Alcoholic
Hemodialysis
Wow Withdrawl

Rapid detoxification of the acute alcoholic with hemodialysis

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Hemodialysis has gained widespread acceptance in the treatment of intoxications by a variety of poisons and drugs.[4] In experimental animals hemodialysis has been shown to be a rapid and effective method for reducing plasma ethanol concentrations.[3] Although amelioration of central nervous system depression should attend the reduction of plasma ethanol concentrations the effect upon symptoms of central nervous system stimulation presumably caused by intermediate breakdown products of ethanol has been unexplored. It was thought that hemodialysis of acutely intoxicated chronic alcoholics might be of theoretical as well as practical value.

MATERIAL AND METHODS

Six acutely intoxicated chronic alcoholic patients have been treated with hemodialysis using a conventional recirculating single-pass dialysis apparatus. For purposes of the study a chronic alcoholic was defined as a patient who consumed more than one pint ethanol equivalent per day for 10 consecutive days during the immediate preceding 2 week period, or one whose alcohol ingestion has resulted in social disruption manifest by unemployment, separation or divorce, or one in whom ethanol consumption has produced blackouts, delirium tremens, pancreatitis, or cirrhosis. Patients were not accepted in the study if they had a history of convulsions, evidence of severe liver disease, acute pancreatitis, intercurrent infection, or if they or their family could not provide informed consent for the procedure.

Each patient was interviewed by a psychiatrist before and within 4 hours of dialysis. Objective measurable personality evaluation was achieved with a standard psychiatric evaluation form (Fig. 1). The Brief Psychiatric Rating Scale (BPRS) is an eighteen-item scale which quantifies inpatient symptoms and signs on seven points in ordered categories.[3] This instrument has been used to measure patient change and was intended to provide a rapid assessment technique using a structured 18 minute interview. It has been employed to evaluate the therapeutic efficacy of different treatment modalities. The scale has been widely used with different samples, raters, methods of analysis, and cultural and language differences. Each question is measured on a 1 to 7 scale. A total BPRS score of eighteen would indicate the absence of all signs and symptoms measured by this scale.

Serum alcohol was measured before, during, and at the end of hemodialysis using the technique of Lundquist.[1]

RESULTS

Six patients were admitted for dialysis during alcoholic episodes; 3 were acutely intoxicated and 3 who appeared clinically

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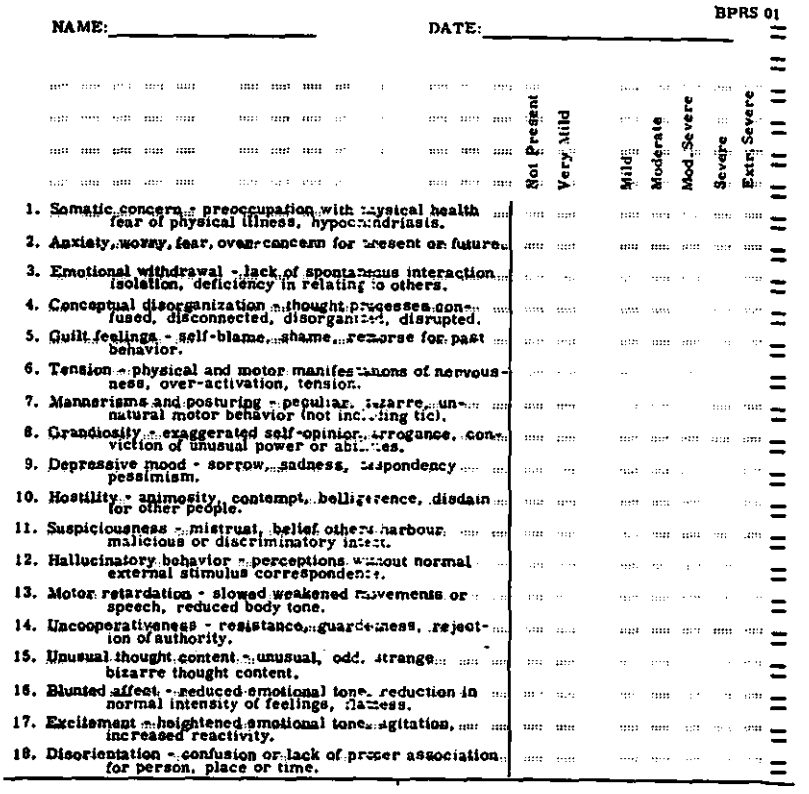

