

IN THE NAME OF GOD

ALCOHOL INTOXICATION

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PRIMARY TOXICITY CAN BE DUE TO:

- PARENT COMPOUND (ETHANOL AND ISOPROPANOL)
- TOXIC METABOLITES (ETHYLENE GLYCOL AND METHANOL)

- **ETHANOL AND ISOPROPANOL** ARE THE MOST COMMON ALCOHOLS INGESTED;
 - GI IRRITATION AND INTOXICATION
 - DO NOT IN THEMSELVES PRODUCE A CLINICALLY RELEVANT METABOLIC ACIDOSIS.
- **METHANOL AND ETHYLENE GLYCOL** ARE TOXIC ALCOHOLS BECAUSE THEY CAUSE SERIOUS MULTI- SYSTEM DAMAGE AND METABOLIC ACIDOSIS.

ETHANOL

- INTOXICATION MOST COMMON FROM:
 - INGESTION
 - INHALATION
 - PERCUTANEOUS EXPOSURE
- ETHANOL MAY BE FOUND IN HIGH CONCENTRATIONS IN MANY OTHER COMMON HOUSEHOLD PRODUCTS SUCH AS MOUTHWASH (MAY CONTAIN UP TO 75% ETHANOL BY VOLUME) AND COLOGNES AND PERFUMES (UP TO 40% TO 60%), AS A DILUENT OR SOLVENT FOR MEDICATIONS (CONCENTRATION VARIES WIDELY BETWEEN 0.4% AND 65%).
- SUCH PRODUCTS ARE OFTEN FLAVORED OR BRIGHTLY COLORED AND MAY BE ATTRACTIVE TO CHILDREN.

PATHOPHYSIOLOGY

- ETHANOL IS RAPIDLY ABSORBED AFTER ORAL ADMINISTRATION
- BLOOD LEVELS PEAK ABOUT 30 TO 60 MINUTES AFTER INGESTION.
- THE PRESENCE OF FOOD IN THE STOMACH PROLONGS ABSORPTION AND DELAYS THE PEAK BLOOD LEVEL.
- HIGH CONCENTRATIONS OF ETHANOL IN THE STOMACH MAY CAUSE PYLOROSPASM, DELAYING GASTRIC EMPTY-ING.

- BECAUSE OF THE PHENOMENON OF TOLERANCE, BLOOD ETHANOL LEVELS CORRELATE POORLY WITH DEGREE OF INTOXICATION
- ETHANOL IS PREDOMINANTLY ELIMINATED BY HEPATIC METABOLISM, WITH ABOUT 10% EXCRETED IN THE URINE, EXHALED BREATH, AND SWEAT.

CLINICAL FEATURES

- CLINICAL INEBRIATION, BEHAVIORAL DISINHIBITION MAY INITIALLY APPEAR AS EUPHORIA OR AGITATION AND
- COMBATIVENESS.
- AS MORE SEVERE, SLURRED SPEECH, NYSTAGMUS, ATAXIA, AND DECREASED MOTOR COORDINATION DEVELOP.
- SEVERE INTOXICATION MAY CAUSE RESPIRATORY DEPRESSION AND COMA.
- NAUSEA AND VOMITING OFTEN OCCUR IN CONJUNCTION WITH NEUROLOGIC DEPRESSION

- PERIPHERAL VASODILATION AND FLUSHED, WARM SKIN, ENABLING LOSS TO THE ENVIRONMENT AND PROMOTING HYPOTHERMIA.
- VASODILATION MAY ALSO LEAD TO ORTHOSTATIC HYPOTENSION AND REFLEX TACHYCARDIA.
- ETHANOL-INDUCED HYPOTENSION IS USUALLY MILD AND TRANSIENT, SO SIGNIFICANT OR PERSISTENT HYPOTENSION WARRANTS INVESTIGATION FOR ALTERNATIVE CAUSES

- HYPOGLYCEMIA, USUALLY IN CHILDREN AND MALNOURISHED INDIVIDUALS DUE TO LOW GLYCOGEN STORES AND REDUCED GLUCONEOGENESIS.
- THE METABOLISM OF A SIGNIFICANT AMOUNT OF ETHANOL INCREASES THE NADH/NAD⁺ RATIO, WHICH THEN PROMOTES THE CONVERSION OF PYRUVATE TO LACTATE, DIVERTING PYRUVATE AWAY FROM THE GLUCONEOGENESIS PATHWAY

