., FACN, FASN
Series Editor

Preface

Humankind has had a complex relationship with alcohol from the beginning of recorded history. In most societies, some level of alcohol consumption is acceptable. In the United States, about 60% of high-school students illegally use alcohol. Alcohol-altered diet and nutrition directly affects ten million alcohol-abusing adults. It costs people in the United States more than $250 billion in health care, lost work, etc. Alcohol research is in a golden era. With more powerful tools for data collection and analysis and increased funding, the epidemiology of alcohol consumption, dietary consequences, role of nutrition in treatment of alcohol's pathology, and alcohol-related health issues are being better elucidated. Therefore, there is an overview section on nutrition and the effects of alcohol use on it to aid the reader. This includes genetics of alcohol metabolism and lessons learned from animal models.

Chronic alcohol use is associated with heart, liver, brain, and other organ pathology. Alcohol is a drug of abuse and a caloric food. It causes poorer intake and absorption of nutrients, thus playing a major role in many aspects of clinical consequences. Alcohol use lowers consumption of fruit and vegetables, lowers tissue nutrients, and, in some cases, requires nutritional therapy by clinicians. Thus the next section deals with diverse chapters relating to oxidation, body weight, health inequalities, specific problems to Native Americans, and biology. Clearly, metabolites of ethanol such as acetaldehyde are important modifiers of nutrients and metabolism of protein which are reviewed. In addition, the effects of alcohol abuse on nutrients' actions including vitamin E, vitamin B12, and zinc in the body's biology are assessed. Alcohol modifies use and metabolism of diverse foods with oats, fish oil, and soy being examples that are reviewed.

Infectious diseases, particularly viral ones including HIV/AIDS and viral infections promoting cancer can be changed by alcohol abuse which is defined in this book. More importantly chronic diseases are susceptible to chronic alcohol abuse. These include a wide range of nutritional diseases such as cataracts, high blood pressure, dyslipidemia, diabetes, obesity, and bulimia. This book helps to define the causes and types of nutritional changes due to alcohol use and how nutrition can be used to ameliorate its consequences. The role of antioxidant nutrients and foods as partial therapies is carefully defined.

Chapters deal with application of current nutritional knowledge by physicians and dietitians in understanding alcohol and cancer promotion. Reviews describe alcohol use in liver, colorectal, urinary, and digestive systems. Of course, toxic metabolites, acetaldehyde plays an important role in digestive tract cancer described in a chapter. An intimate, detailed knowledge of the effects of alcohol on the biochemical reactions and nutritional changes is critical in preventing or treating biomedical consequences.

Specific areas involving alcohol-related damage due to alcohol-combined effects with foods are reviewed, specifically the interaction with caffeine in foods, tobacco smoke and nicotine, and energy drinks. Because of alcohol's effects on the liver with a diverse range of diseases, they become a major section. Therefore the roles of nutrients as therapies for alcoholic liver diseases are defined including the actions of dietary fats, vitamin A, and native plant foods in reducing and exacerbating them.

The book will become a desk reference for alcohol therapists and researchers as well as primary care physicians and dietitians. These professionals frequently need information on the nutritional effects of alcohol as well as the role of nutritional supplementation and diet in the therapy of alcohol pathology. Research progress encourages us to summarize and evaluate in detail advances in understanding changes in nutritional biochemistry and physiology caused by ethanol (alcoholic beverages). It will assist the clinician, student, and dietitian to comprehend the complex changes caused by direct and indirect effects of ethanol at the cellular level via its nutritional modification. This book will stimulate research while educating health-oriented laypersons as well as scientists and health-care professionals.

Tucson, AZ, USA — Ronald Ross Watson
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Introduction

Although alcohol consumption is very frequent in Western countries, nutritional disorders due to alcohol are relatively uncommon, and they are mainly restricted to heavy consumers. However, malnutrition is one of most relevant medical problems of alcoholic patients, since it is related to advanced alcoholism and to survival.

Some years ago, we reviewed general pathogenetic and clinical aspects of alcohol-related malnutrition [1]. Despite intensive research in trace elements and specific nutrients, relatively few new data related to general clinical aspects of alcohol-related malnutrition have appeared in the medical literature. They will be commented in this chapter.