Fig. 1. The Brief Psychiatric Rating Scale used for objective evaluation of emotional symptoms.

Table I. *Brief psychiatric rating scale (BPRS)—total scores*

Patient	*Predialysis*	*Postdialysis*
G. D.	31	23
C. F.	74	34
P. K.	64	44
E. J.	68	30
J. R.	60	43
B. W.	60	46

intoxicated had actually stopped drinking at least 24 hours prior to hospitalization.

CASE REPORTS

The patient (G. D.) is a 35-year-old white male who was admitted for acute alcoholic intoxication, having been drinking heavily and steadily for 13 days. He had a 13 year history of excessive alcohol intake, was twice admitted to state hospitals during the past year for alcoholism, and had multiple arrests for drunkenness (Table II). He was mildly disoriented to time, but not to place or person; he was mildly depressed; there were no hallucinations or delusions. His judgment was markedly impaired. He was nauseated, dizzy, and had mild upper abdominal pain, but no tenderness. His BPRS scores are listed in Table I. His blood alcohol level was 216 mg. percent. After 4 hours of dialysis he was alert, cooperative, and oriented. His blood alcohol level was 102 mg. percent; dialysis was discontinued (Fig. 2). The patient ate breakfast without nausea or vomiting. He was readmitted to the hospital 3 weeks later for elective herniorrhaphy.

The patient (P. K.) is a 39-year-old white male with a 10 year history of severe ethanol intake, 2 weeks of drinking two pints or more of wine per day. He had two previous mental hospital admissions, 9 arrests for alcoholism, several accompanied by episodes of delirium tremens (Table II).

He was markedly disoriented, delusional, hallucinating severely, anxious, agitated, severely depressed. He was nauseated and had been vomiting for 2 days. There was no abdominal tenderness. His BPRS was 64 and blood alcohol 146 mg. percent. After 6 hours of hemodialysis, serum alcohol

Table II. *Summary of alcohol history*

Patient	*Type of alcohol (major)*	*Length of alcoholism problem (years)*	*Hospitalization for alcoholism*		*Arrests for alcoholism*	*Type of drinker*
			Mental	*General*		
G. D.	Wine	13	2	4	9	Continuous
G. F.	Wine	8	1	2	20	Binge
P. K.	Wine	10	2	4	9	Continuous
E. J.	Wine	10	5	10	12	Binge
J. R.	Whiskey	9	1	4	1	Binge
B. W.	Whiskey	14	5	2	5	Continuous

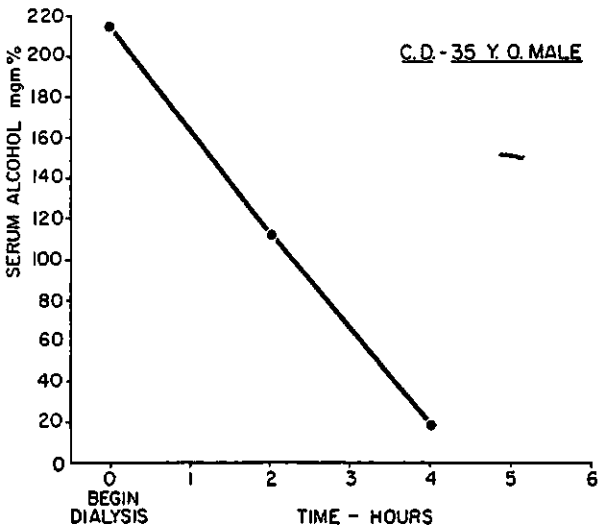

Fig. 2

was zero (Fig. 3), patient was oriented, no longer hallucinating or having delusions of persecution. He was markedly less anxious and depressed, although he had multiple psychosomatic complaints. He ate breakfast without nausea and remained in the hospital on the Plastic Surgical Service for facial reconstruction.

