

Major Pathologies Associated with Acute and Chronic Alcohol Use – a Reference Summary

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Read the Fine Manual

This summary of pathologies was part of a collection of material "left over" when we realized that our Alcohol Withdrawal Syndrome Treatment Manual was getting a bit too long and included too much material not directly related to the treatment of alcohol withdrawal.

We may someday pull all this material together into a second book. In the meantime, we're giving it away (although still reserving our copyright to the material). In view of the price, we have not inserted references for the statements made in the text – it would take a great deal of time, and at the moment we're just a bit busy with other stuff. We also recognize that in some cases we could have gone into more detail – our second book was to include, for example, an entire chapter on alcohol and pregnancy, so the material here is relatively brief. Nonetheless, we think you'll find the summary useful, both as a clinical guide and perhaps even for patient education (Mr. McDonough reports that he never drank alcohol with quite the same carefree attitude after helping to write it!). Our AWS treatment manual is available at <http://www.sagetalk.com>.

Medical Disclaimer

Medicine is a dynamic field. As new research and clinical experience expand our knowledge, changes in treatment and drug therapy are required. The authors of this work have used sources believed to be reliable and informative and have made every effort to present information that is complete and generally in accord with the accepted practices at the time of publication.

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Readers are strongly advised to confirm the information contained in this volume with other sources. Readers are encouraged to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this book is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This is of particular importance when administering new or infrequently used drugs. Readers should also consult their own laboratories for normal values.

1	Major Pathologies Associated With Acute and Chronic Alcohol Use -- A Reference Summary.	1
1.1	Alcohol and the Gastrointestinal System	1
1.1.1	Oral and Pharyngeal Disorders.....	2
1.1.2	Esophageal Cancer	2
1.1.3	Mallory-Weiss Syndrome	2
1.1.4	Boerhaave's Syndrome.....	2
1.1.5	Esophageal Varices.....	2
1.1.6	Erosive Gastritis	2
1.1.7	Cancer of the Liver, Stomach, Intestines, and Colon	3
1.1.8	Colitis, Enteritis, Injury to Intestinal Mucosa.....	3
1.1.9	Hemorrhoids.....	3
1.2	Alcohol and the Liver	3
1.2.1	Fatty Liver	4
1.2.2	Alcoholic Hepatitis	4
1.2.3	Alcoholic Cirrhosis.....	4
1.2.4	Hepatic Encephalopathy.....	5
1.3	Alcohol and the Pancreas	5
1.3.1	Acute Pancreatitis.....	5
1.3.2	Chronic Pancreatitis	6
1.3.3	Pancreatic Cancer.....	6
1.4	Alcohol and the Gallbladder.....	6
1.5	Alcohol and the Cardiovascular System.....	6
1.5.1	Depression of Cardiac Muscles.....	7
1.5.2	Alcoholic Cardiomyopathy	7
1.5.3	Indirect Toxic Cardiovascular Effects: General.....	7
1.5.4	Conductive Disturbances	8
1.5.5	Effects Associated with Adrenaline: General.....	8
1.5.6	"Holiday Heart" Syndrome.....	8
1.5.7	Hypertension.....	8
1.6	Renal Effects of Alcohol	9
1.6.1	Impairment of Water Excretion and Hyponatremia	9
1.6.2	Renal Tubular Dysfunction in Chronic Alcoholism.....	9
1.7	Alcohol and the Respiratory System	9
1.7.1	Acute Respiratory Depression	9
1.7.2	Other Direct Toxic Effects on the Respiratory System	10
1.7.3	Indirect Toxic Effects on the Respiratory System	10
1.8	Alcohol in Pregnancy	10
1.9	Alcohol and the Genitourinary System	10
1.9.1	Male Genitourinary Effects.....	10
1.9.2	Female Genitourinary Effects.....	11
1.10	Toxic Effects on the Musculoskeletal System -- General	11
1.10.1	Acute Skeletal Muscle Myopathy	11
1.10.2	Chronic Skeletal Muscle Myopathy.....	11
1.10.3	Indirect Toxic Effects on the Musculoskeletal System.....	11
1.11	Alcohol-Related Skin Disorders	11
1.12	Hematological Effects of Alcohol	12
1.12.1	Direct Toxic Hematological Effects	12
1.12.2	Indirect Toxic Hematological Effects.....	12
1.13	Effects of Alcohol on the Endocrine System.....	12
1.14	Neurologic Effects of Alcohol	13

1.14.1	Effects of Alcohol on Cognition -- General	13
1.14.2	Effects of Acute Intoxication	13
1.14.3	Wernicke's Encephalopathy	13
1.14.4	Alcoholic Korsakoff's Syndrome.....	13
1.14.5	Alcoholic Dementia	14
1.14.6	Neuropsychiatric Deficits	14
1.14.7	Alcohol and Peripheral Nervous System Pathology	16
1.14.8	Sleep Disturbances and Alcohol	16
1.14.9	General Effects of Alcohol on the Brain.....	16
1.14.10	Cerebellar Degeneration.....	16
1.14.11	Marchiafava-Bignami Disease.....	16
1.14.12	Brain Stem Degeneration	16
1.14.13	Alcoholic Pellagra.....	16
1.15	Alcohol and Nutrition	17
1.15.1	Common Alcohol-Related Nutritional Deficiencies	17

1 Major Pathologies Associated With Acute and Chronic Alcohol Use -- A Reference Summary

Of all mind-altering substances of use and abuse, ethyl alcohol is the agent with the greatest effect on human health. In 1990, there were 18 million people in the U.S. who met criteria for alcohol abuse or alcohol dependence. Approximately 200,000 people per year die in the U.S. of alcohol-related medical problems.