Ethanol is a highly energetic (7.1 kcal/g), readily oxidizable compound, often present in the Western diet. It accounts for 5.6% of the total energy intake of the average American diet, despite the fact that about one-third of the population is teetotaler [2]. Ethanol accounts for up to 10% of the total energy intake among social drinkers, this proportion reaching more than 50% in heavy alcoholics. Due to its high caloric content, ethanol consumption has been considered a risk factor for weight gain and obesity. However, weight loss is common among heavy drinkers [3]. But it is noteworthy that alcohol dependence per se is not a main cause of malnutrition. The alcoholic patient who becomes malnourished is that one with social and familial problems, socially marginated, who loses meals, and finally spent most of money and time in drinking. Another way of malnutrition is the development of organic pathology such as liver cirrhosis with ascites.

Mechanisms of Malnutrition in Alcoholics

Primary Malnutrition

Shift of Nutrients

Moderate ethanol consumption increases rather than decreases dietary intake. Indeed, Westerterp-Plantenga et al. (1999) showed that 24-h energy intake was higher on days in which a drink was consumed as an aperitif [4]. In contrast, heavy alcoholism leads to a substantial reduction of dietary intake, so consumption of other nutrients progressively decreases as ethanol intake increases [5, 6]. Moreover, since heavy alcoholics underreport the amount of ethanol consumed and overreport their nonalcoholic energy intake, this effect is probably even more important [7, 8].

Despite the fact that alcoholic beverages may account for up to 5% of the total energy intake, they should not be considered as a food, or, in the best of the cases, only as a poor-quality food, since they provide only one nutrient, lacking proteins, essential lipids, minerals, and the majority of trace elements and vitamins. Therefore, although the diet of a heavy drinker matches or even surpasses the caloric requirements, it may be inadequate in terms of protein, essential lipids, and other nutrients.

Caloric Wastage

Pirola and Lieber (1972), in classic studies, found a weight loss of about 1 kg after consumption for 14 days of a diet in which 50% of calories were substituted by ethanol. Moreover, no significant weight gain was observed when 2,000 kcal – in the form of ethanol – were added to the diet, whereas subjects experienced a weight gain of nearly 3 kg when the same amount of calories was consumed in the form of chocolate. These findings were attributed to the metabolism of ethanol by energy-wasting pathways in chronic alcoholics [9, 10].

Ethanol is a xenobiotic product, which cannot be stored in the body but becomes rapidly oxidized, displacing other fuels. Two main mechanisms are involved in ethanol metabolism: the alcohol dehydrogenase (ADH) pathway and the microsomal ethanol-oxidizing system (MEOS). The ADH pathway requires reduction of NAD to NADH + H, but MEOS requires oxidation of NADPH to NADP, a process that consumes ATP and dissipates heat. Therefore, the ADH pathway yields 16 mol ATP/mol of ethanol oxidized, whereas MEOS, only 10. MEOS pathway scarcely works in occasional ethanol consumers but is induced in chronic alcoholics [11, 12].

In healthy volunteers, short-term ethanol administered as 25% of the total energy requirements, either added to the diet or given instead of other food, increases 24-h energy expenditure [13, 14]. Since this experiment was carried out in healthy nondrinkers, ethanol should have been mainly metabolized by the ADH system and not by the MEOS. Therefore, mechanisms other than MEOS must be involved in the alcohol-mediated increase in energy expenditure, such as acetaldehyde-induced catecholamine secretion. When moderate amounts of ethanol, 5–10% of total daily calories, were added to the diet (as occurs with social drinkers), no change was observed in resting energy expenditure (REE) [15, 16]. However, Addolorato et al. (1998) report an increase in REE in long-term heavy drinkers (mean consumption of 195 g ethanol/day) when compared with social drinkers; chronic alcoholics show a significantly lower weight due to lower fat mass and increased fat oxidation [17, 18]. Levine et al. (2000) also showed an increased fat oxidation and an increased REE, which is related to ethanol ingestion, since both decrease 4 days after withdrawal [19]. Thus, it seems that ethanol increases REE by an increased catecholamine secretion and uncoupled oxidative phosphorylation due to mitochondrial damage [20, 21].

