Emergency management of alcohol withdrawal

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Since the mean annual per capita consumption of alcohol is increasing in all industrialized countries, physicians can expect to encounter more patients in alcohol withdrawal. The severity of the alcohol withdrawal reaction depends on both the intensity and duration of alcohol consumption. Generally, this withdrawal is mild and usually requires little medical treatment. However, even mild withdrawal may progress to the major withdrawal syndrome of delirium tremens, the mortality of which may be as high as 15%. Morbidity in withdrawal is highest when diagnosis of the syndrome is delayed and when it occurs in patients with other medical or surgical problems.

The proper management of withdrawal reactions depends largely on full assessment and early treatment. Full assessment is intended to detect factors that increase the morbidity of withdrawal (Figure 1), and early treatment is intended to prevent symptoms and signs from progressing to a major reaction (Figure 2). Some complications may be overlooked, while others, such as subdural hematoma, are difficult to diagnose conclusively during withdrawal. The medical and paramedical personnel caring for the alcohol-abusing patient in the emergency department should be sympathetic and nonjudgmental to facilitate full assessment and [illegible] treatment.

Clinical profile of alcoholic withdrawal

In the large doses taken by alcoholics, ethanol has a depressant action on the central nervous system. When alcohol ingestion is abruptly decreased or discontinued, it is the compensatory increase in neuronal excitability that produces most of the signs and symptoms characteristic of the alcohol withdrawal reaction.

Primary dependence (alcohol withdrawal syndrome)

There is considerable individual variation in the clinical signs and symptoms of alcohol withdrawal (Figure 2). In mild reactions, the chief symptoms are hyperacuity, hyperactivity of reflexes, tremor, anxiety, insomnia, and reduction of seizure threshold, all of which appear within a few hours after drinking is stopped and last approximately 48 hours. Seizures during withdrawal are typically grand mal, nonfocal, one or two in number, and are most likely to occur between 12 and 48 hours after cessation of drinking. In severe reactions, tremulousness, seizures, auditory and/or visual hallucinations, and global confusion (delirium) are most evident between 48 and 60 hours after withdrawal, but may rarely persist up to 10 days. Low-grade fever (<38.5°C) is occasionally found in severe withdrawal reactions without appa[illegible]

cause; nevertheless meticulous clinical and laboratory assessment must always be made to exclude infection, regardless of the absolute level of temperature.

