Alcohol Poisoning

ALCOHOLS

- Methanol (CH_3OH)
  Wood alcohol

- Ethanol (CH_3CH_2OH)
  Grain alcohol

- Ethylene Glycol (CH2OHCH2OH)
  Polyhydric alcohol

Alcohol content of common products and medications(0.3% to 75%.)

- Aftershaves lotions 15-18%
- Cold /allergy medications 5-16%
- Cough preparations 2-25%
- Glass Cleaner 10%
- Mouthwashes 15-25%
- Perfumes/Colognes 25-95%

Ethyl Alcohol

- The most commonly abused drug in the world
- 75% of adults drink alcohol regularly
- In the United States, 18% of adults are classified as heavy drinkers
- Approx. 10% are considered alcoholics
- Cost attributed to alcohol abuse exceed 200 billion dollars annually.
- Traffic fatalities, homicides, rapes and suicides are all alcohol related .
- Moderate alcohol use protect against cardiovascular diseases in individuals
- Alcoholism is a complex disorder with a genetic and environmental component

Pharmacokinetics

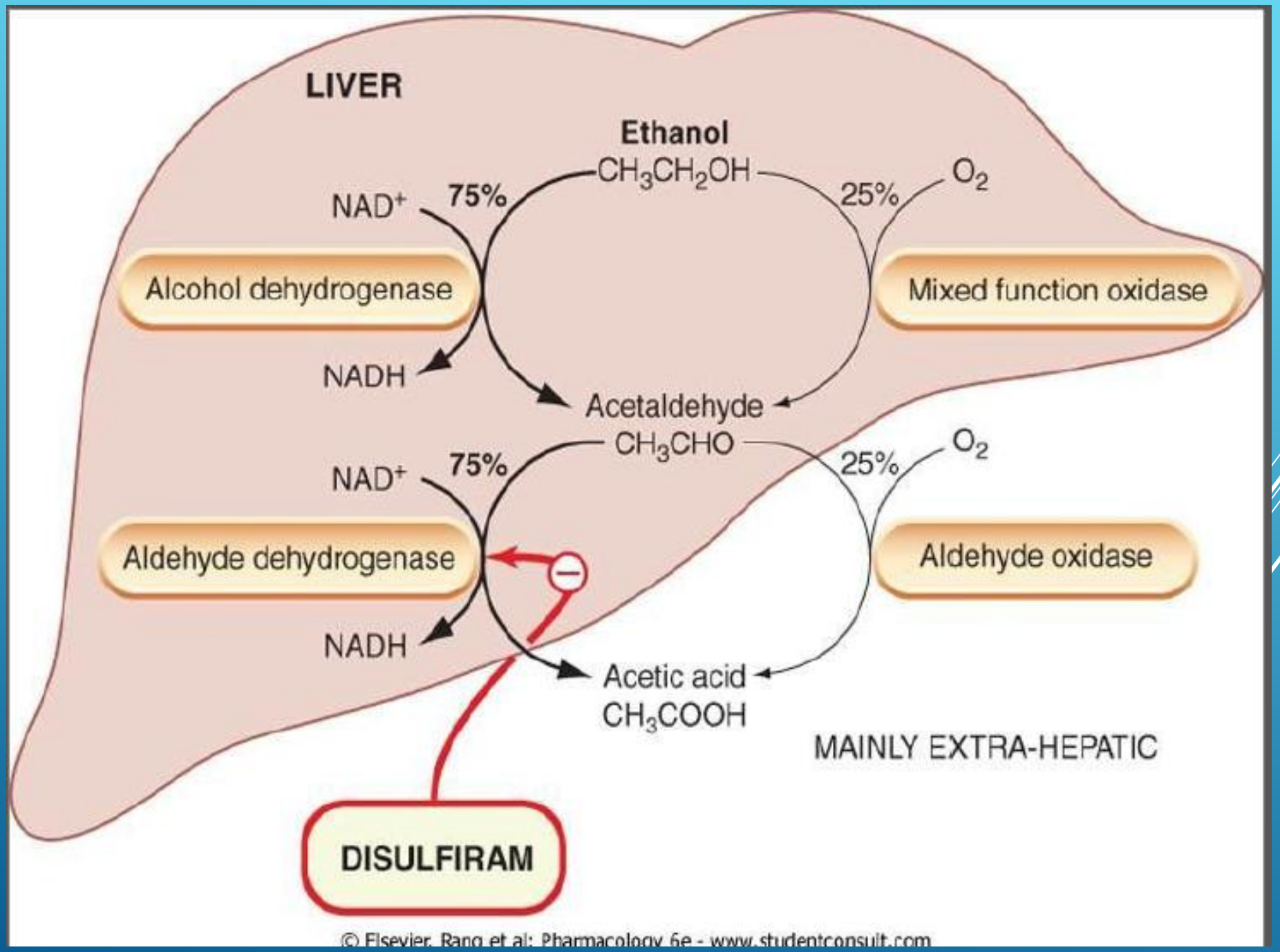
- Ethanol is a small water soluble molecule rapidly absorbed from stomach and small intestine (75%) after oral ingestion.
- Rate of absorption from the stomach is reduced by the presence of food.
- Peak blood alcohol levels are achieved in 30 minutes.
- About 60% of inspired ethanol vapor is absorbed through the lungs and can lead to intoxication.
- Percutaneous absorption also occurs (in infants)
- Distribution is rapid, with tissue levels approximating blood alcohol concentration (BAC).
- BAC for a fixed amount of alcohol depends on sex, age and adiposity.
- Volume of distribution of ethanol is 0.5-0.7 L/kg which is approximately total body water.
- For the same oral dose of alcohol, women will have a higher peak concentration than men because of lower total body water and lower (50 %) gastric Alcohol dehydrogenase (ADH).

Absorption & Metabolism

- Stomach and proximal portion of the small bowel.
- When the stomach is empty, peak blood ethanol levels are reached between 30 and 90 minutes after ingestion.
- The primary pathway of ethanol metabolism occurs in the liver via alcohol dehydrogenase .
- Alcohol dehydrogenase is also located in the gastric mucosa, but this gastric metabolism of alcohol is decreased in women.
- Decreased "first-pass metabolism", combined with a smaller volume of distribution, may explain the enhanced vulnerability of women to acute complications of alcohol intoxication.