Effect of Ethanol on Fat Synthesis and Oxidation

Ethanol may inhibit fat mobilization due to the antilipolytic effect of acetate [22]. In addition, an increased NADH/NAD ratio may enhance liver fatty acid and triglyceride synthesis. These data theoretically favor lipid accumulation and weight gain. However, epidemiologic studies support the conclusion that even moderate ethanol consumers (less than 50 g/day), despite an increase in the total energy intake, show weight loss [23, 24]. So, studies dealing with changes in body composition in chronic heavy drinkers describe fat loss. Addolorato et al. (1998), in chronic heavy drinkers (mean ethanol intake of 195 g/day) without liver cirrhosis or malabsorption, found a lower body weight due to fat mass reduction (the triceps skinfold was reduced but not the midarm muscle circumference) and a preferential use of lipids as fuel when compared with social drinkers [17, 18].

Effects of Ethanol on Protein Metabolism

Ethanol increases urinary nitrogen excretion [25, 26]. Reinus et al. (1989) studied eight alcoholic patients continuously fed by nasogastric tube. When ethanol accounted for 30% of the total caloric intake (about 100 g/day), an amount which does not surpass the hepatic clearance rate, negligible ethanol concentrations were detected in blood, and no increase in urea nitrogen excretion was observed. However, when the amount of ethanol was increased to 40–60% of the total calories (about 180 g), blood ethanol concentration ranged from 250 to 300 mg/dl, urinary urea nitrogen and 3 methylhistidine increased – pointing to muscle wastage – and weight loss ensued [27].

Ethanol administered to rats leads to reduced protein synthesis and type II muscle fiber atrophy, an effect more dependent on acetaldehyde than on ethanol itself. Moreover, type IIb fiber atrophy is more intense when a low protein diet is added to ethanol [28]. The association between ethanol, malnutrition, and muscle atrophy is complex. It has been clearly shown that ethanol leads to muscle atrophy and cardiomyopathy in the absence of nutritional impairment [29]. However, malnutrition is frequently associated to alcoholic myopathy [30]. Histologically assessed muscle atrophy was found

in one-third of 64 heavy alcoholics, drinkers of 217 g ethanol/day. Patients with muscle atrophy consistently showed an impaired nutritional status, affecting not only muscle mass but also subcutaneous fat [31]. Fernandez-Sola et al. (1995) reported that protein-calorie malnutrition is an independent predictive factor of type II fiber atrophy [32, 33]. However, muscle atrophy implies a reduction in total body protein burden, and is, thus in itself, a criterion of malnutrition. In any case, as Fernandez-Sola et al. (2000) show, alcoholic myopathy only appears with heavy ethanol consumption at levels at which malnutrition is frequent. Interestingly, it may recover without total abstinence, only by lowering the dose of ethanol consumption [34].

In addition to muscle protein, ethanol and acetaldehyde may alter protein synthesis in every body tissue. They decrease protein synthesis in the majority of the tissues, such as bone, decreasing collagen; liver, decreasing albumin, prealbumin, IGF-1, its binding protein IGF1BP3, and osteocalcin; and whole-body nitrogen balance. But they also increase liver collagen synthesis [35].

Socioeconomic Status, Social and Family Problems, and Irregular Feeding

Malnutrition has been more frequently reported among skid row and low class alcoholics than in middle class ones [36–38]. In this sense, Goldsmith et al. (1983) found that only 8% of alcoholics of middle and high socioeconomic status were malnourished, in contrast with 32% of those belonging to a low social class [39]. Alcoholics frequently have social and family problems which disrupt social links and lead to an irregular lifestyle. Meals of lonely male alcoholics are often irregular. As alcoholics increase ethanol intake, they change their feeding habits; some meals are missed, and the quality of the diet consumed is poor [6].

In a study performed on drug addicts – mainly heroin consumers – admitted for detoxification, we found that disruption of social and family links were related to anorexia and poor food intake and also to a more intense drug addiction [40]. In our culture, regular meals and adequate food intake are related to family life, and family rupture leads to progressive marginalization and poverty. These factors, together with the anorexigenic effect of alcohol and the lack of interest for everything besides ethanol consumption, may lead to progressive malnutrition. In this line, we studied 181 alcoholic patients, consumers of about 180 g of ethanol daily. The heaviest drinkers showed the most irregular feeding habits and were severely underweighted. The worst situation was suffered by the skid row alcoholics, all of them unemployed, homeless, and without family support. Most of these patients (73%) showed a BMI below 20 kg/m^2, a finding which was observed only in 11% of non-skid row alcoholics and in none of the controls. Skid row alcoholics also showed an intensely decreased lean and fat mass assessed by midarm anthropometry and double-energy X-ray absorptiometry (DEXA), and, subsequently, decreased handgrip strength. However, skid row alcoholics did not show more somatic complications [41].