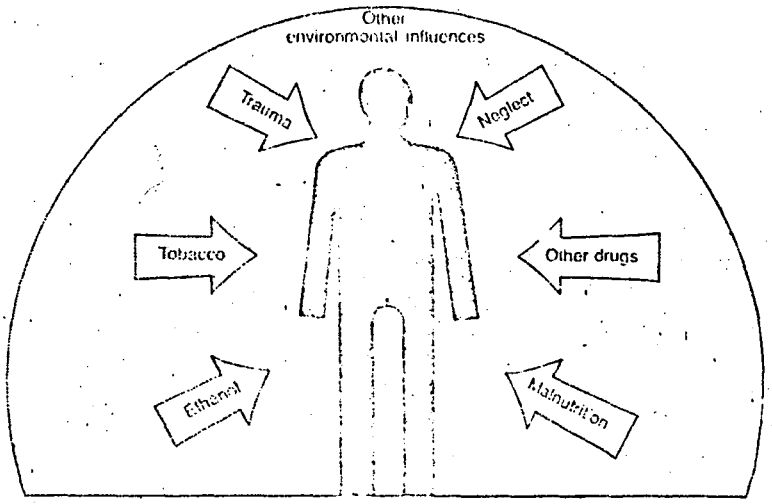
Secondary metabolic effects

Chronic ingestion of ethanol produces a constellation of predictable secondary metabolic changes (Table 1, column 1). Since most of these changes are alcohol induced, they do not usually require treatment other than supportive care and stopping the consumption of alcohol. The lactic acidemia, hyperuricemia, hypertriglyceridemia, and ketosis are all attributed to oxidation of excess nicotinamide adenine nucleotide dehydrogenase (NADH), which is produced during the conversion of alcohol to acetaldehyde by alcohol dehydrogenase. Insulin therapy is not required for hyperglycemia unless there is a clinically important osmotic diuresis, ketoacidosis, or the patient has a history of diabetes mellitus. On the other hand, severe electrolyte abnormalities should be routinely treated since they may affect the prognosis. If hypoglycemia is suspected, a blood-sugar determination should be made, and 50% dextrose is given (50 ml over 60 seconds). Alcohol-induced ketoacidosis with accumulation of β-hydroxybutyrate, acetoacetate, and lactate develops after several days of heavy drinking, with little or no food, and associated vomiting. When these anions account for the metabolic acidosis, the anion gap ($[Na^+]-([Cl^-]+[CO_2])$) will be greater than 15. Arterial blood-gas determinations are necessary to assess the nature and severity of such acid-base abnormalities. Bicarbonate is usually not indicated if the pH is > 7.1 and the actual bicarbonate value is > 15 meq/liter. These patients respond well to solutions of IN saline and glucose that restore hydration and liver glycogen.

Alcohol-induced disease

After prolonged drinking, the direct toxic effects of alcohol produce various organic disorders (Table 1, column 2). A careful history, obtained from either the patient or a relative, should include the amount and type of alcoholic beverage consumed daily and the duration of its excessive use. An average daily intake above 80 g ethanol is associated with an increased risk of cir-

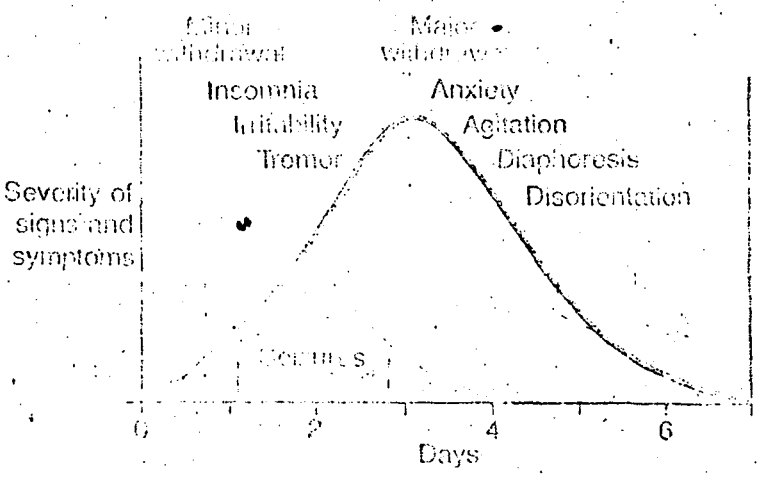
Figure 1: Etiology of organic diseases in the alcoholic patient



rhosis. It is difficult to assess the patient accurately during withdrawal if there is coexistent liver disease (with or without portal encephalopathy), dementia, or other neurologic problems. Excess sedation may precipitate portal encephalopathy, as may the common complications associated with withdrawal—dehydration, electrolyte imbalance, hypoxia associated with pneumonia, infections, and gastrointestinal hemorrhage.

Ascites may be aggravated if saline is aggressively administered to the dehydrated alcoholic with a history or clinical evidence

Figure 2: The time course of two typical clinical instances of untreated alcohol withdrawal



of portal hypertension. In these patients, 10% dextran (molecular weight 40,000) in 5% dextrose in water may temporarily correct serious hypovolemia.

Chest pain, arrhythmias, cardiomegaly, congestive heart failure, or combinations of these symptoms may indicate cardiomyopathy. Results of careful examination of the cardiovascular system, including a chest x-ray to assess cardiomegaly and congestive heart failure, an electrocardiogram, and cardiac monitoring, will help determine whether this complication is present.

Alcohol-associated disorders

Many concurrent clinical problems are related to the "life-style" of the alcoholic (Table 1, column 3). For example, hypothermia, which may occur in the alcoholic exposed to cold, can be missed because most clinical thermometers only register 35°C and above. (Electronic thermometers with expandable scales and flexible probe can be invaluable in the hypothermic restless patient.)