The variety of responses seen in individuals exposed to alcohol suggests that environmental and genetic factors play a role in modulating the expression the toxic effects of the drug. Women, for example, appear to be more sensitive than men to the hepatotoxic effects of the drug when confounding factors such as total exposure are considered. Compared to men, women also appear to have more brain hippocampal damage after exposure to the drug. These gender-based stratifications of toxicity suggest that the gender-related hormonal milieu modifies the toxicity of alcohol.

Evidence is also accumulating that repeated episodes of AWS may be responsible for neuronal loss, especially in the hippocampus, possibly do to the combined effects of AWS on neurotransmitter systems and the high-cortisol state induced by AWS.

Alcohol affects all body systems. It is a systemic toxin having both acute and chronic effects. Acute toxicity is mediated by alcohol and its metabolites. Chronic toxicity can be divided into two general categories: specific cellular injury due to effects on cellular neurotransmitter receptors, and a non-specific cytological toxicity.

Specific injury, such as occurs in the nervous system, may be mediated by changes in the activity of excitatory N-methyl-D-aspartate receptors as a result of adaptive changes to the depressant effects of the drug resulting in specific neuronal losses. General cellular injury may result from a combination of factors: acetaldehyde-protein adducts formed as from intermediate production of acetaldehyde as alcohol is metabolized, glutathione depletion secondary to free radical formation, and changes in cellular metabolism as a result of effects on cellular signal transduction. Toxicity may be enhanced by malnutrition and malabsorption of nutrients and vitamins.

In the development of alcohol-related pathology, certain bodily systems are markedly more vulnerable than others. We will next discuss typical effects of long term use organized by bodily system.

1.1 Alcohol and the Gastrointestinal System

Chronic use of alcohol can produce a wide variety of pathologies in the gastrointestinal system. We discuss these briefly below. While we list cancers

separately, the prevalence of all gastrointestinal cancers rises in the presence of chronic alcoholism.

1.1.1 Oral and Pharyngeal Disorders

There is an increased risk of oral and pharyngeal cancer, a risk which becomes even greater if alcohol use is combined with the smoking of tobacco. Combined use increases the risk to approximately 15 times that of a control population. Another manifestation of chronic alcohol use is glossitis, probably the result of a deficiency of B vitamins. Parotid gland enlargement also occurs in approximately 12% of alcoholics.

1.1.2 Esophageal Cancer

Cancer of the esophagus and esophagogastric cancer is 1.5 times more likely among alcoholics, and increases to 2.1 times more likely if tobacco is co-abused.

1.1.3 Mallory-Weiss Syndrome

Several gastrointestinal syndromes are associated with alcoholism. These include Mallory-Weiss syndrome, which is characterized by mucosal laceration at the gastroesophageal junction. Mallory-Weiss is a common cause of vomiting blood or gastric bleeding. Typically, it presents as painless vomiting of blood, usually occurring after alcohol intake and vomiting or "dry heaves." Diagnosis of Mallory-Weiss can be confirmed by endoscopy. Generally, the syndrome is self-limiting if vomiting can be controlled.

1.1.4 Boerhaave's Syndrome

Boerhaave's syndrome involves rupture of the lower esophagus with leakage of contents into the mediastinum (the space behind the sternum). Typical presentation includes a history of painful severe vomiting from any cause. Boerhaave's syndrome can result in death from overwhelming infection if not appropriately diagnosed.

1.1.5 Esophageal Varices

Esophageal varices occur as a result of portal hypertension secondary to cirrhosis of the liver. Varices do not regress. The patient remains at constant risk of a ruptured varix, which can result in rapid death from exsanguination. Like Mallory-Weiss and erosive gastritis, esophageal varices are associated with hematemesis (vomiting of blood).

1.1.6 Erosive Gastritis

Erosive gastritis is the most common effect of chronic alcohol abuse on the stomach. It is also the most common cause of vomiting blood in alcoholics, accounting for approximately half of all such occurrences.

The mucosal barrier of the stomach ordinarily prevents the stomach lining from being attacked by hydrochloric acid. Exposure to alcohol changes the composition of the mucus so that it is a less effective barrier to acid,

compromising its protective capacity. Alcohol may also intensify this effect by increasing acid production.

Presentation usually includes mid-epigastric or abdominal pain, nausea, vomiting, sometimes of blood, and abdominal distention. The risk of gastric ulceration is increased when alcohol and non-steroidal anti-inflammatory drugs (NSAIDs) are taken together, but only minimally increased by alcohol itself. Upon endoscopic examination, the stomach is seen to be beefy red and bleeding from many small spots; the condition always improves if alcohol intake ceases.

1.1.7 Cancer of the Liver, Stomach, Intestines, and Colon

Alcoholism increases may increase the risk of pancreatic cancer, but may not increase the incidence of stomach or large bowel cancers. Liver cancer may also be increased in alcoholism, but whether this is an independent effect or a cancer promoter effect in patients with hemochromatosis (iron-storage disease) or chronic infection with hepatitis B or C remains undefined, though the data would suggest the latter.

1.1.8 Colitis, Enteritis, Injury to Intestinal Mucosa

Injury to intestinal mucosa is secondary to direct toxic effects of alcohol and results in malabsorption of food and vitamins. Malnutrition, which results in alcoholics from malabsorption, poor diet, and other causes, also results in biochemical injury to the mucosa. Inflammation of the intestinal lining can also lead to enteritis or colitis. Diarrhea is common as a re-feeding phenomenon in malnourished alcoholics, and may represent a combination of malabsorption at the mucosal level, since in the absence of evidence of chronic pancreatitis, it is self-limited in duration.