Alcoholics eat frequently in bars or taverns instead of at home. They miss meals, meals are scanty, and portions are small and deficient in protein. Alcoholics who confessed irregular feeding habits had more social and family problems, drank more ethanol, and suffered a more intense malnutrition with decreased fat, lean, and bone mass (pointing to a relationship between malnutrition and osteopenia); low serum albumin, prealbumin and transferrin, cholesterol and triglyceride, and also serum folate and magnesium; and a decreased handgrip strength when compared with the remaining alcoholics. Thus, loneliness and irregular feeding may be the link between social and family problems and malnutrition [41, 42].

Recently, a Japanese study supports this hypothesis. It included 467 patients with a daily ethanol consumption of 119±65 g; 50.5% of the subjects consumed three meals a day; 32.8%, two meals; 12.2%, one meal; and 4.5% scarcely ate. The meals mainly consisted of carbohydrates and protein, with few vegetables. Daily alcohol consumption was inversely related to the frequency of meals. The subjects who

lived with their family (72.8%) consumed more meals than the subjects living alone. BMI of excessive drinkers directly depends on ethanol consumption and inversely on the number of lost meals. The group with the lowest BMI values (<18.5) accounted for 19.3% of the subjects, and those with the highest BMI values (> or = 25) accounted for 11.5% [43]. So, excessive ethanol intake may cause both overweight and malnutrition. Malnutrition develops mainly in heavy drinkers and is not related to dependence but to marginality and loneliness. Alcoholics with social and familial disturbs are those who lose meals and become malnourished. Menari AP et al. (2003) did not find differences in the degree of malnutrition between the harmful drinkers (mild dependency) and heavily dependent alcoholics. Although the whole population of the study showed one or more deficiencies in macro- or micronutrients intake, one-third were below normal body weights, but one-quarter showed overweight [44].

Serum folate levels are reduced in alcoholics [41, 45–48]. In a study on 103 male alcoholics, drinkers of a mean of 205 g/day, we found decreased serum folate and B6 levels but increased B12. Thirty percent of our alcoholics showed serum folate levels below 3 ng/l. The decrease in serum folate was not related to liver function impairment or to ethanol intake; instead, it was related with nutritional data and especially, again, with irregular feeding habits (only one meal per day and one dish per meal) and poor consumption of one or more of the main food groups. Decreased B6 levels were also related to malnutrition [48]. As serum folate and B6 levels were inversely related to homocysteinemia, ethanol abuse may lead to hyperhomocysteinemia [46–48].

Early start in alcohol abuse. Alcohol intake in teenagers may impair growth. The height of alcoholic patients was 4 cm less than that of the controls. Height of the alcoholics was related to age at the onset of drinking, which was before 15 years in nearly half the cases. Alcoholics who drank before 15 years of age were 3 cm shorter than the remaining alcoholics who did not drink at this age and also showed a higher current ethanol intake [41, 49]. Alcohol intake was related to decreased serum IGF-1 and osteocalcin levels, even among those alcoholics without liver disease [41, 42, 45]. Two studies performed on Harris lines, which may be related to growth arrest due to metabolic stress, showed a relation with ethanol intake during growth [49, 50].

Secondary Malnutrition

Many alcohol-related diseases may lead to malnutrition, mainly by interfering with intake or absorption of nutrients. Chronic alcoholic gastritis, with anorexia and vomiting, and chronic diarrhea are common complications of alcohol consumption. However, chronic pancreatitis and liver disease are the two main causes of secondary malnutrition in alcoholics. Moreover, alcoholics frequently suffer episodes of infection and injuries, leading to superimposed stress malnutrition. Nicolas et al. (1993), in a study performed on 250 male chronic alcoholics, who drank a mean of 235 g ethanol per day, with stable social status and familial support, who entered a treatment program for alcoholism, found that impaired nutritional status was mainly due to organic complications but not to alcohol itself or dependence. Indeed, nutritional status of alcoholics without organic complications was similar to that of the controls [51]. Alcohol dependence does not seem to play an important role in alcoholic malnutrition, provided that social and familial links are not disturbed. Alcoholics with major withdrawal symptoms either at admission or during hospital stay showed a nutritional status similar to those without withdrawal symptoms [41].