الکل دهیدروژناز:

- ✓ فعالیت این آنزیم در خانمها نسبت به آقایان کمتر میباشد.
- ✓ فعالیت این آنزیم با معده خالی کاهش می یابد.(احتمال مسمومیت)
- ✓ مهم ترین آنزیم مسیر متابولیسم الکل است، اتانول را به استالدئید تبدیل میکند.(این واکنش در میکروزومها توسط 2E1 ودر پراکسی زومها توسط کاتالازها هم میتواند انجام شود.)
- ✓ استالدئید به میتوکندری رفته و در انجا توسط آلدئید دهیدروژناز به اسید استیک تبدیل میشود.
- ✓ مصرف مزمن الکل باعث القای 2E1 میشود. (افراد دایم الخمر دیرتر مست میشوند.)


LIVER
Ethanol
CH_3CH_2OH
NAD^+
75%
25%
O_2
Alcohol dehydrogenase
Mixed function oxidase
NADH
Acetaldehyde
CH_3CHO
NAD^+
75%
25%
O_2
Aldehyde dehydrogenase
Aldehyde oxidase
NADH
Acetic acid
CH_3COOH
MAINLY EXTRA-HEPATIC
DISULFIRAM
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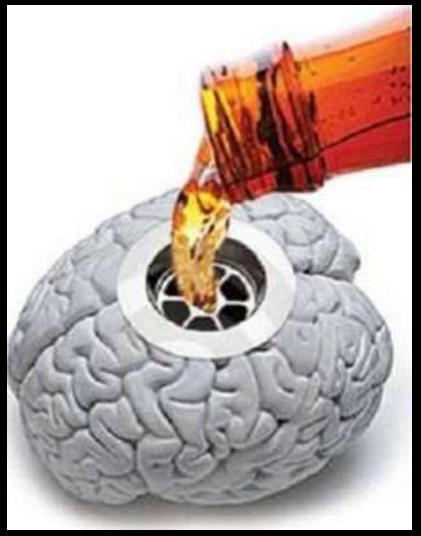
Pharmacokinetics: Gender Differences



- Gender Differences
  - in absorption
    - Differences in gastric ADH activity
  - in volume of distribution
    - Differences in body composition and total body water (TBW)
  - in metabolism
    - Differences in liver volume, ADH activity

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Acetaldehyde Metabolism

- Several other drugs **(eg, metronidazole, cefotetan, trimethoprim)** inhibit aldehyde dehydrogenase and can cause a disulfiram-like reaction if combined with ethanol.

- Some people, primarily of Asian descent, have a genetic deficiency in the activity of the mitochondrial form of aldehyde dehydrogenase.

- When these individuals drink alcohol, they develop high blood acetaldehyde concentrations and experience a flushing reaction similar to that seen with the combination of disulfiram and ethanol.

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Commonly Used Medications That Cause Disulfiram-Like Reactions (i.e., Flushing, Nausea, Vomiting, Sweating) After Alcohol Consumption

Type of Medication Generic Names Brand Names

Analgesics (NSAIDs)
Phenacetin
Phenylbutazone
Antibiotics :
Cefamandole, Mandol, Cefoperazone, Cefobid, Cefotetan, Cefotan
Chloramphenicol
Griseofulvin, Grifulvin,
Isoniazid ,Rifamate,
Metronidazole
Nitrofurantoin
Sulfamethoxazole
Cardiovascular medications Isosorbide dinitrate ,Sorbitrate
(nitrates) Nitroglycerin
Diabetes medications Chlorpropamide
(sulfonylureas) Glyburide
Tolazamide generic
Tolbutamide

CNS EFFECTS OF ETHANOL

- Ethanol is a sedative-hypnotic agent
- Membrane-active CNS depressant similar to anesthetic agents

- Mechanism of CNS action involves the potentiation of GABA receptor and inhibition of Glutamate receptor neurotransmission

- Ethanol could induce the release of endogenous opiates (basis for opiate antagonist Naltrexone treatment)