1.1.9 Hemorrhoids

Hemorrhoids, like esophageal varices, can be a result of portal hypertension. Significant bleeding can occur from internal and external hemorrhoids, and in a patient with a cirrhosis-induced clotting disorder, loss of blood may be substantial.

1.2 Alcohol and the Liver

The liver is a major site of alcohol toxicity. Since all blood from the intestines must pass through the liver, it is one of the first organs exposed to any toxin, including alcohol. Cirrhosis can result from chronic heavy alcohol consumption and is directly proportional to alcohol intake. Genetic factors may play a role in differences in susceptibility between individuals and ethnic groups. Women are more likely to develop cirrhosis than men. Good nutrition does not protect the liver from alcohol-induced damage, but poor nutrition may hasten the development of cirrhosis. A 10% to 30% death rate is seen among affected individuals.

Alcohol has three common health effects on the liver: fatty liver, alcoholic hepatitis and alcoholic cirrhosis. These three conditions may represent a

continuum of liver injury, with different degrees of reversibility and recovery when alcohol intake stops. The last condition, with associated portal hypertension, is in turn responsible for a wide variety of other pathologies seen in alcoholics, ranging from clotting deficiencies to esophageal varices.

1.2.1 Fatty Liver

Fatty liver, which can occur with moderate quantities of alcohol, is completely reversible with cessation of alcohol use. It results when alcohol inhibits the ability of liver cells to dispose of lipids, with resultant accumulation of lipids inside the liver cell. Fatty liver is generally asymptomatic; on occasion it can cause abdominal pain from distention of the liver capsule and may present as an enlarged liver (hepatomegaly) on physical examination.

1.2.2 Alcoholic Hepatitis

Alcoholic hepatitis occurs in 27% of male alcoholics and 47% of females. Genetic factors may play a role in determining susceptibility. It occurs after heavy alcohol use and is secondary to inflammation, injury and necrosis of liver cells. Repeated episodes of alcoholic hepatitis are associated with deposition of collagen in perivenular spaces, which may be a factor leading to fibrosis and consequent cirrhosis.

Alcoholic hepatitis may vary in severity from asymptomatic to a syndrome characterized by liver failure. Depending on the severity, clinical presentation can include decreased appetite to severe nausea and vomiting, weakness, mild abdominal discomfort to severe abdominal pain, jaundice, fever, tender liver enlargement (hepatomegaly), enlarged spleen (splenomegaly), and in severe cases which may be superimposed on pre-existing cirrhosis, evidence of ascites, peripheral edema, clotting disorders, thrombocytopenia, and hepatic encephalopathy. Laboratory examination reveals an increased WBC and elevated liver function tests with SGOT > SGPT. PT and PTT may be severely elevated. Severe hyperbilirubinemia, elevated serum creatinine, elevated PT > 1.5 times control, ascites, and symptoms of hepatic encephalopathy are associated with a 50% in-hospital mortality rate.

Alcoholic hepatitis as a manifestation of acute liver cell injury itself is usually reversible, since the immediate symptoms are generally due to damage to the liver cells, which have a marked capacity for regeneration. However, as fibrosis supervenes, the architectural structure of the liver is disrupted, and with each repeated insult can lead to alcoholic cirrhosis. Regenerating liver cells do not have proper architectural support. This results in formation of nodules, in which some architecture is preserved, surrounded fibrous bands. This pattern begins to increase the resistance to blood flow through the organ, resulting in elevated venous pressures associated with portal hypertension.

1.2.3 Alcoholic Cirrhosis

Alcoholic cirrhosis is irreversible and can be progressive and represents a dose-response curve of alcohol toxicity. It is estimated that at least one pint of

whiskey or equivalent alcohol per day over ten years in Northern European Caucasian males is associated with development of cirrhosis. Presentation includes portal hypertension, ascites, and edema. The patient may appear to be malnourished, with prominent wasting of muscle mass. The liver is firm and nodular, and may be large or small. The spleen is enlarged and the patient exhibits continuously abnormal blood chemistry with elevated bilirubin and elevations of the PT and PTT which can manifest as easy bruisability. Cirrhosis usually occurs in the end stage of alcoholism and in its extreme manifestations is associated with hepatic failure and portal hypertension: esophageal varices, ascites, peripheral edema, hepatic encephalopathy, and coma. An increased risk of bacterial infection of ascitic fluid (spontaneous bacterial peritonitis) may occur.

Electrolyte abnormalities due to an increase in the serum level of aldosterone due to intravascular volume depletion can result in hyponatremia though total body sodium is increased. Cirrhosis from any cause is also associated with increased urinary losses of potassium, magnesium, and zinc and associated hypophosphatemia. Intravascular volume depletion from a severely lowered plasma oncotic pressure due to failure of albumin synthesis can result in pre-renal azotemia. In severe cases, the patient may develop cirrhosis-associated renal failure (hepatorenal syndrome), which may often be due to aggressive attempts at diuresis or removal of large amounts of ascitic fluid. The syndrome tends to be fatal.

1.2.4 Hepatic Encephalopathy

When liver function deteriorates, the organ is unable to clear toxins, including those produced by bacteria in the colon as part of normal metabolic functions. These toxins may severely affect mental and neurological functions, producing a syndrome known as hepatic encephalopathy. This syndrome is characterized by decreased mental status, "liver flap" (asterixis), and ultimately coma. Hepatic encephalopathy can be temporarily reversed in 70% of cases by administration of a benzodiazepine antagonist, flumazenil (Romazicon) suggesting that increased GABAergic tone in the CNS may contribute to symptoms. An elevated blood ammonia level supports the diagnosis, but is not a prerequisite. Benzodiazepine administration should be avoided in a patient with marginal liver function or a history of hepatic encephalopathy as it may precipitate encephalopathy.