DIAGNOSIS

- ETHANOL-INTOXICATED PATIENTS OFTEN HAVE OTHER DISEASE PROCESSES, SUCH AS INFECTIONS AND TRAUMATIC INJURIES
- PERFORM A DETAILED PHYSICAL EXAMINATION, LOOKING ESPECIALLY FOR EVIDENCE OF TRAUMA, AND OBTAIN AS MUCH HISTORY AS POSSIBLE.
- UNCOMPLICATED ETHANOL INTOXICATION IMPROVES OVER A FEW HOURS.
- IF DEPRESSED MENTAL STATUS FAILS TO IMPROVE OR DETERIORATES, CONSIDER OTHER CAUSES OF ALTERED MENTAL STATUS AND EVALUATE APPROPRIATELY.

- THE CLINICAL ASSESSMENT GUIDES THE SELECTION OF LABORATORY TESTS.
- FOR ALTERED LEVELS OF CONSCIOUSNESS, OBTAIN A POINT-OF-CARE GLUCOSE LEVEL.
- ETHANOL LEVELS ARE NOT NECESSARILY REQUIRED IN CASES OF MILD OR MODERATE INTOXICATION WHEN NO OTHER ABNORMALITY IS SUSPECTED, BUT MEASURE SERUM ALCOHOL LEVELS IN PATIENTS WITH ALTERED MENTAL STATUS OF UNCLEAR CAUSE.

- ESTIMATION OF ETHANOL LEVEL IS UNRELIABLE, PARTICULARLY AROUND LEVELS OF 100 MILLIGRAMS/DL (22 MMOL/L) OR IN ALCOHOL-TOLERANT PATIENTS.
- IN ISOLATED ETHANOL INTOXICATION, THE PRESENCE OF HORIZONTAL GAZE NYSTAGMUS HAS A SENSITIVITY OF 70% TO 80% FOR A BLOOD ETHANOL LEVEL OF 80 MILLIGRAMS/DL (17 MMOL/L) AND A SENSITIVITY OF 80% TO 90% FOR BLOOD ETHANOL LEVELS >100 MILLIGRAMS/DL (22 MMOL/L).

- ASK ABOUT CONCOMITANT DRUG USE, ESPECIALLY COCAINE.
- THE ATTRACTION OF ABUSING THESE DRUGS TOGETHER MAY RELATE TO THE FORMATION OF THE ACTIVE COCAINE METABOLITE COCAETHYLENE, WHICH, ALTHOUGH LESS POTENT THAN THE PARENT COMPOUND, HAS A HALF-LIFE THAT IS THREE TO FIVE TIMES LONGER.
- THE RISK OF SUDDEN DEATH AMONG USERS OF BOTH DRUGS SIMULTANEOUSLY IS HIGHER THAN THAT AMONG COCAINE USERS ALONE.

- ETHANOL INGESTION IS THE MOST COMMON CAUSE OF AN OSMOLAR GAP ON SERUM ELECTROLYTE ANALYSIS AND MAY BE ASSOCIATED WITH A MILD METABOLIC ACIDOSIS
- A SIGNIFICANT ANION GAP METABOLIC ACIDOSIS SUGGESTS THE PRESENCE OF LACTIC ACIDOSIS, KETOACIDOSIS, OR METHANOL OR ETHYLENE GLYCOL TOXICITY.

TREATMENT

- MANAGEMENT IS OBSERVATION UNTIL SOBRIETY.
- ACTIVATED CHARCOAL IS NOT USEFUL SINCE ETHANOL IS RAPIDLY ABSORBED
- CONSIDER ACTIVATED CHARCOAL ONLY IF TOXIC ADSORBABLE SUBSTANCES HAVE BEEN CO-INGESTED WITHIN THE PAST HOUR.
- TREAT HYPOGLYCEMIA WITH IV DEXTROSE 0.5 TO 1 GRAM/KG
- ACUTE WERNICKE'S ENCEPHALOPATHY CAN BE PRECIPITATED BY PROLONGED SUSTAINED ADMINISTRATION OF IV CARBOHYDRATE, THERE IS NO EVIDENCE THAT A SINGLE DOSE OF IV GLUCOSE CAN CAUSE THIS SYNDROME.