2.2. Stages of EtOH intoxication

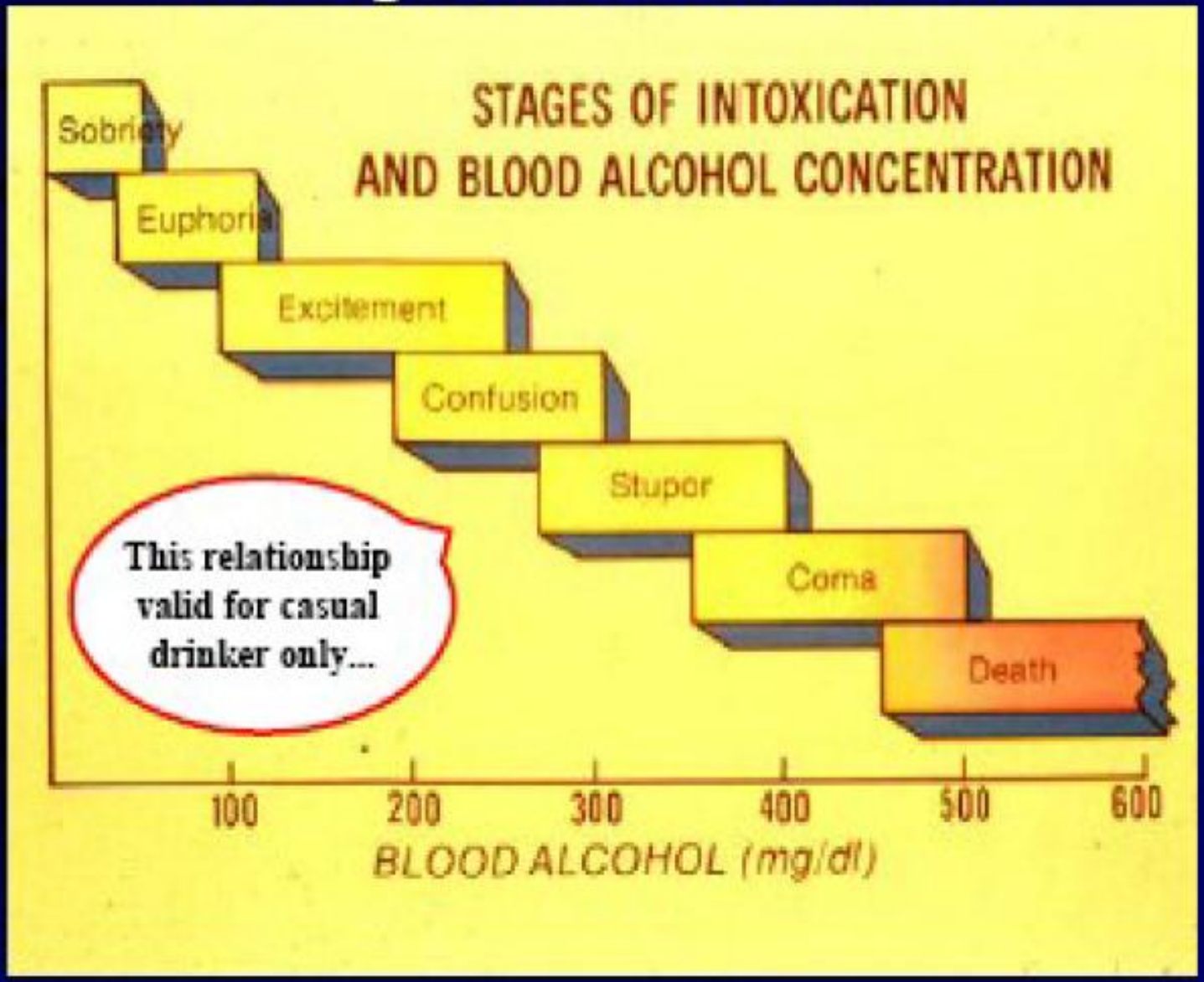


TABLE 31-4 Signs and Symptoms of Intoxication and Blood Ethanol Concentrations in a Non-Alcohol-Dependent Population*

ETHANOL CONCENTRATION (MG%)	SIGNS AND SYMPTOMS
<25	Sense of warmth Sense of well-being Talkativeness Mild incoordination
25–50	Euphoria Clumsiness Decreased judgment and control
50–100	Decreased sensorium Worsened coordination, ataxia Decreased reflexes/increased reaction time Emotional lability
100–250	Cerebellar/vestibular dysfunction (ataxia, diplopia, slurred speech, visual impairment, nystagmus) Severe emotional lability, confusion, stupor Nausea, vomiting
250–400	Stupor or coma Little response to stimuli Incontinence Respiratory depression
>400	Respiratory paralysis Loss of protective reflexes Hypothermia Death

*Correlation between signs and symptoms and blood ethanol levels show wide variability among individuals.

A toxic dose is considered to be 5 g/kg in an adult or 3 g/kg in a child.

Fatal dose is 6-10 ml/kg in adults and 4ml/kg in children.

Cardiovascular Effects of Ethanol

ACUTE EFFECTS:

- Cutaneous vasodilation with increased blood flow to the skin
- Increased coronary blood flow
- Depressed myocardial contractility
- Acetaldehyde induce cathecholamine release result in tachycardia
- Vasoconstriction in cerebral and renal vascular beds

CHRONIC EFFECTS

- Dilated cardiomyopathy
- Ventricular hypertrophy
- Atrial & Ventricular arrhythmias
- Mild Anemia from Folate deficiency

Gastrointestinal Effects of Ethanol

- Gastrin release and gastric acid secretion
- Inflammation and bleeding by ulceration of the stomach lining
- Retards intestinal absorption of glucose, amino acid, folic acid, thiamine & vitamin B_{12} (alcoholics)
- Chronic CNS effects (Korsakoff Psychosis & Wernicke encephalopathy occurs from thiamine deficiency
- Liver acidosis, hypoglycemia, increased fatty acid and lactate formation; steatosis
- Alcoholic hepatitis; Liver Cirrhosis; Liver failure (Alcoholism)