Hepatic coma, if survived by the patient, may result in a number of residual neurological symptoms such as coarse tremor of the head or arms, asterixis, grimacing, choreoathetotic movements of the limbs, dysarthria, ataxia of gait, and cognitive deterioration termed chronic hepatocerebral degeneration.

1.3 Alcohol and the Pancreas

1.3.1 Acute Pancreatitis

Alcoholism can account for about 50% of all cases of pancreatitis. Presenting features include abdominal pain, centered in the midepigastrium and radiating

to the back. Lying down exacerbates the pain in some patients. The patient may also complain of severe nausea, vomiting, and a feeling of fullness in the abdomen due to a decrease in intestinal motility. On exam, the patient may be tachycardic due to peripheral vasodilation coupled with intravascular volume depletion from poor oral intake as well as a phenomenon known as "third-spacing" due to increased permeability of the vascular system and transudation of fluid into the abdominal cavity.

Laboratory examination may reveal an elevated WBC count, elevations of serum amylase and lipase, hyperbilirubinemia, elevated LDH, hypocalcaemia, hyperglycemia, and low oxygen tension on blood gas determination. EKG abnormalities may be present and consist of ST and T wave abnormalities. Chest x-ray can reveal pulmonary infiltrates, and abdominal films can show the presence of intestinal paralysis (ileus). In severe cases, mass lesions of the pancreas can occur: pancreatic pseudocyst, phlegmon, or abscess.

In susceptible individuals, especially alcoholics with previous episodes of pancreatitis, even a small amount of alcohol (the equivalent of 1 - 2 beers) can precipitate an episode of acute pancreatitis, which may be superimposed on symptoms of chronic pancreatitis which are discussed below.

1.3.2 Chronic Pancreatitis

Chronic pancreatitis may occur with ingestion of relatively low amounts of alcohol over a long period of time. The syndrome is characterized by a slow, insidious onset. Presentation generally includes: chronic abdominal pain made worse by large, fatty meals, weight loss, malabsorption, foul-smelling bulky stools, and diarrhea. Endocrine insufficiency resulting from damage to the gland can result in diabetes, which may be severe if glucagon secretion is also impaired. A syndrome of vitamin B12 deficiency may commonly occur with chronic pancreatitis from malabsorption of B12, which can be corrected by exogenous administration of pancreatic enzymes.

1.3.3 Pancreatic Cancer

Alcoholism also doubles the risk of pancreatic cancer. Painless jaundice or hypercoagulability, or a change in pain associated with chronic pancreatitis in the alcohol-dependent patient should prompt the clinician to search for evidence of pancreatic cancer.

1.4 Alcohol and the Gallbladder

The gallbladder is also affected by chronic alcohol abuse. Gallstones are more common in alcoholics, and may be associated with repeated bouts of pancreatitis. The gallbladder can become infected causing fever, jaundice, and abdominal pain.

1.5 Alcohol and the Cardiovascular System

Alcohol has a wide variety of toxic effects on the cardiovascular system. These effects include both direct toxic effects and indirect toxic effects secondary to

other alcohol-related medical conditions. Alcohol abuse can lead to the development of several potentially life-threatening cardiac conditions, as outlined below.

1.5.1 Depression of Cardiac Muscles

Acute toxic effects of alcohol on the cardiovascular system include depression of cardiac function by alcohol, which can precipitate congestive heart failure in a patient with pre-existing alcoholic cardiomyopathy. Alcohol-induced left ventricular dysfunction can lead to a decrease in cardiac output, with decreased exercise tolerance, shortness of breath, peripheral edema, and pulmonary edema.

1.5.2 Alcoholic Cardiomyopathy

A large proportion of dilated cardiomyopathy is due to the effects of alcohol consumption on the heart. There appears to be a dose-response curve between alcohol exposure and myocardial damage. In one study, mean age at time of evaluation was 54 years with use of 82 gm alcohol/day over 34 years. In the absence of symptoms of heart failure, the diagnosis should be suspected in any patient with chronic heavy alcohol use, especially in the presence of findings of skeletal muscle weakness or cirrhosis, as the prevalence of these conditions is increased in the disease.

Cardiomyopathy is characterized pathologically by interstitial fibrosis, hypertrophy of myocytes, and myocytolysis. Patients with alcoholic cardiomyopathy who continue to use alcohol are at risk for out of hospital death with a rate of 14.1% over 4 years of follow-up.

Presentation of cardiomyopathy may be divided into early and progressive phases. Early on, patients may be completely asymptomatic. Gradually, symptoms can include weakness, shortness of breath on exertion or on reclining, paroxysmal nocturnal dyspnea, peripheral edema, and palpitations. Some patients may describe some of these symptoms upon using alcohol, and on close questioning will reveal that they have moderated their alcohol intake as a result. Progressive cardiomyopathy leads to rate and rhythm disturbances and to symptomatic congestive heart failure. Rate and rhythm symptoms include atrial fibrillation, premature ventricular contractions, premature atrial contractions, paroxysmal atrial tachycardia, and ventricular tachycardia. Symptoms of congestive heart failure include cardiomegaly, cough, chest pain, shortness of breath, pulmonary and peripheral edema, ascites, and prominent pulsation of an enlarged liver.

1.5.3 Indirect Toxic Cardiovascular Effects: General

Indirect toxic effects of alcoholism include cardiac conduction disturbances, cardiac problems exacerbated by over-hydration, and hyperadrenergic symptoms related to alcohol withdrawal (Type B symptoms).