The patient (C. F.) is a 38-year-old white male with an 8 year history of chronic alcoholism marked by 20 arrests and one admission to a state hospital for alcoholism (Table II). These were punctuated by several previous episodes of delirium tremens. The patient was admitted after 10 days of drinking more than two pints of wine per day. He was markedly disoriented, had delusions of persecution and visual hallucinations; judgment was impaired. He was extremely anxious, depressed, and markedly agitated. He was nauseated, had been vomiting. His speech was slurred. His BPRS scores are listed in Table I. Blood alcohol level was 166 mg. percent, and after 6 hours of dialysis was reduced to 24 mg. percent. (Fig. 4). At the end of dialysis he was alert and oriented. The anxiety, depression, and agitation were markedly diminished. The delusions and hallucinations had disappeared completely. He ate breakfast without nausea.

The patient (E. J.) is a 67-year-old white male with a 10 year history of excessive ethanol intake who had consumed more than two pints per day of wine for the immediate preceding 21 days. He had 12 previous arrests for alcoholism, five mental hospital admissions for drinking and reported having had delirium tremens on most of his previous admissions and arrests (Table II). He was disoriented to time, place, and person, had delusions and visual hallucinations, was anxious, depressed, tense, and agitated. His judgment was markedly impaired. He was nauseated and reported having vomited several times during the previous three days. His BPRS scores are listed in Table I. His blood alcohol level was zero before dialysis. After dialysis he was oriented, no longer having delusions or hallucinations, and was no longer agitated.

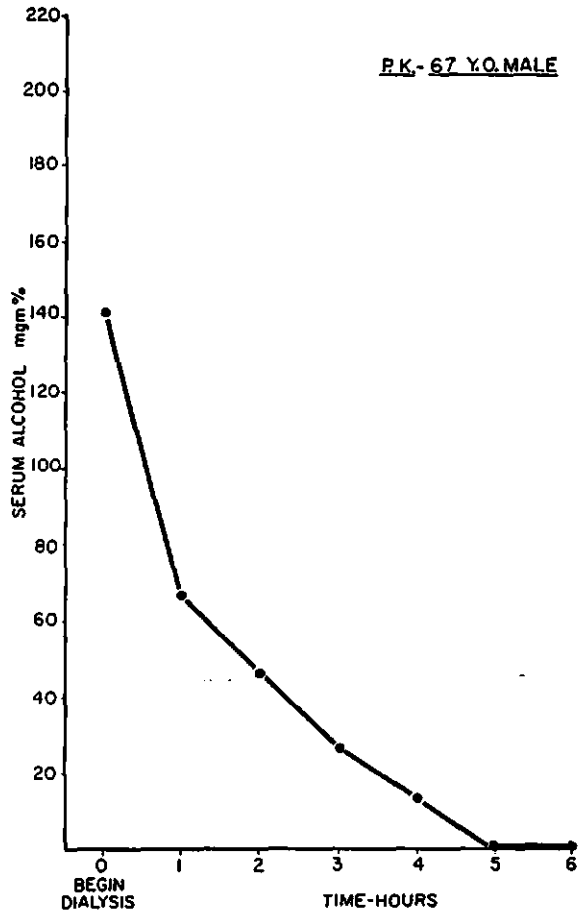

Fig. 3

Mild anxiety and depression persisted. He ate breakfast without nausea.

Clinical improvement in this patient in spite of the negligible blood ethanol concentration led us to believe that perhaps intermediate metabolites of ethanol were responsible for the neuromuscular disorders seen during spontaneous detoxification. We, therefore, entertained the hemodialysis of alcoholics who were clinically intoxicated but who had no measurable serum ethanol.