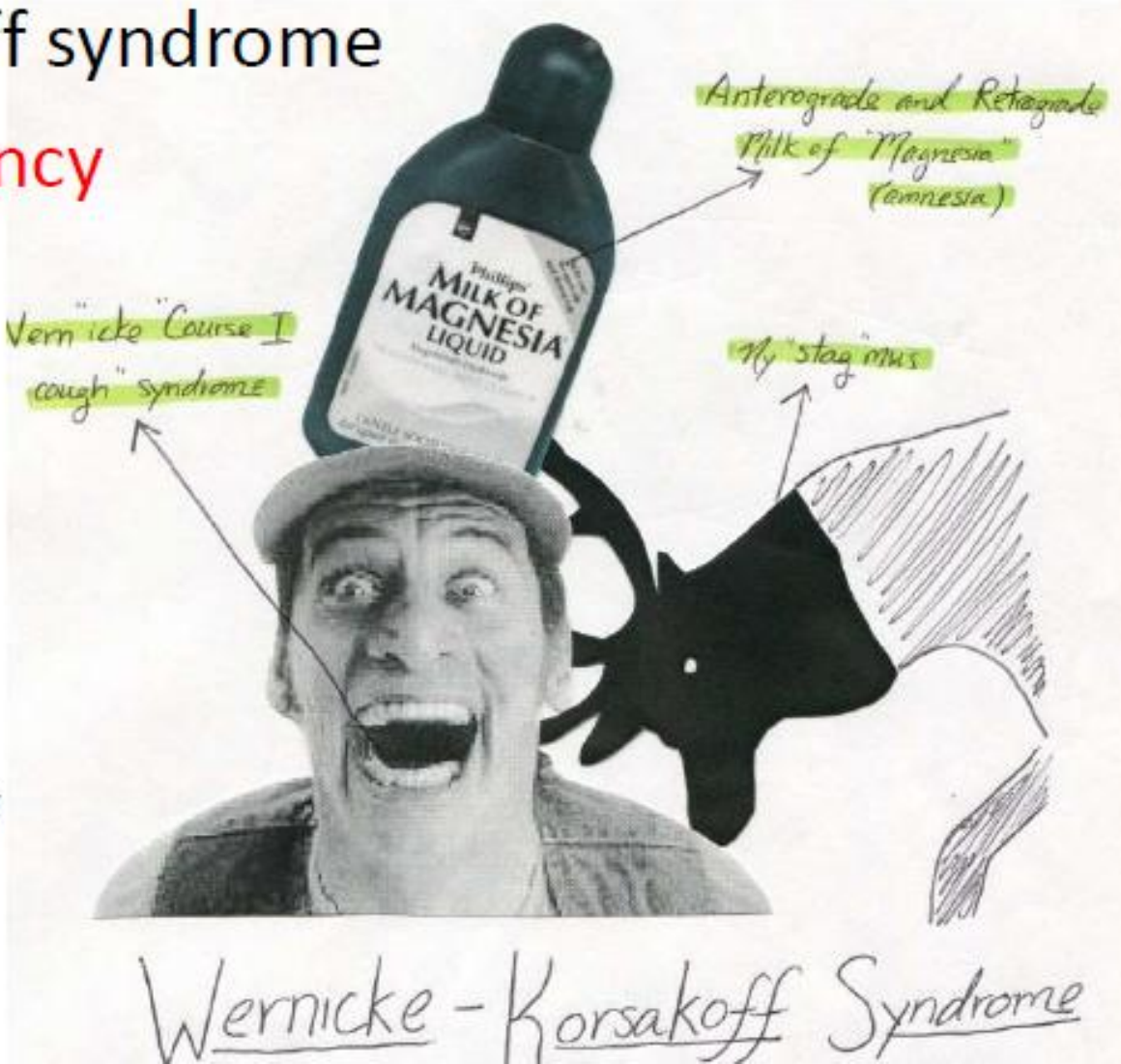
CHRONIC TOXICITY

Wernicke-Korsakoff syndrome

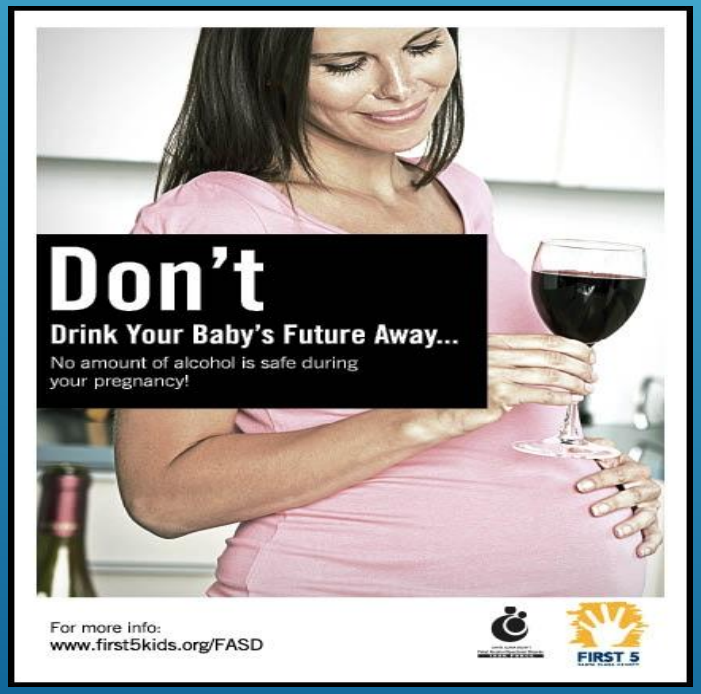
- thiamine deficiency

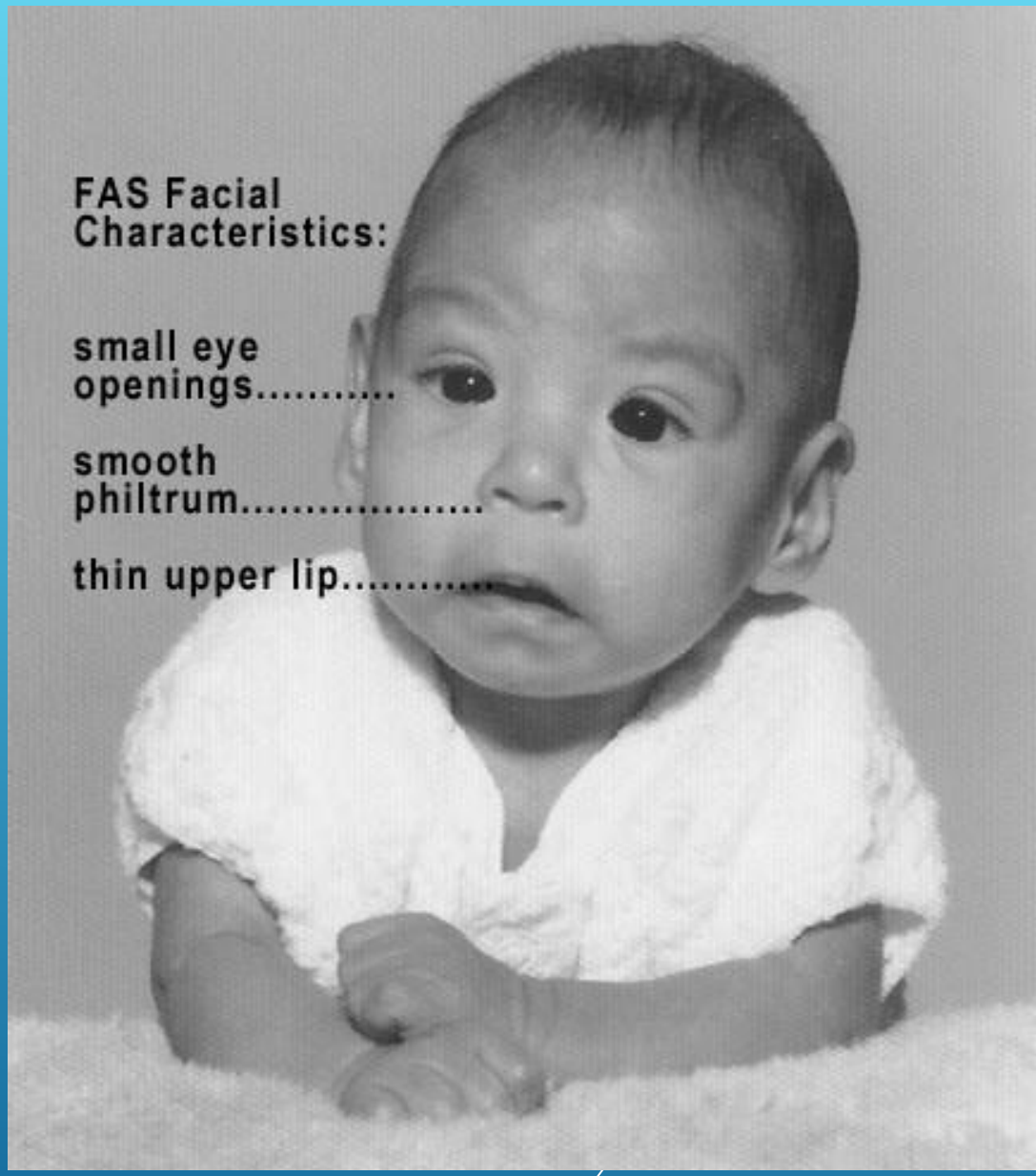
- Korsakoff's Psychosis

- Wernicke's encephalopathy



FATAL ALCOHOL SYNDROME





Fetal Alcohol Syndrome

- Specific pattern of facial features
- Pre- ad/or postnatal growth deficiency
- Evidence of central nervous system dysfunction

Photo courtesy of Teresa Kellerman

Acute Ethanol Intoxication

- Occurs from consumption of large quantities
- Degree of intoxication depends on

1. Blood ethanol concentration (BAC)
2. How fast the blood ethanol level rises
3. How long the BAC is maintained

Other factors are: Drinking patterns, G.I. Absorptive surface, other medications.

- Acute Effects: Vasodilation, Tachycardia
  G.I. Irritation, respiratory depression
- **Management: Prevention of respiratory depression; aspiration of vomitus**
- **Treatment of: Hypoglycemia & ketosis with glucose**
- **Treatment of dehydration with electrolytes**

Mild ethanol intoxication

1- Observation and serial examination.

2- In patients with a clear history of alcohol intake and mild ethanol intoxication, and without signs of volume depletion, intravenous (IV) catheter insertion and fluid hydration are not usually necessary.

3-The unhabituated drinker clears ethanol from the blood stream occurs at an approximate rate of 15-20 mg/dL per hour.

4-Patients with chronic ethanol abuse can clear ethanol at a rate of 25-35 mg/dL per hour, or even faster in some cases .

5-Patients with mild intoxication can be safely discharged when no longer clinically intoxicated and deemed by the clinician to be no danger to themselves or others.