1.5.4 Conductive Disturbances

Conductive disturbances in the context of alcoholism can be caused by many factors. Acute alcohol intake or withdrawal results in an increased level of circulating catecholamines and may be associated with an increased response of the myocardium to the chronotropic and inotropic effects of these neurohormones. Depletion of body stores of magnesium and potassium may also increase cardiac irritability which can lead to arrhythmias. If the patient has an underlying alcoholic cardiomyopathy, this further increases the risk of a cardiac arrhythmia.

1.5.5 Effects Associated with Adrenaline: General

Adrenaline is produced in large amounts during certain phases of both mild and severe alcohol withdrawal. Increased circulating levels of adrenaline place stress on the entire cardiovascular system. The effects are particularly dangerous in the presence of pre-existing angina or heart disease and can result in impaired cardiac function resulting in heart failure, or myocardial infarction. Underlying hypertension may also be exacerbated by the hyperadrenergic state. For a discussion of the hyperadrenergic state and related symptoms (Type A AWS), diagnosis and treatment in much greater detail, see our Alcohol Withdrawal Syndrome Treatment Manual.

1.5.6 "Holiday Heart" Syndrome

One common syndrome caused by increased adrenaline levels is so-called "holiday heart." In this syndrome, the patient has generally engaged in binge drinking over a period of time, perhaps a weekend or holiday. When the patient reduces or ceases alcohol consumption, the resulting withdrawal triggers the release of excess adrenaline which in turn can lead to atrial and ventricular arrhythmias. The patient may complain of palpitations and in some cases, chest pain. Failure to recognize the underlying cause of the syndrome can lead either to inappropriate medical therapy. Except in the presence of cardiomyopathy or other irreversible cardiac conditions, remission of the holiday heart syndrome is possible with cessation of alcohol intake.

1.5.7 Hypertension

Risk of hypertension is approximately doubled by alcoholism. Alcohol acts to increase vascular reactivity to endogenous vasopressors and also increases levels of circulating catecholamines. Alcohol-related hypertension can enter an acute phase in Alcohol Withdrawal Syndrome, as one of the common effects of withdrawal is a large rise in circulating levels of adrenaline. In this context, alcoholics may require immediate pharmacologic treatment to control hypertension and thus reduce the risk of cerebrovascular or cardiac events. For more information on treatment of hypertension in a context of AWS, see our Alcohol Withdrawal Syndrome Treatment Manual.

1.6 Renal Effects of Alcohol

1.6.1 Impairment of Water Excretion and Hyponatremia

Hyponatremia in alcoholism is generally secondary to rebound hyperexcretion of antidiuretic hormone, with resultant inability to excrete free water. Total body sodium is normal in the absence of significant liver disease. Anti-diuretic hormone (ADH) is inhibited by rising and stable BAL, promoting a free water diuresis. With falling BAL, the process is reversed. ADH rebounds, thirst increases and the patient's intake of free water increases in the presence of impaired excretion. In an inpatient setting, an alcoholic patient may also receive inappropriate and vigorous hydration and the resultant increases in vascular volume can lead to acute heart failure as a result of increased left ventricular pressure while worsening the hyponatremia.

1.6.2 Renal Tubular Dysfunction in Chronic Alcoholism

Only recently have the effects of chronic alcohol use on renal function been evaluated. Even in the presence of normal glomerular function, a wide range of tubular reabsorption defects were found in subjects meeting criteria for chronic alcoholism who were studied immediately after alcohol consumption and after 4 weeks of abstinence. Hypophosphatemia and hypomagnesaemia were found in 30% of patients, 21 percent had hypocalcaemia and 13 percent had hypokalemia. 36 percent of patients had a variety of simple and mixed acid-base disorders. Defects in renal tubular function included decreases in the threshold and maximal reabsorptive ability for glucose in 38 percent of patients and in the renal threshold for phosphate excretion in 36 percent of patients. Increases in the fractional excretion of calcium, and magnesium occurred in 23% and 21% of patients. Aminoaciduria was present in 38%. 28% had a defect in tubular acidification, and 8% had an impairment in urinary concentrating ability. The effects of alcohol on renal function in the absence of liver disease appears reversible, since in this group of patients, blood chemistry parameters and renal tubular function normalized after four weeks of abstinence.

1.7 Alcohol and the Respiratory System

Effects of alcohol on the respiratory system include both direct and indirect toxic effects. In addition, effects can be either acute or chronic.

1.7.1 Acute Respiratory Depression

Acute ingestion of alcohol sufficient to produce blood alcohol levels of > 400 mg% in non-tolerant individuals may result in death due to hypoventilation as a result of depression of the breathing centers in the brain stem. In a tolerant individual, the lethal dose may be considerably higher. Alcohol does depress the ventilatory response to carbon dioxide. Ventilation volume may be increased or decreased with moderate doses. A history of alcohol use may increase the risk of sleep apnea. Age appears to be a risk factor for this effect.

1.7.2 Other Direct Toxic Effects on the Respiratory System

Alcohol use impairs the natural defense mechanisms of the lungs against bacterial and viral invasion. Upper airway reflex sensitivity is impaired with alcohol levels > 100 mg%, and it is unknown whether tolerance to this phenomenon occurs. Cough and gag reflexes are both impaired during intoxication, while mucociliary clearance is decreased. Alcohol use is associated with an increased incidence of lung infections, which include both community-acquired pneumonias, as well as tuberculosis and anaerobic lung infections from aspiration of gastric contents which may occur during a heavily intoxicated state or after vomiting.