- THE PREVALENCE OF VITAMIN DEFICIENCIES IN ACUTELY INTOXICATED ED PATIENTS IS LOW AND DOES NOT JUSTIFY THE ROUTINE USE OF IV VITAMIN-CONTAINING FLUIDS.
- LONG-TERM DRINKERS MAY BE VITAMIN DEFICIENT AND ARE SOMETIMES TREATED WITH IV FLUIDS CONTAINING MAGNESIUM, FOLATE, THIAMINE, AND MULTIVITAMINS, TERMED A BANANA BAG BECAUSE OF THE YELLOW COLOR IMPARTED BY THE MULTIVITAMIN MIXTURE.

- FLUID ADMINISTRATION DOES NOT HASTEN ALCOHOL ELIMINATION, SO ESTABLISHMENT OF IV ACCESS FOR FLUID ADMINISTRATION ALONE IS UNNECESSARY IN UNCOMPLICATED MILD TO MODERATE INTOXICATION.
- METADOXINE, WHICH IS NOT CURRENTLY AVAILABLE IN THE UNITED STATES BUT IS AVAILABLE IN LATIN AMERICA, MEXICO, ASIA, AFRICA, AND EASTERN EUROPE, ENHANCES THE METABOLISM OF ETHANOL AND ACCELERATES RECOVERY.

WERNICKE'S ENCEPHALOPATHY

- ABNORMAL MENTAL STATUS, ATAXIA, AND NYSTAGMUS
- REQUIRES DAILY TREATMENT WITH THIAMINE, 100 MILLIGRAMS, UNTIL NORMAL DIET IS RESUMED.

DISPOSITION AND FOLLOW-UP

- PATIENTS WITH ACUTE ETHANOL INTOXICATION AS THE ONLY CLINICAL PROBLEM REQUIRE ED OBSERVATION UNTIL SOBER.
- PRIOR TO DISCHARGE, REASSESS FOR AN UNDERLYING MENTAL HEALTH DISORDER, SUCH AS SUICIDAL OR HOMICIDAL IDEATION, THAT REQUIRES FURTHER CARE OR HOSPITAL ADMISSION.

- SCREENING FOR ALCOHOL USE DISORDER PRIOR TO DISCHARGE WITH BRIEF INTERVENTION AND REFERRAL TO APPROPRIATE OUTPATIENT SERVICES IS RECOMMENDED TO REDUCE FUTURE HARM.
- CLINICAL JUDGMENT, RATHER THAN A SERUM ETHANOL LEVEL, DETERMINES THE APPROPRIATENESS OF DISCHARGE.
- DISCHARGE THE PATIENT IN THE CARE OF A RESPONSIBLE COMPANION.
- PATIENTS TREATED FOR ALCOHOL INTOXICATION SHOULD NOT BE RESPONSIBLE FOR THEIR OWN TRANSPORTATION HOME

ALCOHOL WITHDRAWAL SYNDROMES

- HAND TREMORS
- HEADACHE
- LOSS OF APPETITE
- NAUSEA AND VOMITING
- DIAPHORESIS
- INSOMNIA
- TACHYCARDIA
- HYPERTENSION
- FEVER
- PSYCHO-MOTOR AGITATION
- HYPERAROUSAL
- CRAVING
- ANXIETY
- SEIZURES
- HALLUCINATIONS
- DELIRIUM

- EARLY AND DISTINGUISH WITHDRAWAL FROM MIMICS
- TOXIC-METABOLIC ABNORMALITIES (HYPONATREMIA, HYPOGLYCEMIA, HYPOMAGNESEMIA, DIABETIC KETOACIDOSIS, WERNICKE'S ENCEPHALOPATHY)
- TOXIC ALCOHOL INGESTIONS (ETHYLENE GLYCOL, METHANOL)
- OPIOID OR SEDATIVE WITHDRAWAL
- PRESCRIPTION OR ILLICIT DRUG INGESTIONS (ANTICHOLINERGIC DRUGS, STIMULANTS)
- NEUROLOGIC ABNORMALITIES (PRIMARY GENERALIZED SEIZURES, WITHDRAWAL SEIZURES)
- SEPSIS