Moderate ethanol intoxication

- Patients with moderate ethanol intoxication with signs of **volume depletion, hypotension or malnutrition may require IV catheter insertion and fluid hydration**.
- At a moderate to severe level of intoxication any alteration in the level of consciousness must be further investigated.
- If there is a clear history of alcohol consumption and serial examinations demonstrate improvement in the patient's mental status, further work-up may not be necessary.
- However, if there is any question of possible occult trauma or if the patient's mental status does not improve after serial examinations a computed tomographic scan of the head should be obtained and other diagnostic tests as needed.

Severe ethanol intoxication

- All patients with severe ethanol intoxication must obtain **aggressive supportive care**.
- In patients with evidence of volume depletion and hypotension, IV fluid hydration should be instituted.
- At high blood alcohol concentrations special attention must be paid to the **patients respiratory status with a frequent assessment of airway and breathing**.
- If the patient is unable to protect his or her airway or has inadequate respiration then endotracheal tube **insertion and mechanical ventilation may be required**.
- All patients presenting with coma secondary to ethanol intoxication should receive thiamine (100 mg IV) to prevent or treat Wernicke's encephalopathy.

Toxicity Management:

- Supportive care
- Charcoal: No benefit
- IV Fluids
- Dextrose: for hypoglycemia
- Thiamine
- Diazepam