1.7.3 Indirect Toxic Effects on the Respiratory System

Indirect toxic effects of alcohol on the respiratory system include immune system suppression. This contributes to a greater prevalence of the infectious pathologies mentioned immediately above. The toxic effects of alcohol intake on the respiratory system increase if tobacco is also consumed.

1.8 Alcohol in Pregnancy

It is, of course, unwise to consume any drug during pregnancy unless it is an absolute medical necessity. Approximately 5% of pregnant women are problem drinkers.

The prevalence of full-blown fetal alcohol syndrome is approximately 1 to 3 births per thousand in the U.S.

Spontaneous abortions show a two-fold increase in chronic drinkers and there is a much higher incidence of congenital cranio-facial and cardiac defects. Alcohol use in pregnancy is also associated with decreased birth weight, retarded intellectual development, and lowered IQ scores.

1.9 Alcohol and the Genitourinary System

Alcohol has several effects on the genitourinary system. In both males and females, it is associated with an increase in the severity of kidney infections. An increase in genitourinary infections is also seen in both sexes. Other manifestations are gender-dependent, as outlined below.

1.9.1 Male Genitourinary Effects

In the male system, alcohol has a direct toxic effect on the testes. Patients may exhibit decreased plasma testosterone levels, infertility, and atrophic testes. Male patients may exhibit decreased secondary sex characteristics, an effect also secondary to the liver's failure to clear estrogen.

Typical presentation of male genitourinary effects may include: impotence, decreased libido, decreased beard growth, and prostatic atrophy. Hyperestrogenism leads to gynecomastia, decreased body hair, and hypogastric and pelvic fat pads.

1.9.2 Female Genitourinary Effects

In women, alcoholism can result in a wide range of problems including decreased libido, dyspareunia secondary to impaired lubrication, dysmenorrhea, and amenorrhea.

1.10 Toxic Effects on the Musculoskeletal System -- General

Alcohol also has direct and indirect toxic effects on the musculoskeletal system. In clinical presentations, these include skeletal muscle myopathy and breakdown. Subclinically, history may be positive for transient muscle cramps, weakness, and dark urine; often subclinical effects are asymptomatic. Toxic effects of alcohol on muscles will result in elevated muscle enzymes, SGOT, LDH, CPK, and aldolase in lab results.

1.10.1 Acute Skeletal Muscle Myopathy

Acute skeletal muscle myopathy is usually seen after a large amount of alcohol intake. Long periods of immobility increase the risk. Presentation typically includes weakness of limb girdle and musculature, muscle pain, edema of muscles, markedly elevated muscle enzymes, and myoglobinuria. This last effect may precipitate renal failure.

1.10.2 Chronic Skeletal Muscle Myopathy

Chronic skeletal muscle myopathy can occur after many acute episodes or without previous history. Presentation includes limb-girdle muscle weakness and wasting. There is an absence of pain, tenderness, or elevated muscle enzymes.

1.10.3 Indirect Toxic Effects on the Musculoskeletal System

Indirect toxic effects of alcohol on the musculoskeletal system include a high incidence of skeletal and muscular trauma secondary to intoxication and osteoporosis secondary to calcium depletion, poor diet, and decreased activity. Rarely, alcohol abuse can be associated with osteonecrosis of the hip. This is secondary to hyperlipidemia and occurs when fat blocks arteries supplying the hip joint. Presentation includes severe bilateral hip pain and limping with no history of arthritis.

1.11 Alcohol-Related Skin Disorders

Alcohol has many toxic effects on the skin, primarily indirect. One class of lesions is secondary to liver pathology. These include linear excoriations secondary to pruritis, gray skin pigment, jaundice, dorsal tongue furrows, scant body hair, spider nevi, and palmar and plantar erythema. Lesions secondary to malnutrition include glossitis secondary to folate deficiency, purpura secondary to impaired prothrombin production. In addition any type of tissue damage will heal more slowly in a malnourished individual.

Lesions exacerbated by alcohol consumption include rhinophyma, acne rosacea, psoriasis, seborrheic dermatitis, wine sores, and Dupuytren's contractures. Alcoholics also experience an increase in infection, co-incident with poor

hygiene. Alcoholic pellagra also produces characteristic skin lesions secondary to niacin deficiency.

1.12 Hematological Effects of Alcohol

The effects of alcohol on the hematopoietic system are both direct and indirect. Many of the latter are caused by nutritional deficiencies and/or gastrointestinal pathologies.

1.12.1 Direct Toxic Hematological Effects

Direct toxic effects of alcohol on the hematopoietic system include interference with maturation of all marrow cellular elements: red blood cells, white blood cells and platelets.

Blockage of WBC synthesis by alcohol leads to leukopenia, impaired leukocyte mobilization, function, and chemotactic properties. This in turn leads to increased vulnerability to infections.

Blockage of thrombocyte maturation leads to decreased platelet life span, inhibited platelet function, and reduced clotting activity.

1.12.2 Indirect Toxic Hematological Effects

Indirect toxic effects of alcohol on the hematopoietic system include folic acid deficiency. Folate absorption is blocked by alcohol both at the cellular level and by alcohol-induced changes in the intestinal mucosa. Prevention of proper metabolizing of Vitamin B6 can lead to both megaloblastic and sideroblastic anemia.

Iron deficiency anemia can occur secondary to alcohol-induced bleeding, usually in the GI tract. Alcohol does not block absorption of iron via the intestinal mucosa. Alcohol consumption may also lead to hemochromatosis due to an increase in tissue iron stores from ingestion of iron-rich alcoholic beverages. Genetically predisposed individuals are at greater risk for developing hemochromatosis if they drink alcohol; it can cause liver and pancreatic damage.