Wernicke's encephalopathy (ataxia, ocular palsies, nystagmus) often improves rapidly with parenteral thiamine. Trauma (fractures, visceral injury, head injury, and subdural hematoma) may easily be missed in the patient who is already confused, drowsy, and/or hallucinating. Acute bronchitis, aspiration, or pneumonia is often a more difficult problem to manage in alcoholics who smoke heavily.

Concurrent unrelated disease

Chronic alcoholics may have coincidental diseases that are etiologically unrelated to alcohol consumption and the withdrawal syndrome (Table 1, column 4). Problems arising from the concurrent use of sedatives, tranquilizers, and alcohol often coexist. The alcoholic with diabetes mellitus may have hypoglycemia, hyperglycemia, or diabetic ketoacidosis. Alcoholics with epilepsy may discontinue anticonvulsant therapy and develop status epilepticus. Systolic and diastolic hypertension may subside to normal or mildly elevated values after withdrawal has been accomplished.

Laboratory investigation

Table 2 lists important tests that should

Table 1: Clinical profiles of chronic alcoholic withdrawal

	Primary alcohol dependence (withdrawal syndrome)		
Secondary metabolic effects	Alcohol-induced diseases	Alcohol-associated disorders	Concurrent problems not alcohol related
Electrolyte imbalances Hypokalemia Hypomagnesemia Hypocalcemia Metabolic ketoacidosis Dyslipidemia Overhydration Hyperglycemia Hypoglycemia Hypertriglyceridemia Hyperuricemia	Cirrhosis Ascites Encephalopathy Varices Hepatorenal syndrome Hepatitis Peptic ulcer GI hemorrhage Pancreatitis Cerebellar degeneration Dementia Peripheral myopathy Cardiomyopathy	Dehydration Anemia Malnutrition Hypothermia Wernicke's encephalopathy Trauma Sepsis Carcinoma Oropharyngeal Laryngeal Bronchial Chronic obstructive lung disease Aspiration pneumonia Tuberculosis Dysrhythmias Subdural hematoma	Use of sedatives, tranquilizers Diabetes mellitus Epilepsy Hypertension Myocardial infarction Other systemic diseases

Table 2: Clinical workup for assessing patients in alcohol withdrawal

Primary		Additional tests
Barbiturate screening[1]	Urine	Blood may be drawn and stored for later measurement of:
Urine	Analysis	Calcium
	Microscopy	Magnesium
Stool	Occult blood	Amylase
Hematology	CBC and differential	Serum glutamic oxaloacetic transaminase (SGOT)
Biochemistry	Glucose	Serum bilirubin
	Urea	Alkaline phosphatase
	Electrolytes (Na^+, K^+, Cl^-)	Total protein albumin globulin
	Carbon dioxide	Prothrombin time
	Anion gap[2]	Creatinine phosphokinase (CPK)
Arterial	Blood gases	Lactic dehydrogenase (LDH)
X-ray	Skull	Hydroxybutyric dehydrogenase (HBD)
	Bones	Lactate
	Chest	β-hydroxybutyrate
Electrocardiogram		Acetoacetate

1. Other qualitative or quantitative screening of urine or blood is ordered on the basis of clinical assessment (eg, blood ethanol, benzodiazepines, salicylates), provided that facilities are available.
2. Calculated by physician ($([Na^+] - ([Cl^-] + CO_2))$; if CO_2 content or anion gap is abnormal, arterial blood gases should be evaluated.

usually be considered when studying a patient in alcohol withdrawal. Additional helpful diagnostic tests are also cited. The extent to which these patients can be assessed will depend upon the available laboratory facilities, the severity of the withdrawal, and the presence of associated and unrelated clinical problems.

Treatment

Many patients with mild-to-moderate withdrawal reactions can be treated initially in the emergency room and then safely managed at home. Patients with severe uncontrolled withdrawal reactions or complicating problems require hospitalization. General emergency management includes reassurance in surroundings that are well lighted and quiet, monitoring of vital signs as frequently as clinically indicated (eg, cardiac monitoring if there are arrhythmias), hydration, correction of electrolyte abnormalities, and administration of thiamine, 100 mg parenterally.

