TREATMENT ALCOHOLIC KETOACIDOSIS

Extracellular fluid deficits almost always accompany AKA and should be repleted by IV administration of saline and glucose (5% dextrose in 0.9% NaCl). Hypophosphatemia, hypokalemia, and hypomagnesemia may coexist and should be corrected. Hypophosphatemia usually emerges 12–24 h after admission, may be exacerbated by glucose infusion, and, if severe, may induce rhabdomyolysis or even respiratory arrest. Upper gastrointestinal hemorrhage, pancreatitis, and pneumonia may accompany this disorder.

Drug- and Toxin-Induced Acidosis • ***SALICYLATES*** (See also Chap. 472e)
Salicylate intoxication in adults usually causes respiratory alkalosis or a mixture of high-AG metabolic acidosis and respiratory alkalosis. Only a portion of the AG is due to salicylates. Lactic acid production is also often increased.

TREATMENT SALICYLATE-INDUCED ACIDOSIS

Vigorous gastric lavage with isotonic saline (not $NaHCO_3$) should be initiated immediately, followed by administration of activated charcoal per nasogastric tube. In the acidotic patient, to facilitate removal of salicylate, IV $NaHCO_3$ is administered in amounts adequate to alkalinize the urine and to maintain urine output (urine pH >7.5). While this form of therapy is straightforward in acidotic patients, a coexisting respiratory alkalosis may make this approach hazardous. Alkalemic patients should not receive $NaHCO_3$. Acetazolamide may be administered in the face of alkalemia, when an alkaline diuresis cannot be achieved, or to ameliorate volume overload associated with $NaHCO_3$ administration, but this drug can cause systemic metabolic acidosis if HCO_3^- is not replaced. Hypokalemia should be anticipated with an alkaline diuresis and should be treated promptly and aggressively. Glucose-containing fluids should be administered because of the danger of hypoglycemia. Excessive insensible fluid losses may cause severe volume depletion and hypernatremia. If renal failure prevents rapid clearance of salicylate, hemodialysis can be performed against a bicarbonate dialysate.

ALCOHOLS Under most physiologic conditions, sodium, urea, and glucose generate the osmotic pressure of blood. Plasma osmolality is calculated according to the following expression: $P_{osm} = 2Na^+ + Glu + BUN$ (all in mmol/L), or, using conventional laboratory values in which glucose and BUN are expressed in milligrams per deciliter: $P_{osm} = 2Na^+ + Glu/18 + BUN/2.8$. The calculated and determined osmolality should agree within 10–15 mmol/kg H_2O. When the measured osmolality exceeds the calculated osmolality by >10–15 mmol/kg H_2O, one of two circumstances prevails. Either the serum sodium is spuriously low, as with hyperlipidemia or hyperproteinemia (pseudohyponatremia), or osmolytes other than sodium salts, glucose, or urea have accumulated in plasma. Examples of such osmolytes include mannitol, radiocontrast media, ethanol, isopropyl alcohol, ethylene glycol, propylene glycol, methanol, and acetone. In this situation, the difference between the calculated osmolality and the measured osmolality (*osmolar gap*) is proportional to the concentration of the unmeasured solute. With an appropriate clinical history and index of suspicion, identification of an osmolar gap is helpful in identifying the presence of poison-associated AG acidosis. Three alcohols may cause fatal intoxications: ethylene glycol, methanol, and isopropyl alcohol. All cause an elevated osmolal gap, but only the first two cause a high-AG acidosis.

ETHYLENE GLYCOL (See also Chap. 472e) Ingestion of ethylene glycol (commonly used in antifreeze) leads to a metabolic acidosis and severe damage to the CNS, heart, lungs, and kidneys. The increased AG and osmolar gap are attributable to ethylene glycol and its metabolites, oxalic acid, glycolic acid, and other organic acids. Lactic acid production increases secondary to inhibition of the tricarboxylic acid cycle and altered intracellular redox state. Diagnosis is facilitated by recognizing oxalate crystals in the urine, the presence of an osmolar gap in serum, and a high-AG acidosis. Although use of a Wood's lamp to visualize the fluorescent additive to commercial antifreeze in the urine of patients with ethylene glycol ingestion, this is rarely reproducible. The combination of a high AG and high osmolar gap in a patient suspected of ethylene glycol ingestion should be taken as evidence of ethylene glycol toxicity. Treatment should not be delayed while awaiting measurement of ethylene glycol levels in this setting.

TREATMENT ETHYLENE GLYCOL-INDUCED ACIDOSIS

This includes the prompt institution of a saline or osmotic diuresis, thiamine and pyridoxine supplements, fomepizole, and usually, hemodialysis. The IV administration of the alcohol dehydrogenase inhibitor fomepizole (4-methylpyrazole; 15 mg/kg as a loading dose) is the agent of choice and offers the advantages of a predictable decline in ethylene glycol levels without excessive obtundation as seen during ethyl alcohol infusion. If used, ethanol IV should be infused to achieve a blood level of 22 mmol/L (100 mg/dL). Both fomepizole and ethanol reduce toxicity because they compete with ethylene glycol for metabolism by alcohol dehydrogenase. Hemodialysis is indicated when the arterial pH is <7.3 or the osmolar gap exceeds 20 mOsm/kg.

METHANOL (See also Chap. 472e) The ingestion of methanol (wood alcohol) causes metabolic acidosis, and its metabolites formaldehyde and formic acid cause severe optic nerve and CNS damage. Lactic acid, ketoacids, and other unidentified organic acids may contribute to the acidosis. Due to its low molecular mass (32 Da), an osmolar gap is usually present.

TREATMENT METHANOL-INDUCED ACIDOSIS

This is similar to that for ethylene glycol intoxication, including general supportive measures, fomepizole, and hemodialysis (as above).

PROPYLENE GLYCOL Propylene glycol is the vehicle used in IV administration of diazepam, lorazepam, phenobarbital, nitroglycerine, etomidate, enoximone, and phenytoin. Propylene glycol is generally safe for limited use in these IV preparations, but toxicity has been reported, most often in the setting of the intensive care unit in patients receiving frequent or continuous therapy. This form of high-gap acidosis should be considered in patients with unexplained high-gap acidosis, hyperosmolality, and clinical deterioration. Propylene glycol, like ethylene glycol and methanol, is metabolized by alcohol dehydrogenase. With intoxication by propylene glycol, the first response is to stop the offending infusion. Additionally, fomepizole should also be administered in acidotic patients.

ISOPROPYL ALCOHOL Ingested isopropanol is absorbed rapidly and may be fatal when as little as 150 mL of rubbing alcohol, solvent, or deicer is consumed. A plasma level >400 mg/dL is life-threatening. Isopropyl alcohol is metabolized by alcohol dehydrogenase to acetone. The characteristic features differ from ethylene glycol and methanol in that the parent compound, not the metabolites, causes toxicity, and an AG acidosis is *not* present because acetone is rapidly excreted. Both isopropyl alcohol and acetone increase the osmolal gap, and hypoglycemia is common. Alternative diagnoses should be considered if the patient does not improve significantly within a few hours. Patients with hemodynamic instability with plasma levels above 400 mg/dL should be considered for hemodialysis.

TREATMENT ISOPROPYL ALCOHOL TOXICITY

Isopropanol alcohol toxicity is treated by watchful waiting and supportive therapy, IV fluids, pressors, ventilatory support if needed, and occasionally hemodialysis for prolonged coma, hemodynamic instability, or levels >400 mg/dL.