1.13 Effects of Alcohol on the Endocrine System

Disturbances in catecholamine metabolism are the most prominent endocrine effect of chronic alcohol abuse. Elevated levels of circulating catecholamines are found in the case of rising, stable, and falling BALs. They can be most severe in the presence of falling BALs. Hyperadrenergia thus constitutes one of the major symptom groups of AWS, referred to in this text as Type B. For a complete discussion of Type B symptomatology and treatment, see our Alcohol Withdrawal Syndrome Treatment Manual.

Alcohol-related disturbances in catecholamine metabolism can have very serious medical consequences. Elevated levels of adrenaline and other endogenous vasopressors are associated with hypertension and a variety of cardiac

pathologies. Serious and potentially lethal effects of this syndrome include acute and chronic hypertension, cerebrovascular events, myocardial infarction and cardiac arrhythmias.

Other toxic effects of alcohol on the endocrine system are covered above as part of its effects on the genitourinary system.

1.14 Neurologic Effects of Alcohol

Alcohol has an extraordinary range of effects on the neurological system. Many of them are capable of producing serious and often irreversible cognitive and neurological impairment. We discuss some of the more common pathologies below.

1.14.1 Effects of Alcohol on Cognition -- General

The neuropsychiatric deficits which can be attributed to chronic alcohol exposure may appear as obviously dramatic clinical syndromes such as Wernicke's encephalopathy, or as sub-clinical deficits, such as decreases in associative learning functions. The recognition of these syndromes is important, since their presence may influence the kind of treatment program which may be offered to an alcoholic in early recovery, after the detoxification process is complete.

1.14.2 Effects of Acute Intoxication

Acutely, alcohol use may lead to an alcoholic blackout, a form of amnesia associated with high BALs. While the person may appear in control during these episodes, they feature irretrievable short-term memory loss. A person can do high-level tasks during an episode because they are able to draw on long-term memory.

1.14.3 Wernicke's Encephalopathy

Another nervous system effect of alcohol is Wernicke-Korsakoff syndrome, which is secondary to thiamine deficiency. Wernicke encephalopathy is caused by bleeding into the brainstem and hypothalamus. Presentation includes progressive external ophthalmoplegia, horizontal nystagmus, bilateral rectus palsy, and concomitant ataxia, confusion, and disorientation. The syndrome is progressive to complete paralysis. If not treated, it is progressive to Korsakoff's Psychosis (see below).

Prevention and treatment of Wernicke-Korsakoff focus on thiamine replacement. All alcoholics should be given parenteral thiamine prior to intervention. Thiamine replacement can cure this syndrome completely.

1.14.4 Alcoholic Korsakoff's Syndrome

Alcoholic Korsakoff's syndrome is a chronic sequelae resulting from thiamine deficiency, and usually preceded by an episode of Wernicke's encephalopathy. The syndrome is due to neuronal degeneration, especially in mamillary bodies. Presentation includes loss of recent memory, inability to store recent memory

into long term memory, poor insight and judgment, apathy or flattened affect. Confabulation may be more common early in the course of the syndrome and tends to completely extinguish with time. Once the syndrome has developed, there appears to be little response to treatment, although some workers have seen some improvement in the disorder with clonidine.

1.14.5 Alcoholic Dementia

Alcoholic dementia is a diagnosis of exclusion, arrived at after all other causes of dementia have been ruled out. Its presence is inferred by the history of chronic alcohol use, deteriorating intellectual function, and stabilization of function once the individual stops alcohol use. Using these criteria, as many as 24% of institutionalized elderly may be suffering from alcoholic dementia. As a group, these patients tended to be 10 years younger than patients with Alzheimer's type dementia.

In early stages, presentation includes: fatigue, listlessness, loss of interest, depression, anxiety and agitation. Typical personality changes include social withdrawal, irritability, impulsive and socially unacceptable behavior.

In later stages presentation of alcoholic dementia includes: confusion, disorientation, recent memory loss, poor judgment, and lack of insight. There is deterioration of learning and memory processes including problem-solving, visuo-motor and constructional skills. Physical symptoms include: spasticity of the lower extremities, scissor gait, and fine picking movements. The patient may come to require a structured and supervised living situation to avoid self-harm.

Differentiation from Alzheimer's type dementia appears to be best made by following intellectual function over time. Alzheimer's type dementia would show a gradual progression of deficits, whereas an alcoholic dementia usually remains more stable over time, if one can be assured that alcohol intake has stopped. It is also possible that alcohol use in the past is a significant risk-factor for developing Alzheimer's dementia especially when this condition develops at a later age.

1.14.6 Neuropsychiatric Deficits

Chronic alcoholics often have significant impairments in problem-solving, which appear to result from failure to generate context-appropriate hypothesis-testing strategies. In addition, chronic alcoholics exhibit impairments in the ability to modify behavior based on feedback, suggesting a change in evaluative capacities. These defects in cognitive function related to the failure to use hypothesis-testing strategies in a structured fashion appear to be relatively specific effects of chronic heavy alcohol use, and according to certain workers, may be the basis for the information-processing deficits found in this population.

The clinician needs to be aware of the level of neuropsychological impairment present in the detoxified patient, as this will have a major impact on the kind of post-detoxification treatments which can be offered to the patient. Selecting cognitively appropriate treatment will increase the chances that the patient will benefit from these interventions.

Alcohol-related neuropsychological impairment can be roughly divided into short-term and long-term defects in cognitive processing. This division is somewhat arbitrary, in that in any particular patient, there is a continuum of deficits, some of which tend to remit quickly, and some of which may not remit at all, even with prolonged (> 5 years) abstinence. In general, short-term memory capacity and psychomotor skills tended to return to normal levels, but deficits in verbal association and learning tended to persist.

