

# The Toxic Alcohols

Historical Treatment and Use of  
**Antizol<sup>®</sup>** for Methanol and  
Ethylene Glycol Poisoning

# Ethylene Glycol

- ◆ Sweet, odorless, often brightly colored liquid
- ◆ Common uses include:
  - Automotive antifreeze and coolant
  - Hydraulic brake fluid
  - Glass cleaner
- ◆ Lethal dose 1.4-1.6 ml/kg

# Ethylene Glycol Poisoning: Incidence

- ◆ In the United States, 1999:
  - 6,077 exposures
  - 254 near-fatalities
  - 40 fatalities

Watson WA, *et al.*, 2002: Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *American Journal of Emergency Medicine* 2003; 21(5):353-421.

# Ethylene Glycol Poisoning: Incidence

- ◆ Ingestions are nearly always a medical emergency
  - Intentional as an alcohol substitute or suicide attempt (adults)
  - Unintentional due to accidental ingestion (children)

# Ethylene Glycol Poisoning

- ◆ Ethylene glycol itself is not very toxic
- ◆ Symptoms of serious poisoning are due to the accumulation of toxic quantities of metabolites (glycolic and oxalic acids)

# Ethylene Glycol: Metabolism

Ethylene Glycol



(Alcohol Dehydrogenase)

Glycoaldehyde



(Aldehyde Dehydrogenase)

Glycolic Acid



Glyoxylic Acid



Oxalic Acid

# Ethylene Glycol Poisoning: Clinical Course

- ◆ Stage 1 (30 minutes-12 hours)
  - Central Nervous System
- ◆ Stage 2 (12 hours- 24 hours)
  - Cardiopulmonary
- ◆ Stage 3 (24 hours- 3 days)
  - Renal

# Ethylene Glycol Poisoning: Diagnosis Often Difficult

- ◆ Clinical signs and symptoms are nonspecific and may resemble other poisonings or illnesses
- ◆ Patients are frequently unwilling or unable to provide information regarding ingestion
- ◆ Little correlation between blood concentrations of ethylene glycol and severity of poisoning
- ◆ Some patients present asymptomatic
- ◆ Timely ethylene glycol laboratory results are often unavailable

# Ethylene Glycol Poisoning: Treatment Objectives

- ◆ Stabilize the Patient
- ◆ Correct Metabolic Acidosis
- ◆ Prevent further metabolism of ethylene glycol
- ◆ Hemodialysis to enhance elimination of unmetabolized toxin (and metabolites)

# Methanol

- ◆ Clear, flammable liquid
- ◆ Common uses include:
  - Windshield wiper fluid
  - Gas line antifreeze
  - Fuel for small stoves
  - Adulterant in “bootleg” whiskey
- ◆ Lethal dose 1 ml/kg

# Methanol Poisoning Exposures

- ◆ In the United States, 2002:
  - 2,610 exposures
  - 55 near-fatalities
  - 18 fatalities

Watson WA, *et al.*, 2002: Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *American Journal of Emergency Medicine* 2003; 21(5):353-421.

# Methanol Poisoning: Incidence

- ◆ Ingestions are always a medical emergency
  - Intentional as an alcohol substitute or suicide attempt (adults)
  - Unintentional due to accidental ingestion (children)

# Methanol Poisoning

- ◆ Methanol itself is not very toxic
- ◆ Symptoms of serious poisoning are due to the accumulation of toxic quantities of metabolite (formic acid)

# Methanol Metabolism

Methanol



(Alcohol Dehydrogenase)

Formaldehyde



(Aldehyde Dehydrogenase)

Formic Acid

# Methanol Poisoning: Clinical Course

- ◆ Drowsiness, confusion, ataxia
- ◆ Severe anion gap metabolic acidosis
- ◆ Ocular injury, blindness
- ◆ Coma, seizures, hypotension, death

# Methanol Poisoning: Diagnosis Often Difficult

- ◆ Clinical signs and symptoms are specific for other poisonings and illnesses
- ◆ Patients are frequently unwilling or unable to provide information regarding ingestion
- ◆ Some patients present asymptomatic
- ◆ Timely methanol laboratory results may be unavailable