The patient (J. R.) is a 44-year-old white male, with a 9 year history of chronic alcoholism, admitted after 2 weeks of steady ingestion of at least four-fifths quart per day of blended whiskey. Although he had stopped drinking 48 hours before admission, he came to the hospital because of active hallucinations in the previous 24 hours. He had one previous mental hospital admission and one previous arrest for drinking, four previous general hospital admissions for drinking and two known episodes of delirium tremens (Table II). The patient was disoriented, actively hallucinating, and having delusions of persecution. He was anxious, but not depressed. He was agitated and tense. His judgment was very badly impaired. His BPRS scores are recorded in Table I. His blood alcohol level prior to dialysis was zero. After 6 hours of dialysis the patient was still having hallucinations and delusions and was mildly disoriented. However, his agitation was decreased and he was less anxious. He remained in this state for 3 days after which his mental status changed. He became oriented, the delusions and hallucinations ceased, and he became less agitated.

The patient (B. W.) is a 43-year-old Negro,

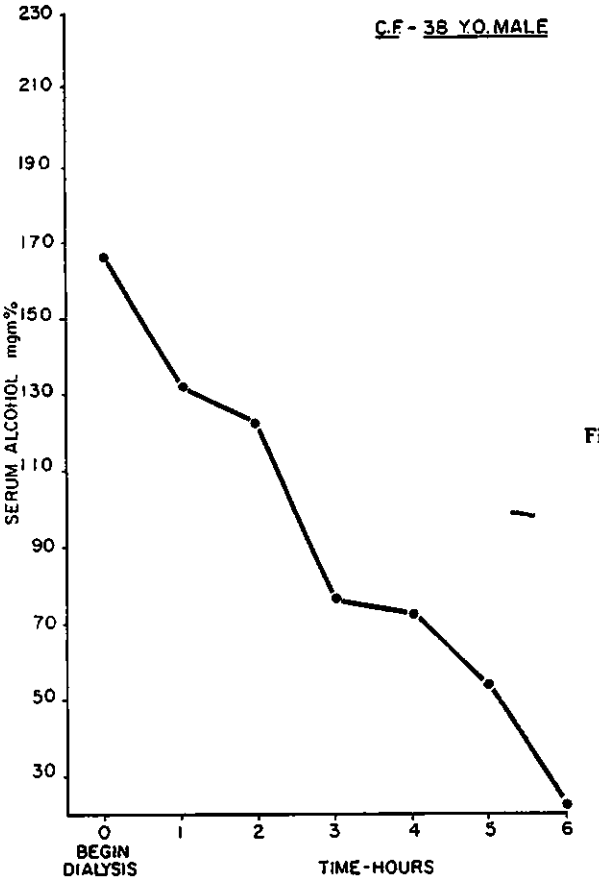

Fig. 4

with a 14 year history of chronic alcoholism, brought to the hospital by the Police Department. He had been arrested the previous day on the charge of disorderly conduct and after 24 hours was remanded to the hospital by a judge in keeping with recent State legislative action indicating that alcoholics were to be treated in hospitals, not in prisons. The patient had five previous admissions to mental institutions for alcoholism, and five previous arrests for intoxication (Table II). He was disoriented, hallucinating, delusional, anxious, uncooperative, and agitated. His BPRS scores are listed in Table I. His blood alcohol level was zero. After 6 hours of dialysis he was still delusional, hallucinating, and had evidence of anxiety and disorientation.