METHANOL POISONING

Overview

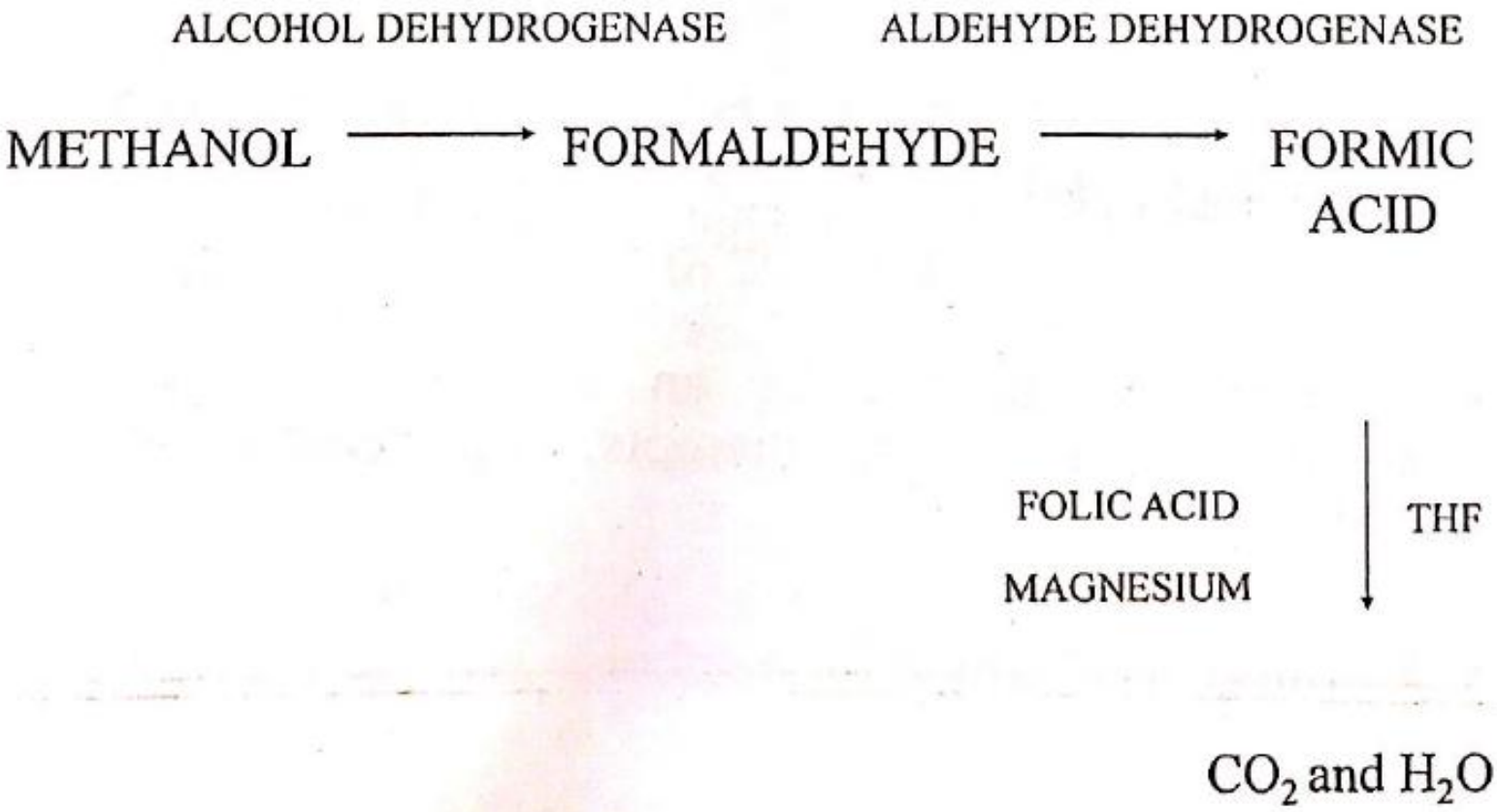
- Methyl alcohol /wood alcohol, CH_3OH.
  Colorless, volatile, flammable, light odor and readily miscible in water .

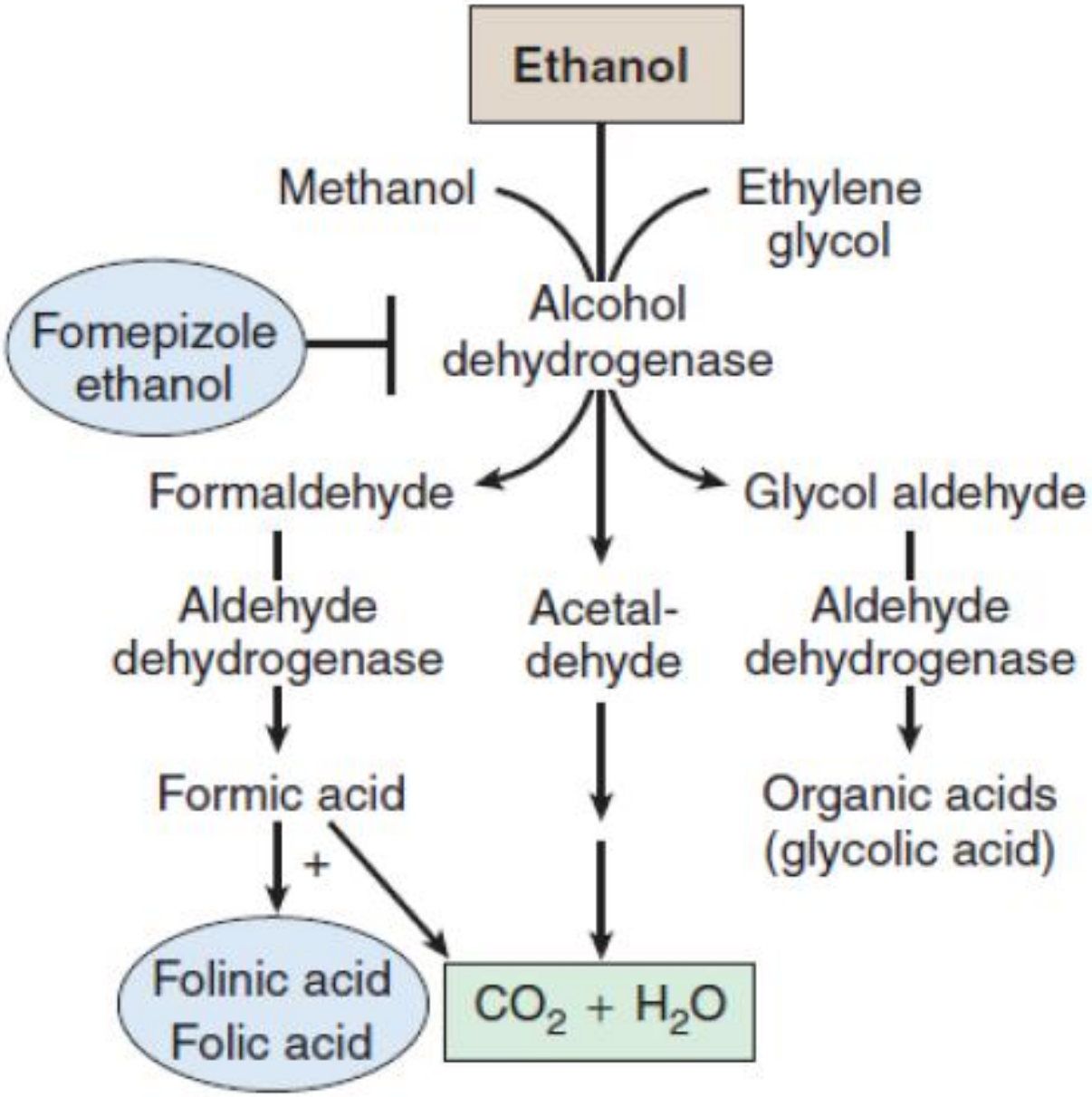
- The clinical course of methanol poisoning occurs over a number of hours. While methanol itself is only mildly intoxicating, it is converted to highly toxic metabolites responsible for **acidosis, blindness, and potentially death**.
- Because the morbidity for methanol poisoning is related to **delay in treatment**, real or suspected methanol poisoning creates many challenges for clinicians because **laboratory tests, antidotes and intensive care facilities are not always available.**
- The **lethal dose of pure methanol is estimates to be 1-2 mL/kg** ; however, permanent blindness and death have been reported with as little as **0.1 mL/kg** (6-10 mL in adults) .