Compensated liver cirrhosis may be associated with a normal or only slightly impaired nutritional status, even with overweight. In cirrhotics, interpretation of decreased serum albumin, transferrin, and prealbumin levels may be difficult, since they may be secondary to liver failure rather than to malnutrition or may be even related to infection or injury [52]. Serum IGF-1 and IGFBP3 levels show a better correlation with liver function than with nutritional status [45, 53].

Alcoholics with liver disease show some metabolic disturbances which may clearly influence nutritional status. A hypermetabolic state with increased thermogenesis has been observed in these patients, especially in those with superimposed alcoholic hepatitis [54–56]. However, these changes are not specific of alcoholic liver disease, since they are also observed in other forms of liver disease as postviral cirrhosis [57]. Furthermore, not all cirrhotics are hypermetabolic. In fact, Muller et al. (1992) report hypermetabolism in 18% and hypometabolism in 31% of their cirrhotics. Those who were hypermetabolic showed a reduced muscle mass, whereas those who were hypometabolic, an increased fat mass [58]. Hypermetabolism has been related to increased serum levels of pro- and anti-inflammatory cytokines [59].

In contrast to cirrhotics with ascites, compensated cirrhotics show a better nutritional status, even with overweight in half of cases. This overweight is related to an excess of fat, as lean mass was shown to be reduced both by creatinine excretion and by DEXA. Indeed, arm lean mass and handgrip strength were both decreased to a similar degree in compensated cirrhotics and noncirrhotic alcoholics [41, 42, 45, 60]. Other studies have also shown an excess of fat in cirrhosis. Overweight was reported in 18% of the 883 male cirrhotics who entered the Italian Multicentre Study (1994), and Bunout et al. (1983) found higher values of body weight (110% of ideal weight) and midarm fat area (113% of the standard) in alcoholics with cirrhosis or alcoholic hepatitis [61, 62]. Therefore, obesity is not an uncommon finding in cirrhotics. However, the increased fat mass often coexists with a decreased lean mass, which is a criterion of malnutrition: obese-type malnutrition [63].

Nutritional status of decompensated cirrhotics (mainly by ascites or alcoholic hepatitis) is worse than that of noncirrhotic alcoholics [41, 42, 60, 64, 65]. Cirrhotics with ascites showed reduced lean and fat mass. Ascites causes anorexia and early satiety due to gastric compression and abdominal distension but not to altered gastric emptying: large-volume paracentesis improves satiety and dietary intake but has no effect on gastric emptying [66]. Ascites drainage by peritoneovenous shunting improves fat and muscle mass, serum albumin and transferrin, and lymphocyte count [67, 68]. Transjugular intrahepatic portosystemic shunt (TIPS), as therapy for refractory ascites, decreases portal hypertension and improves intestinal absorption. Allard et al. (2001) studied ten cirrhotics with refractory ascites who underwent TIPS. Total body nitrogen, body fat, REE, caloric intake, and muscle strength were all reduced at baseline and showed a marked improvement 12 months later [69].

Thus, body weight is a misleading method to detect nutritional changes in cirrhotics. Both fluid retention and obese-type malnutrition (decreased lean mass with increased fat mass) are common in cirrhotics, emphasizing the importance of nutritional assessment by compartments. Moreover, decreased albumin, prealbumin, transferrin, and IGF-1 are unreliable nutritional markers in alcoholics, since they may depend more on liver function, infection, and injury than on nutritional impairment.

Nutritional assessment by body compartments may be performed either by anthropometry, bioelectrical impedance, or absorptiometry. DEXA is the most accurate of these procedures and allows a separate evaluation of fat, lean, and bone mass, although it has the drawback that retained water – as ascites or edema – is counted as lean mass [70]. However, since fluid retention is habitually less pronounced, or absent, in arms, compartmental analysis of the upper limbs allows an accurate assessment of lean mass [41].