DISCUSSION

Recent legislative action in several states has removed the acutely intoxicated alcoholic from the ranks of legal offenders and declared him a sick person. Accordingly, the patients are brought to hospitals for medical care rather than to prisons for incarceration. Conventional in-hospital techniques for treating such patients permit spontaneous detoxification under sedation with psychiatric assistance and electrolyte management. The usual hospital stay for each patient in the general hospital is 5 to 7 days and in the alcohol study wards 14 to 16 days. Nausea, vomiting, and tremors are frequent and in patients with cirrhosis, prolonged episodes of continuous drinking or a history of previous delirium tremens the incidence of acute delirium tremens is high. Mortality from delirium tremens in such patients is variously stated to be between 15 and 30 percent.[5]

Hemodialysis of the acutely intoxicated chronic alcoholic was introduced with a

view toward reduction of the necessary hospital stay for treatment of acute alcoholism, prevention of neuromuscular disorders in the alcoholic, and more efficient handling of the chronic alcoholic during an acute episode. The effective use of hemodialysis in acute poisonings is well established and is based on the assumptions that the poison molecule can diffuse through the cellophane dialysis membrane and has a reasonable removal rate; that the poison is sufficiently well distributed in accessible body fluid compartments; that there is a relationship between toxicity and blood concentration and duration of exposure to the circulating poison; and the amount of poison dialyzed constitutes a significant addition to the normal body mechanisms for dealing with the particular poison under consideration. Effective treatment of patients poisoned by voluntary or involuntary exposure to excessive salicylate ingestion, acute barbiturate poisoning, glutethimide (Doriden), bromium, diphenylhydantoin (Dilantin), and others have been well established.[2] It is also apparent that dialysis therapy for a number of poisons which might fulfill the theoretical criteria listed above has not actually been given extensive experimental clinical trial. Such a list would include ethyl alcohol, methyl alcohol, isoniazid, and certain long-acting antibiotics in sensitivity states.

The first 3 patients showed evidence of recent ethanol intake which was reflected in high blood alcohol levels. They all had a history of chronic alcoholism and previous withdrawal symptoms. Hemodialysis without any medication resulted in marked relief of physical and mental symptoms without delirium tremens. All patients had previous episodes of delirium tremens, and were potentially good candidates for this complication. In Patient E. J. who had active acute alcoholic hallucinosis, tremor, and nausea but whose serum ethanol level was zero, the symptoms ceased during dialysis. This led us to believe that perhaps active delirium tremens was related causally to serum concentration of an intermediate metabolite of ethanol.

Patient J. R. had abstained for 48 hours prior to admission and was in severe alcoholic hallucinosis when he was dialyzed. The procedure did not markedly improve his psychological status which in fact continued for several days before spontaneously clearing.

The last subject (B. W.) who was a chronic alcoholic had abstained during the 24 hours prior to admission and had no measurable level of alcohol in his blood. It became apparent from his clinical status and history that the patient is a chronic paranoid schizophrenic whose symptoms were merely exacerbated by ethanol.

From the initial experience with three patients, dialysis of the acutely intoxicated, agitated, chronic alcoholic was found to markedly improve their physical and psychological status. Hallucinations, delusions, and anxiety cease and the patient is able to eat without nausea and vomiting and be discharged from the hospital within 24 hours of dialysis.

All postdialysis BPRS scores were lower than at the initial interview. In Patients J. R. and B. W. the psychotic symptoms (measured in questions 4, 12, 14, and 18) remained prominent. In Patient C. F. the psychotic symptoms were relieved, but persistence of prominent psychosomatic symptoms (questions 1, 5, 14, and 16) was responsible for higher scores than anticipated.

The clinical impression of improvement in these patients permitted extension of the study to include alcoholics whose withdrawal symptoms were far advanced and had already metabolized the ingested alcohol. However, when psychological symptoms persist after ethanol has been metabolized, dialysis does not appear to be indicated. Hemodialysis is judged to be a suitable procedure for rapid detoxification of an acute episode of alcoholic intoxication in a chronic alcoholic.

SUMMARY

Six acutely intoxicated chronic alcoholic patients have been treated with hemodialysis. Each subject has undergone thorough psychiatric evaluation before and after dialysis.

Plasma ethanol levels were obtained repeatedly during dialysis and declined rapidly. Delirium tremens ceased or failed to occur even in subjects who frequently experienced delirium tremens with spontaneous detoxification. Hemodialysis appears to be a practical approach to the problem of severe acute intoxication in the chronic alcoholic.