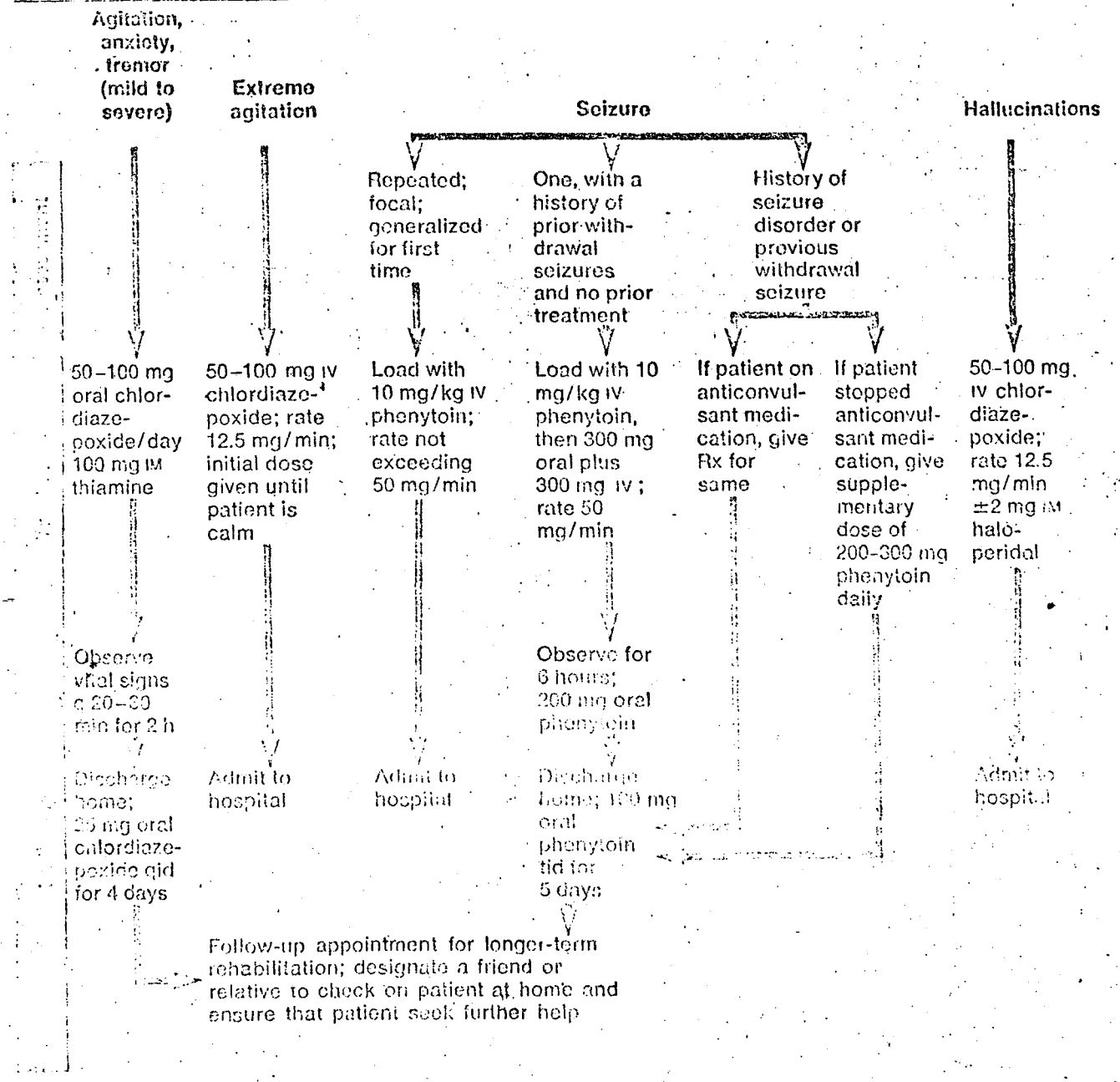
Pharmacotherapeutic objectives

Drug therapy for alcohol-withdrawal reactions is intended to relieve symptoms, prevent or treat more serious complications (eg, seizures, arrhythmias), and prepare the patient for long-term rehabilitation without introducing new drug-dependence problems or therapy-related toxicity.