Complications of Alcohol Abuse Closely Related to Malnutrition

Some complications of alcoholism are more frequent among severely malnourished alcoholics. Some of them are the logical consequence of vitamin and trace element deficiencies. Diverse studies such as the Italian Multicentre (1994), Leo and Lieber (1999), and Bergheim et al. (2003) have shown vitamin and trace element deficiencies in alcoholics with and without liver disease, with decreased serum levels of vitamin C, retinol, carotene, selenium, and zinc [61, 71, 72]. Manari et al. (2003)

report in UK alcohol abusers' low intakes of vitamin E and folate, selenium and vitamin D, calcium and zinc, and vitamins A, B1, B2, B6, and C below UK recommended standards [44]. Wernicke encephalopathy (vitamin B1 deficiency), pellagra (niacin), xerophthalmia (vitamin A), scurvy (vitamin C), and folate and B12 deficiencies are only seen in severely malnourished alcoholics [73–76]. Interestingly, consequences of B12 deficiency, such as megaloblastic anemia, are sometimes observed among alcoholics with normal cobalamin serum levels (Fragaso A 2010), pointing out to the existence of nonfunctional forms of cobalamin [77].

Other alcohol complications, such as cerebral and cerebellar shrinkage, hypophosphatemic rhabdomyolysis, chronic alcoholic myopathy, bone disease with decreased bone mineral density, and paralysis associated with hypokalemia and hypomagnesemia, have not a direct relation with vitamin deficiency but globally with malnutrition. In all of them, a close relationship with malnutrition has been reported but also a remarkable improvement after abstinence [78–83].

Alcohol Abuse, Malnutrition, and Survival

Malnutrition, irrespective of its etiology, is related to a poor prognosis, since it depresses immunity and favors infection. Therefore, mortality of malnourished alcoholic inpatients is increased to a similar degree to that of similarly undernourished nonalcoholics [83].

The prognostic value of malnutrition in alcoholics has been extensively analyzed in those affected by liver disease: acute alcoholic hepatitis and liver cirrhosis. The prognosis of decompensated liver cirrhosis is very poor, with a 2–5-year mortality of 50% [84, 85]. The Child system, a widely used prognostic score of liver disease, included in its first version (Child and Turcotte classification 1964) a subjective nutritional assessment. However, this parameter was later substituted by prothrombin in the Child-Pugh score (1973) [86, 87]. Therefore, in the current version of the Child-Pugh score, no nutritional parameter is included.

The question is, therefore, whether nutritional data – other than liver-synthesized proteins and BMI in cases of fluid retention – may improve the prognostic value of the Child-Pugh score regarding survival. In this line, Abad et al. (1993) showed that midarm circumference (MAC) improves the prognostic capacity of the Child-Pugh score, a result also obtained by Alberino et al. (2001) with midarm muscle circumference (MAMC) and triceps skinfold (TSF), with MAMC yielding a closer prognostic value than TSF [84, 88]. Merli et al. (1996) found that a MAMC below the fifth percentile is associated with an increased mortality in Child A and B patients but not in class C ones, whereas a decrease in adipose tissue did not worsen the prognosis in any of the Child groups [85]. Mendenhall et al. (1995), in patients with acute alcoholic hepatitis, report that creatinine excretion and handgrip strength – both related to muscle mass – are better indicators of survival than other nutritional parameters [89].

Our group (2008) reported that lean arm mass assessed by DEXA yields a long-term survival value after a follow-up period of 88 months [90, 91]. Moreover, loss of lean mass after a 6-month period is related to impaired prognosis. One hundred and five alcoholic patients (including 66 of those who underwent two DEXA assessments) were followed up for a median of 18 months. During this period, 33 died (including 20 of those who had undergone a second DEXA assessment).

Forty-two of the patients had abstained from alcohol. Of these, 69.04% gained lean mass, compared with only 35.71% of those who had continued drinking ($p=0.006$). However, no associations were found between alcohol abstinence and changes in fat parameters. Analysis by means of Kaplan-Meier curves showed that loss of total lean mass and loss of total fat mass were all significantly associated with reduced survival. However, within 30 months of the second evaluation, significant associations were observed between changes related to lean mass and mortality, but no association between changes in fat parameters and mortality [92]. Taken together, these observations suggest that the protein compartment, especially muscle protein, is clinically more important than body fat stores