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DISCUSSION

Dr. Ward O. Griffen, Jr. (Lexington, Ky.). I wonder if you have considered performing arteriovenous shunts in chronic alcoholics to facilitate this detoxification. One would need only to put a needle in, dry them out, and send them home.

Dr. Marshall J. Orloff (San Diego, Calif.). Dr. Walder's paper recalls an old idea which is firmly ingrained in the minds of the medical profession; namely, that delirium tremens is due to alcohol withdrawal.

Perhaps such is not the case, since you rapidly withdraw these patients from alcohol and in the process relieve the delirium tremens.

This has been a controversial concept, but I think the evidence indicates that delirium tremens is not due to alcohol withdrawal.

Dr. Nicholas A. Halasz (San Diego, Calif.). In recent experience with Doriden intoxication investigators have found that with a lipid phase dialysate considerably more rapid extraction is obtained because of the partitioning coefficient of Doriden and some barbiturates between fat versus water.

Dr. Walder, have you studied clearances through the dialysis coil? Is alcohol totally removed with an aqueous dialysate medium? If not, with sesame oil or another lipid phase dialysate one might achieve complete dialysis more rapidly.

Dr. William S. Blakemore (Philadelphia, Pa.). We did work on peritoneal dialysis for alcoholism in the Navy in 1947. Dialysis was equally effective against methanol.

How often have you found methanol in these patients?

Might not dialysis be applicable in urgent surgical problems when acute alcoholism increases operative risk? The work of Watts Webb and others makes us acutely aware of the toxic effects of high alcoholic levels on the cardiovascular system.

Dr. Robert J. White (Cleveland, Ohio). A difficult problem for neurosurgeons is the possibility that an alcoholic even though not recently injured may still have a chronic subdural hematoma.

I am delighted to hear psychiatrists are interviewing these patients, but have the patients been carefully examined neurologically? Such simple things as echoencephalography or brain scans decrease the risk of missing a subdural hematoma which might be a major problem since the dialysis patients must be anticoagulated.

Dr. Kaplan (Chicago, Ill.). Have the authors investigated any of the intermediates of alcohol? Perhaps the alcohol level itself is not the key consideration?

Dr. Walder (Closing). I would like to thank the discussants for their questions and comments.

Dr. Griffen, we have thought of preparing arteriovenous anastomoses for chronic dialysis of alcoholic patients. The biggest problem has been acquiring informed consent, and while the patient is sober he feels he will not return, although most do.

In view of possible head injury all patients have complete physical examinations by us and by the psychiatrist. One can use regional anticoagulation if dialysis seems urgent in intoxicated patients.

All alcohol is removed in the aqueous phase. We are familiar with the work with lipid dialysis for Doriden poisoning. I don't know whether this is applicable for alcohol.

As to what causes delirium *tremens*, there is some very preliminary work implicating acetaldehyde. Alcohol is oxidized to acetaldehyde requiring an enzyme, alcohol dehydrogenase, and DPN. This reaction tends greatly to the left and goes to the right to oxidation only in an alkaline pH.

is the widely preferred route. Percutaneous absorption is said to be negligible, but severe intoxications have been reported in young children from the practice of tucking alcohol-soaked cloths under rubber pants (Gimenez *et al.*, 1968).

Ethanol is destributed throughout the body water, and over 90% of a dose is metabolized by oxidation to acetaldehyde, to acetate, and to carbon dioxide and water, in that order. The first two steps in the sequence are mediated by alcohol and acetaldehyde dehydrogenases, respectively. Both enzymes require oxidized nicotinamide adenine dinucleotide (NAD) as a cofactor, and both enzymes are found in the cytosol. The rate of metabolic degradation is unexpectedly constant, and within wide limits it is independent of the amount consumed; an average adult is said to be able to oxidize each hour the equivalent of ⅔ oz. of 100-proof whiskey (*e.g.*, Forney and Hughes, 1963). Most authorities no longer hold that this rate can be materially increased by the administration of hormones, glucose, cofactors, or vitamins (Loomis, 1950; Jacobsen, 1952). Less than 10% of the absorbed alcohol is excreted, chiefly in urine, measurably in expired air, and detectably in sweat (Haggard and Greenberg, 1934a and b). Excretion cannot be accelerated to a beneficial degree by diuretic drugs, by hyperventilation, or by the induction of sweating.