- THE GATHERING OF COLLATERAL HISTORY, THOROUGH SERIAL EXAMINATIONS OF THE UNDRESSED PATIENT
- REPEATED MONITORING OF VITAL SIGNS
- MEASUREMENT OF OXYGEN SATURATION AND POINT-OF-CARE TESTING FOR BLOOD GLUCOSE
- LABORATORY ASSESSMENT OF METABOLIC CONDITIONS
- IMAGING AS CLINICALLY INDICATED CAN DETECT MOST COMORBIDITIES

Condition	Treatment (see text)
Uncomplicated alcohol withdrawal (no seizures, no delirium)	<p>Lorazepam 2 milligrams PO <i>or</i> Diazepam 10–20 milligrams PO <i>or</i> Oxazepam 15–30 milligrams PO <i>or</i> Chlordiazepoxide 50–100 milligrams PO</p> <p><i>If vomiting:</i> Diazepam 10–20 milligrams IV <i>or</i> Lorazepam 2–4 milligrams IV <i>and</i> Ondansetron 4 milligrams IV</p>
Alcohol withdrawal seizures	Lorazepam 2 milligrams IV
Alcohol withdrawal delirium tremens	<p>Lorazepam 2–4 milligrams IV; double the dose and repeat every 15–20 min until light somnolence <i>or</i> Diazepam 10–20 milligrams IV over 2 min; double the dose and repeat every 5–10 min until light somnolence</p> <p><i>If refractory to benzodiazepines:</i> Phenobarbital 65 milligrams IV every 15–30 min to maximum of 260 milligrams⁷ (respiratory depression more common than with benzodiazepines; typically requires intubation) <i>or</i> Propofol 5 micrograms/kg per minute (or 0.3 milligram/kg per hour) titrated to effect; typically requires intubation (unlabeled use, primarily case reports of effectiveness)</p>
Alcohol-induced psychotic disorder	<p>Abstinence from alcohol Antipsychotics until symptoms remit</p>

- INITIAL THERAPY IS USUALLY WITH BENZODIAZEPINES
- NO SPECIFIC AGENT IS SUPERIOR TO THE OTHERS
- IV ADMINISTRATION WORKS THE FASTEST, WITH 5 MINUTES FOR DIAZEPAM, 2 TO 5 MINUTES FOR MIDAZOLAM, AND 5 TO 20 MINUTES FOR LORAZEPAM IN ALCOHOL WITHDRAWAL
- INTRAMUSCULAR ABSORPTION OF LORAZEPAM AND MIDAZOLAM IS ADEQUATE, BUT ABSORPTION OF IM DIAZEPAM IS ERRATIC, AND THEREFORE, IM DIAZEPAM IS NOT RECOMMENDED

DISPOSITION

- PATIENTS WITH MILD OR MODERATE UNCOMPLICATED ALCOHOL WITHDRAWAL THAT RESPONDS WELL TO INITIAL ED TREATMENT, WITHOUT TRAUMA OR MAJOR MEDICAL COMORBIDITIES, WITH NO SUICIDAL OR HOMICIDAL IDEATION, AND WITHOUT A SEIZURE DISORDER CAN BE MANAGED SUCCESSFULLY IN A DETOXIFICATION UNIT OR **DISCHARGED** TO A SUPPORTIVE FAMILY WITH REFERRAL TO AN OUTPATIENT PROGRAM.
- INDICATIONS FOR **ADMISSION** INCLUDE ADVANCED AGE, MILD OR MODERATE WITHDRAWAL THAT DOES NOT RESPOND WELL TO ED TREATMENT, THE PRESENCE OF ACTIVE MEDICAL COMORBIDITIES, A PRIOR HISTORY OF DELIRIUM TREMENS, AND ALCOHOL WITHDRAWAL SEIZURES.
- CONSIDER **INTENSIVE CARE UNIT** ADMISSION FOR MODERATE WITHDRAWAL WITH COMORBID CONDITIONS OR SEVERE WITHDRAWAL IN WHICH SEDATIVE REQUIREMENTS NECESSITATE CLOSE MONITORING TO MONITOR RESPIRATORY STATUS.