Pharmacokinetics

- Methanol is readily absorbed from the gut, skin, and lungs.
- Peak serum concentration usually occurs in 30-60 minutes following oral ingestions.
- Methanol distributes widely in body water with a volume distribution of 0.6 L/kg.
- Methanol is slowly and erratically metabolized in the liver and follows zero order kinetics.
- Approximately 3% of a methanol dose is excreted through the lungs or excreted unchanged in the urine.
- The half-life of methanol is prolonged to 30-50 hours during antidotal therapy .

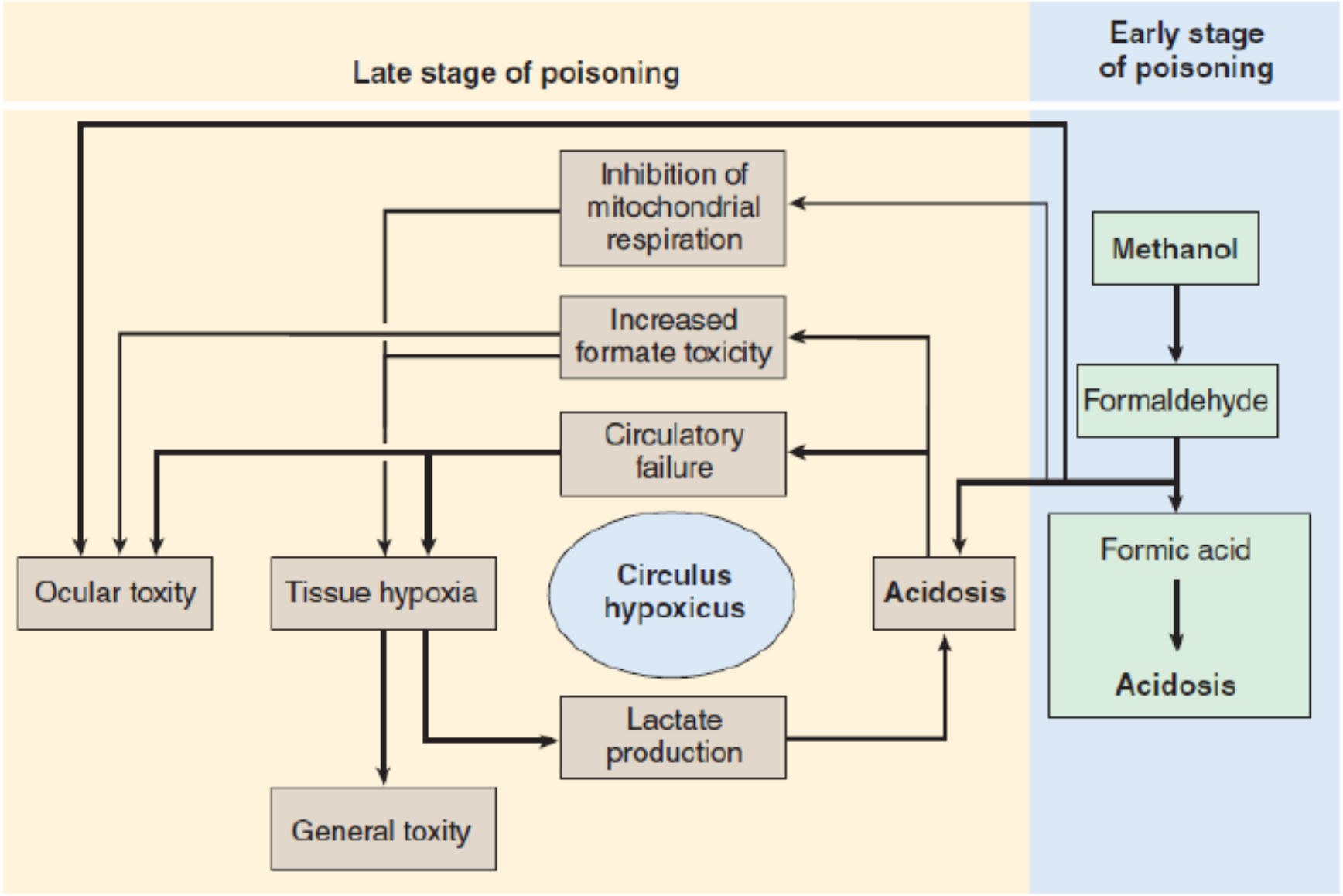
METABOLISM


ALCOHOL DEHYDROGENASE
ALDEHYDE DEHYDROGENASE
METHANOL
FORMALDEHYDE
FORMIC ACID
FOLIC ACID
MAGNESIUM
THF
CO_2 and H_2O


Ethanol
Methanol
Ethylene glycol
Fomepizole ethanol
Alcohol dehydrogenase
Formaldehyde
Glycol aldehyde
Aldehyde dehydrogenase
Acetal-dehyde
Aldehyde dehydrogenase
Formic acid
Organic acids (glycolic acid)
+
Folinic acid
Folic acid
$CO_2 + H_2O$

Mechanism of Toxicity

- Methanol is relatively **non-toxic**; however, it is metabolized to **highly toxic** compounds that are responsible for the **acidosis** and **blindness** characteristic of methanol poisoning.
- The initial step in the metabolism of methanol involves the enzyme alcohol dehydrogenase (ADH)
- First, methanol is slowly oxidized by ADH to yield formaldehyde. Next,formaldehyde is oxidized by formaldehyde dehydrogenase to yield formic acid (or formate, depending on the pH).
- This oxidation occurs rapidly so that little formaldehyde accumulates in the serum. Finally, formic acid is metabolized to carbon dioxide and water, which are excreted by the kidneys and lungs.