# Methanol Poisoning: Treatment Objectives

- ◆ Stabilize the patient
- ◆ Correct metabolic acidosis
- ◆ Prevent further metabolism of methanol
- ◆ Enhance elimination of unmetabolized toxin (and metabolites)

# Summary: Methanol and Ethylene Glycol Poisoning

- ◆ Metabolism of these compounds via alcohol dehydrogenase is responsible for the clinical effects characteristic of poisoning with these compounds
- ◆ Inhibition of alcohol dehydrogenase will prevent the formation of toxic metabolites

# Historical Treatment of Ethylene Glycol and Methanol Poisoning

- ◆ Ethanol therapy has been the historical treatment
- ◆ Ethanol inhibits the production of the toxic metabolites of ethylene glycol and methanol
- ◆ Effective ethanol therapy is often difficult to accomplish and highly labor-intensive

# Challenges of Ethanol Therapy

- ◆ Is very labor-intensive
- ◆ Requires toxic concentrations of ethanol
  - Appropriate level of ethanol may be difficult to achieve
- ◆ Not FDA-Approved

# Antizol<sup>®</sup> (fomepizole) Injection

- ◆ Antizol<sup>®</sup>, commonly referred to as fomepizole, 4-methylpyrazole, 4-MP
- ◆ Studied as an antidote since late 1960s
- ◆ Indicated as an antidote for confirmed or suspected ethylene glycol or methanol poisoning

# Antizol<sup>®</sup> Treatment Rationale

- ◆ Antizol is a competitive inhibitor of alcohol dehydrogenase
- ◆ Antizol blocks the metabolism of ethylene glycol and methanol to their toxic metabolites
- ◆ Antizol is safe and easy to administer

# Antizol<sup>®</sup> (fomepizole) Injection

- ◆ Antizol is safe
  - Low side-effect profile
  - Can be administered on suspicion while waiting for lab results; stopped if needed
  - For referring institutions, patients can be given a loading dose to stabilize and then transferred
- ◆ Most frequent adverse reactions:
  - Headache (14%), nausea (11%), dizziness, increased drowsiness, and bad taste/metallic taste (6% each)

# Antizol<sup>®</sup> (fomepizole) Injection

- ◆ Antizol should be diluted before use
- ◆ Ethylene glycol serum and urine concentrations as well as the presence of urinary oxalate crystals should be monitored in ethylene glycol poisoning throughout treatment
- ◆ Methanol serum concentrations should be monitored throughout treatment in methanol poisoning
- ◆ Dialysis should be considered in some cases

# Advantages of Antizol®

- ◆ Monitoring of serum Antizol not required
- ◆ Does not cause sedation or hypoglycemia
- ◆ Hemodialysis may be unnecessary in some cases
- ◆ Is FDA-approved

# Antizol<sup>®</sup> Treatment Guidelines

- ◆ Begin Antizol treatment on suspicion of ethylene glycol or methanol poisoning or in presence of serum concentration  $>20$  mg/dL
- ◆ Discontinue therapy when serum concentration is zero or when  $< 20$  mg/dL *and* the patient is asymptomatic with normal pH
- ◆ Consider hemodialysis when serum concentration  $>50$  mg/dL

# Antizol<sup>®</sup> Administration

- ◆ Dilute dose in 100 ml normal saline or D5W, infuse over 30 minutes
- ◆ Dosed on a mg/kg basis
- ◆ Doses Q12H until ethylene glycol or methanol concentration sub toxic
- ◆ During hemodialysis, dose Q4H

# Antizol<sup>®</sup> Formulation

- ◆ Provided as a sterile, preservative-free solution for intravenous use
- ◆ Supplied in packages of four 1.5 ml vials, with 1 gm/ml
- ◆ 3 year shelf life, return goods policy for unopened tray packs
- ◆ Sterile for at least 24 hours, discard diluted solution after that time

# Antizol<sup>®</sup> Injection Additional Information

- ◆ To order Antizol, call 1-800-359-4304
- ◆ For questions of a medical nature, call 1-888-8ORPHAN (1-888-867-7426)