METHANOL AND ETHYLENE GLYCOL

	Methanol	Ethylene Glycol
Sources	Windshield cleaners, gas line antifreeze, solvents, solid fuel for stoves, adulterated alcoholic beverages, moonshine	Glycerin substitute, hydraulic fluid, antifreeze, adulterated alcoholic beverage, adulterated toothpaste (diethylene glycol)
Absorption	30–60 min	1–4 h
Metabolism (untreated)	Decreases 8.5 milligrams/dL per hour (2.7 mmol/L per hour)	Elimination half-life \approx 3–8 h
Minimum lethal dose without treatment	1 gram/kg or about 100 mL in an adult	1.1–1.7 grams/kg or about 100 mL in an adult
Metabolism	Methanol \rightarrow formaldehyde \rightarrow formic acid	Ethylene glycol \rightarrow glycoaldehyde \rightarrow glycolic acid \rightarrow glyoxylic acid \rightarrow oxalic acid
Toxic effects	Formic acid blocks oxidative phosphorylation; metabolic acidosis from formic and lactic acids	Metabolic acidosis and tissue toxicity from glycolic acid and calcium oxalate crystals
Clinical features	Inebriation from parent compound, then 12–14 h later: metabolic acidosis; blurred or snow field vision; nausea, vomiting, abdominal pain	Inebriation from parent compound, then 4–12 h later: CNS effects, hypocalcemia, metabolic acidosis; 12–24 h: multisystem organ failure; 24–72 h: renal failure

Diagnosis	<p>Methanol level >20 milligrams/dL (>6 mmol/L)</p> <p>Early: unexplained osmolal gap >10 mOsm/kg H₂O</p> <p>Later: elevated anion gap metabolic acidosis</p>	<p>Ethylene glycol level >20 milligrams/dL (>3.2 mmol/L)</p> <p>Early: unexplained osmolal gap >10 mOsm/kg H₂O</p> <p>Later: elevated anion gap metabolic acidosis and calcium oxalate crystals in urine</p>
Treatment	<p>Fomepizole 15 milligrams/kg IV over 30 min and then 10 milligrams/kg IV over 30 min every 12 h</p> <p><i>or</i></p> <p>Ethanol 10 mL/kg of 10% IV ethanol at 100 milligrams/kg per hour to keep ethanol level 100–150 milligrams/dL (22–33 mmol/L)</p>	<p>Fomepizole 15 milligrams/kg IV over 30 min and then 10 milligrams/kg IV over 30 min every 12 h</p> <p><i>or</i></p> <p>Ethanol 10 mL/kg of 10% IV ethanol at 100 milligrams/kg per hour to keep ethanol level 100–150 milligrams/dL (22–33 mmol/L)</p>
	<p>Folinic or folic acid 1 milligram/kg IV every 4–6 h (up to 50 milligrams per dose), continue until toxicity resolved</p>	<p>Pyridoxine 50–100 milligrams IV every 6 h for 24–48 h</p> <p>Thiamine 100 milligrams IV every 6 h for 24–48 h</p> <p>Magnesium sulfate 2 grams IV (once)</p>
	<p>IV sodium bicarbonate to maintain serum pH >7.30</p>	<p>IV sodium bicarbonate to maintain serum pH >7.20</p>
	<p>See text for indications for hemodialysis</p>	<p>See text for indications for hemodialysis</p>

TREATMENT

- PERFORMING INITIAL RESUSCITATION
- PROVIDING CARDIOPULMONARY SUPPORT
- CORRECTING ACIDOSIS
- PREVENTING FORMATION OF TOXIC METABOLITES
- ENHANCING THE CLEARANCE OF THE PARENT COMPOUND AND TOXIC METABOLITES