Remission is also influenced by age, with alcoholics older than 40 years demonstrating persistent defects in visuo-spatial cognitive defects while those younger than 40 years appearing to recover within a period of 2-3 weeks.

Table 1: Prognosis of Neuropsychological deficits in chronic alcoholics

Deficit	Time Expected to Recover	Chance of Complete Recovery
Simple language skills	< 4 weeks	Good
Decreased short-term memory capacity	> 1 year	Fair
Abstract reasoning ability	> 1 year	Fair
Decreased visuo-spatial reasoning	> 1 year	Fair
Associative learning and memory	> 7 years	Poor

Alcohol affects cognition and neuropsychiatric performance. Acute intoxication results in a familiar syndrome characterized in part by increased reaction time and decreased short and long term memory. Chronic use leads to decreased numerical and verbal recall and a decreased ability to manipulate 3-dimensional figures. When alcohol consumption ceases, cognitive ability may return to a baseline over a period of 1 year, occurring faster in younger patients.

Alcohol also produces a variety of central nervous system pathology. In the most general sense, these include intoxication, dependence, and Alcohol Withdrawal Syndrome (AWS).

1.14.7 Alcohol and Peripheral Nervous System Pathology

Alcohol can also lead to peripheral nervous system pathology, most notably neuropathy. This may be secondary to thiamine deficiency or may be secondary to the direct toxic effects of alcohol on nerve cells. Presentation includes: progressive numbness, pain, and paresthesias in distal extremities. Effects are symmetrical, with sensory loss preceding motor dysfunction, weakness, and ataxia. Numbness often shows a stocking and glove distribution. Deep tendon reflexes, vibratory, and position sense are diminished or absent.

1.14.8 Sleep Disturbances and Alcohol

Sleep disturbances are a very common result of alcohol use and are often not diagnosed as being related to alcohol consumption.

Alcohol can provoke alteration of normal sleep patterns, including REM deprivation followed by REM rebound on cessation of drinking. There may be an absence of stage 4 sleep in alcoholics, whether they are drinking or not. During drinking, there is a decrease of stage 3 sleep. Alcohol generally produces no alteration of stage 1 and 2 sleep.

Presentation generally includes insomnia (this may be severe), restlessness, frequent awakenings, and night terrors.

1.14.9 General Effects of Alcohol on the Brain

Chronic alcohol use can also cause a drop out of nerve cells. Certain effects of alcohol result in lasting specific brain damage. CT scans of chronic alcoholics show a decrease in brain mass.

1.14.10 Cerebellar Degeneration

Alcohol can also lead to cerebellar degeneration. This may be seen as an acute crisis or a chronic effect. This results in loss of balance and incoordination. It may respond to thiamine replacement and cessation of drinking.

1.14.11 Marchiafava-Bignami Disease

Marchiafava-Bignami Disease, caused by the loss of anterior corpus callosum fibers, is another possible effect of chronic alcohol use. It is characterized by a loss of frontal lobe functions. Patients are disinhibited and exhibit impaired judgement. The condition is permanent.

1.14.12 Brain Stem Degeneration

Chronic alcohol intake can also lead to central pontine myelinolysis. In this acute degeneration of brain stem structures, no nerve signals get past the brain stem. The consequence is total quadriplegia. The condition can also cause respiratory arrest and is usually permanent.

1.14.13 Alcoholic Pellagra

Niacin deficiency in alcoholics can produce alcoholic pellagra. In addition to the condition's characteristic dermatitis, presentation includes both psychiatric and gastrointestinal disturbances (leading to the alliterative diagnostic

mnemonic “diarrhea, dermatitis, and dementia”). Specific psychiatric symptoms include confusion, hallucinations, depression and delirium. Gastrointestinal disturbances include glossitis, diarrhea, stomatitis, and constipation.

1.15 Alcohol and Nutrition

Chronic alcohol consumption can also produce a variety of nutritional deficiencies. Specific nutritional deficiencies are outlined briefly below.

While alcohol has a carbohydrate yield of 7 calories per gram, it does not supply any essential nutrients. Alcohol can supply most daily caloric needs. When calories are obtained primarily or exclusively from alcohol, hunger is diminished. Weight is maintained, but muscle mass decreases while fat mass increases.

Alcohol-related malnutrition is due to two causes, either separately or in combination. In the alcoholic, alcohol often displaces food containing essential nutrients. This indirect toxic effect can lead to severe nutritional deficiencies. Additionally, alcohol and alcohol-related pathologies block absorption, modification and storage of nutrients by a variety of mechanisms. Malabsorption is associated with damage to gastric and intestinal mucosa. Progressive liver damage also plays a key role in avitaminosis and malnutrition.

1.15.1 Common Alcohol-Related Nutritional Deficiencies

Thiamine is directly destroyed by alcohol consumption, as it is used to metabolize alcohol. Thiamine deficiency is the most common alcohol-related nutritional deficiency. All alcoholics should be given parenteral thiamine prior to intervention.

Folic acid is blocked at the intestinal and cellular level.

In vitamin B6, production of the active form of the vitamin is inhibited.

Niacin, like Thiamine, is used in to metabolize alcohol, and is thus directly destroyed. Alcoholic pellagra, a potential result of niacin deficiency, is discussed above in section 1.14.13.

Riboflavin is both directly destroyed and dropped at the intestinal level.

There is profound alteration of amino acid metabolism.

Iron is diminished through bleeding.

Alcohol distorts metabolic functions relating to magnesium, calcium, potassium and zinc. This can lead to serious and potentially life-threatening electrolyte imbalances during AWS.