An exceptional carbohydrate that can increase ethanol metabolism to a small but significant degree is fructose (Clark and Hulpieu, 1958). Fructose metabolism results in the oxidation of $NADH_2$ to NAD. The supply of the latter can be rate-limiting for alcohol metabolism. In a study of patients admitted in acute alcoholism, fructose accelerated the rate of fall of blood alcohol concentration by 25% (Brown *et al.*, 1972). Other studies in volunteers indicate that the oxidation of alcohol can be increased by 40 to 50% (Lowenstein *et al.*, 1970; Lundquist and Wolthers, 1958).

Hemodialysis has been employed in acute ethyl alcohol intoxications. In one case it was said to have decreased the plasma half-life over natural processes of elimination by a factor of 11 (Jørgensen and Wieth, 1963). Marc-Aurele and Schreiner (1960) have estimated that the dialysance of ethyl alcohol in a commercial hemodialysis unit tested on dogs is about 200 ml./min. Although this represents a very favorable value of dialysance in comparison with other drugs, at a blood alcohol concentration of 3 mg./ml., hemodialysis would be predicted to remove alcohol somewhat more slowly than oxidative metabolism does, so that the combined elimination rate would be less than doubled. This expectation was substantiated in one child subjected to peritoneal dialysis (Dickerman *et al.*, 1968). Thus hemodialysis may be justifiable with potentially lethal blood alcohol concentrations, but its use should certainly be reserved for those life-threatening cases. Curiously, six patients detoxified acutely by hemodialysis did not develop delirium tremens, even though some of them had previously experienced that syndrome on spontaneous detoxication (Walder *et al.*, 1969).

Severe hypoglycemia in certain individuals following a heavy drinking bout is now well established (Fredericks and Lazor, 1963; Gumpel and Kaufman, 1964; Steer *et al.*, 1969). Although originally reported for denatured alcohols ("smoke") or Solox® (Brown and Harvey, 1941; Tucker and Porter, 1942), alcohol and not the other ingredients is recognized as the major precipitant of the reaction. Because hypoglycemia and convulsions have occurred in children after ingestion of both an alcoholic beverage and cologne (Cummins, 1961; Neame and Joubert, 1961), chronic alcohol intake is not necessary for this reaction.

Hypoglycemic reactions, however, appear to be more frequent with fasting, malnutrition or marginal endogenous carbohydrate balance (Freinkel *et al.*, 1965). Hypoglycemia may occur within 12 to 16 hours of drinking and at blood alcohol levels associated with mild intoxication. Thus, an inebriated patient may lapse into a fatal hypoglycemic coma. This effect is apparently due to an inhibition of gluconeogenesis because of the activity of alcohol dehydrogenase and not a direct effect of alcohol (Freinkel *et al.*, 1965). Perhaps alcohol-hypoglycemia is more common in infants and children than in adults. This could account for the clinical impressions that children are more susceptible to alcohol than adults and that the syndrome differs somewhat in character in that the coma is sometimes punctuated by severe convulsions (Turai *et al.*, 1961; Verron, 1969).

The subject of the interaction of alcohol with other drugs has received an enormous amount of attention, as attested to in a separate monograph (Forney and Hughes, 1968). Certain general principles are beginning to emerge. For example, although the "knock out" effect is now regarded as myth, there can be little doubt that the depressant effects of alcohol are potentiated by chloral hydrate. *In vivo* chloral hydrate is reduced to the more potent central depressant trichloroethanol. Trichloroethanol is a competi-