Various drugs are more effective than placebo for accomplishing these objectives. However, the benzodiazepines have replaced most of the older drugs because of their wide margin of safety. Chlordiazepoxide (Libritabs, Menrium) is the most frequently studied benzodiazepine (although there is no evidence that any one of the benzodiazepines is therapeutically superior to any other). Chlordiazepoxide effectively prevents the reactions from becoming more severe by decreasing anxiety, restlessness, tremor, and the frequency of seizures.

Benzodiazepines are superior to phenothiazines in preventing seizures during withdrawal. (Guidelines for managing seizures are given in Table 3.) There is no direct evidence that the potent antihallucinatory activity of major tranquilizers in schizophrenia has such a specific effect in alcohol withdrawal or on alcoholic halluci-

Table 3: Guidelines for the emergency management of alcohol withdrawal (complete history, physical, laboratory assessment)



nations. Phenothiazines lower the seizure threshold and cause neuroendocrine, dermatologic, and hematologic side effects. Butyrophenones (eg, haloperidol [Haldol]) cause less sedation or hypotension than chlorpromazine and can be reasonably tried for the control of hallucinations, particularly after the risk of seizures has passed. The clinical efficacy of haloperidol can be quite dramatic. Concurrent use of a benzodiazepine will decrease the risk of haloperidol-induced seizures. Acute dystonic reactions, such as oculogyric crisis, may be treated with benztropine mesylate (Cogentin), 2 mg intravenously, followed by 1–2 mg bid orally or parenterally. All patients with hallucinations should be admitted to the hospital.

In general, indications for hospitalization of patients in withdrawal include:

- The presence of a medical or surgical condition requiring treatment (hepatic decompensation, infection, dehydration, mal-

nutrition, cardiovascular collapse, cardiac arrhythmias, trauma)

- Hallucinations, tachycardia > 100 beats/minute, severe tremor, extreme agitation, or a history of severe withdrawal symptoms
- Fever > 38.5 C
- Wernicke's encephalopathy (confusion, ataxia, nystagmus, and ophthalmoplegia)
- Confusion or delirium
- Seizures: Generalized seizure occurring for the first time in the withdrawal state, focal seizures, status epilepticus, seizures in patients withdrawing from a combination of alcohol and other drugs
- Recent history of head injury with loss of consciousness
- Social isolation