- BECAUSE TOXIC ALCOHOLS ARE ABSORBED SO RAPIDLY, GASTRIC DECONTAMINATION IS UNLIKELY TO BE OF BENEFIT, AND THERE IS NO EVIDENCE TO SUPPORT ITS ROUTINE USE
- ACTIVATED CHARCOAL MAY BE USED IF THERE IS A RECENT CO-INGESTANT KNOWN TO ADSORB TO CHARCOAL

CORRECT ACIDOSIS

- IMPROVE THE OUTCOME IN PATIENTS POISONED WITH METHANOL; RAPID IMPROVEMENT IN VISUAL AND OTHER SYSTEMIC SYMPTOMS
- ALKALINIZATION MAY HELP INCREASE FORMIC ACID CLEARANCE BY DECREASING REABSORPTION IN THE PROXIMAL RENAL TUBULES
- WHEN USED IN METHANOL POISONING, GIVE IV SODIUM BICARBONATE INFUSIONS TO MAINTAIN A SERUM pH OF >7.30 .⁵⁹ THERE IS NO EVIDENCE THAT ALKALINIZATION IS SPECIFICALLY BENEFICIAL IN ETHYLENE GLYCOL POISONING, BUT IT SEEMS REASONABLE TO USE SODIUM BICARBONATE IV IF THERE IS A SEVERE METABOLIC ACIDOSIS WITH pH <7.20 .

HEMODIALYSIS

- HEMODIALYSIS CAN RAPIDLY CLEAR THE TOXIC ALCOHOLS AND METABOLITES, AS WELL AS CORRECT ACID-BASE DISORDERS, THEREBY SHORTENING THE DURATION OF METABOLIC BLOCKADE TREATMENT.
- CONVERSELY, WITH FOMEPIZOLE, PATIENTS CAN RECEIVE PROLONGED TREATMENT WITH FEW SIDE EFFECTS AND WITHOUT THE NEED FOR HEMODIALYSIS AND ATTENDANT RISKS

TABLE 185-7**Indications for Hemodialysis After Methanol or Ethylene Glycol Ingestion**

- Refractory metabolic acidosis: pH <7.25 with anion gap >30 mEq/L and/or base deficit <−15
- Visual abnormalities*
- Renal insufficiency
- Deteriorating vital signs despite aggressive supportive care
- Electrolyte abnormalities refractory to conventional therapy
- Serum methanol or ethylene glycol level of >50 milligrams/dL†

DISPOSITION AND FOLLOW-UP

- CONSULTATION WITH A MEDICAL TOXICOLOGIST OR A REGIONAL POISON CONTROL CENTER IS STRONGLY RECOMMENDED
- SYMPTOMS OF METHANOL OR ETHYLENE GLYCOL INTOXICATION MAY BE DELAYED, PARTICULARLY IF ETHANOL HAS BEEN CO-INGESTED.
- A PATIENT WITH SUSPECTED ETHYLENE GLYCOL INGESTION SHOULD BE OBSERVED AND MONITORED FOR 6 HOURS.
- IF NO ETHANOL IS PRESENT, THE PATIENT REMAINS COMPLETELY ASYMPTOMATIC, THERE IS NO OSMOLAR GAP, AND NO METABOLIC ACIDOSIS DEVELOPS, THE PATIENT CAN BE DISCHARGED.
- METHANOL TOXICITY MAY BE DELAYED LONGER, SO A PATIENT WITH SUSPECTED METHANOL INGESTION SHOULD BE OBSERVED FOR 12 HOURS USING THE SAME CRITERIA.

- PATIENTS WITH SIGNIFICANT SIGNS AND SYMPTOMS SHOULD BE ADMITTED TO AN INTENSIVE CARE SETTING.
- PATIENTS SEEN AT FACILITIES UNABLE TO PROVIDE HEMODIALYSIS OR INTENSIVE CARE SHOULD BE TRANSFERRED AS SOON AS POSSIBLE, IF IN SUFFICIENTLY STABLE CONDITION, TO INSTITUTIONS CAPABLE OF PROVIDING SUCH CARE.
- SUICIDAL PATIENTS SHOULD RECEIVE A PSYCHIATRIC EVALUATION WHEN THEIR CONDITION IMPROVES AND PRIOR TO DISCHARGE.

THANK YOU