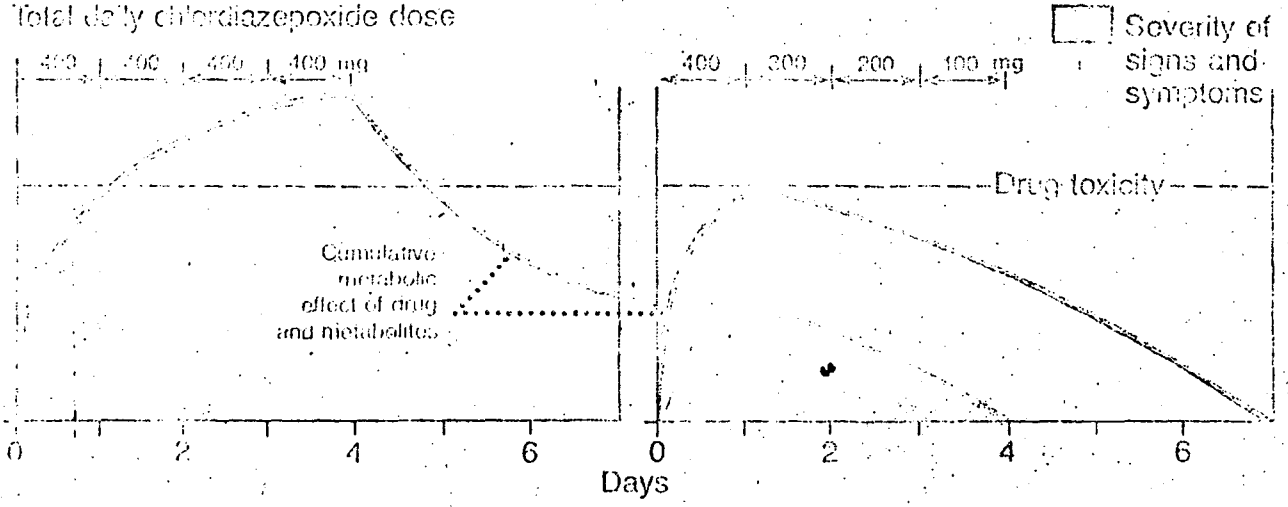
Patients in status epilepticus should be treated initially with 5–10 mg diazepam (Valium) IV as needed, at a rate of 2.5 mg/minute, until seizures are controlled. Equipment for maintenance of an airway and for mechanical support of ventilation must be immediately available. Subsequent doses of 5–10 mg every 20–30 minutes IV as needed, may be given if seizures recur. Appropriate maintenance therapy with other agents should be instituted promptly. Seizures require treatment if they are repeated, continuous, or life threatening. However, there is uncertainty about the therapeutic and prophylactic value of phenytoin in alcohol-withdrawal seizures. Phenytoin should be given orally or intravenously, since it is poorly absorbed from intramuscular injection sites.

Intravenous phenytoin is infused directly. The loading dose is 10 mg/kg, and the oral maintenance dosages are 100 mg tid (Table 3). Phenytoin need not be continued past the withdrawal period except in patients with a preexisting seizure disorder. Patients withdrawing from a combination of alcohol and other drugs, particularly barbiturates and nonbarbiturate hypnotics, should also be hospitalized, since withdrawal seizures from more than one drug can be more serious and difficult to manage elsewhere.

Drug accumulation

Since chlordiazepoxide and diazepam are both long-acting drugs with pharmacologically active metabolites, repeated daily dosages allow either the drug and/or its metabolite to accumulate, and desired therapeutic (or unwanted toxic) effects may not appear until several days of continuous therapy (Fig. 3). Some drowsiness may be of therapeutic benefit, but if dos-

Figure 3: Effect of chlordiazepoxide on clinical course of withdrawal reaction



Left panel indicates the slow cumulative pharmacologic effect of chlordiazepoxide and its active metabolite, desmethylchlordiazepoxide, during repeated daily administration of the same dose. Maximum sedative effects may only be seen after the withdrawal period.

Right panel shows chlordiazepoxide dose to avoid excessive sedation.

ages are not titrated against the clinical state of the individual patient, excessive drowsiness, lethargy, ataxia, diplopia, confusion, respiratory depression, and increased risk of aspiration may follow. To circumvent the consequences of drug cumulation, doses should usually be reduced progressively (Figure 3, right panel). On the first day of treatment, large doses of chlordiazepoxide in the range of 100–400 mg should be given. (Occasionally, doses as high as 1600 mg may be required; this situation is usually associated with delayed treatment.) Thereafter, smaller doses, approximately 25% less than the initial dose, are given daily if required. There

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cannot be a "standard" or "routine" dosage schedule because of the variability in the severity of withdrawal symptoms, the metabolic fate of the drugs, and the presence of other diseases.

Chlordiazepoxide and diazepam are absorbed slowly and incompletely from intramuscular injection sites. When a rapid and predictable clinical effect is required, the oral or intravenous route is preferred. Smaller doses should be given to patients with severe liver disease and/or low serum albumin, since the concentrations of free active chlordiazepoxide and diazepam will be higher, and diazepam is metabolized more slowly in cirrhosis.

In conclusion

Considerable clinical skill and attention are required for the management of alcohol withdrawal. Optimal management of the alcohol-abusing patient includes an adequate opportunity for long-term rehabilitation. ☐

References

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