Late stage of poisoning
Early stage of poisoning
Inhibition of mitochondrial respiration
Increased formate toxicity
Circulatory failure
Methanol
Formaldehyde
Formic acid
Acidosis
Ocular toxity
Tissue hypoxia
Circulus hypoxicus
Acidosis
Lactate production
General toxity

Mode of action

- The accumulation of **formic acid** is responsible for the presence of metabolic acidosis.
- Formic acid also inhibits cellular respiration leading to lactic acidosis.
- The ocular injury caused by methanol may be due to retinal injury, which results from **intra-retinal metabolism of methanol and the accumulation of formic acid**.
- Alternatively, it may be caused by the **inhibition of normal metabolism in optic nerve calls** .

SIGNS AND SYMPTOMS

INITIAL INEBRIATION - ESPECIALLY IF ETHANOL COINGESTED

AFTER 6- 24 HOUR DELAY - PROGRESSION TO ACIDOSIS AND OTHER SIGNS AND SYMPTOMS

MAY BE FURTHER DELAY WITH CONTINUED INGESTION OF ETHANOL

SIGNS AND SYMPTOMS

CNS - INEBRIATION PROGRESSING TO COMA, CONVULSIONS

GIT - NAUSEA, VOMITING

RETINAL - BLURRED VISION, PHOTOPHOBIA, VISUAL ACUITY LOSS, DILATED NON-REACTIVE PUPILS, OPTIC NERVE HYPERAEMIC - BECOMING OEDEMATOUS

CARDIAC - TACHYCARDIA, HYPERTENSION PROGRESSING TO HYPOTENSION AND CARDIOGENIC SHOCK

RESPIRATORY – TACHYPNEA, DYSPNEA

Diagnosis (1)

- Difficult to diagnose
- Diagnosis requires both clinical and laboratory data.
- It is often difficult for a clinician to distinguish between poisoning by methanol or by ethylene glycol.
- The most direct means of diagnosing methanol poisoning is through the measurement of serum methanol concentration.

Diagnosis (2)

- The **co-ingestion of ethanol** may produce a **confusing clinical picture** as the toxic effects of methanol may be masked or delayed .
- Other diagnostic clues are **ophthalmic changes .**
- A serum methanol concentration greater than **20 mg/dL** soon after ingestion generally indicates the need for antidotal therapy; however, in late-presenting patients, any concentration of methanol in the presence of systemic toxicity should be treated.
- Serum amylase: **Hemorrhagic pancreatitis** has been described in as many as two thirds of the patients.

Summary of clinical effects

- Neurological: Early signs are slight drowsiness. Delayed signs appear after 8 - 36 h: headache, vertigo, drowsiness, coma, and, occasionally, convulsions. Dilated pupils, with sluggish or absent light reflex, occur in conscious patients.
- Visual disturbances: Vision becomes blurred, and may be sufficient to impair perception of light or cause complete blindness. There is impaired pupillary response to light, and contraction of visual fields. Visual disturbances can be permanent.
- Other: Abdominal pain is frequent; acute pancreatitis may occur.

TREATMENT

CORRECTION OF METABOLIC ACIDOSIS

BICARBONATE (AGGRESSIVE TREATMENT)

CAN REVERSE VISUAL IMPAIRMENT
REDUCES MOVEMENT OF FORMATE TO THE CNS
MAY REQUIRE 400 TO 600 MMOL DURING FIRST FEW HOURS

TREATMENT

ETHANOL
(REDUCES FORMATION OF TOXIC METABOLITES)

Ethanol Indications:

ingestion > 0.4 ml/kg

methanol > 20 mg/100 ml, symptomatic acidosis, need for HD.

Loading Dose:

achieve BAC of 100- 150 mg /100 ml

loading 0.8gm/ kg of 5 – 10% ethanol
followed by 130mg/kg/hr.
oral loading if no iv preparation
if dialysis, 250-350 mg/kg/hr.

TREATMENT

4-methyl pyrazole(fomepizole, Antizol)

Loading dose: 15-20 mg/kg up to 1g iv (Dilute in NS or DW5%, 30 min. infusion.

Maintenance: 10 mg/kg every 12 hrs for 48 hrs

Folic acid 30 mg every 4 hrly

Leucovorin 1-2mg/kg iv

$MgSO_4$ TITRATED AGAINST BLOOD MAGNESIUM LEVELS

TREATMENT

HAEMODIALYSIS

INDICATIONS:

Haemodialysis indications:

- methanol >50 mg/100ml
- acidosis not responsive to bicarbonate
- formate levels > 20 mg/100ml
- visual impairment
- renal impairment

Treatment Objectives

- The three primary goals of therapy include **treatment of metabolic acidosis**, **inhibition of the methanol metabolism** and **enhanced elimination** of the unmetabolized compound and existing toxic metabolites.
- **Gastric decontamination** is unlikely to be beneficial because methanol is rapidly and completely absorbed from the gut.
- **Ipecac-induced emesis is contraindicated** due to the risk of rapid loss of consciousness.
- It is doubtful activated charcoal has the ability to absorb significant amounts of methanol; however, it may be useful if a **co- ingesting** is suspected. Gastric lavage would need to be performed soon after ingestion to be beneficial.
- Stabilization of the critical patient must be performed before other therapies can be instituted. **Correcting acid/base status should be a priority because serious metabolic acidosis is common and a pH less than 7 is associated with poor prognosis.**
- Sodium bicarbonate should be administered to correct serum pH.
- Fluid and electrolyte replacement, airway management and the treatment of serious cardiovascular and neurological signs, such as hypotension and seizures, should also be a primary concern.
- The elimination of methanol may be enhanced by administering **folic acid**, a cofactor in the conversion of formic acid to carbon dioxide, and by performing hemodialysis

Management

General principles

Treatment consists of:

- Emptying the stomach (if indicated)
- Correction of acidosis
- Correction of seizure
- Ethanol or fomepizole administration to inhibit the formation of toxic metabolites;
- Rapid reduction of the body burden of methanol and formate by haemodialysis
- Intensive supportive care for multiple organ/system failures.

Prognosis

- Outcomes are excellent when asymptomatic methanol-poisoned patients are treated promptly. Reversal of presenting blindness, in one reported case, was attributed to prompt treatment .
- According to one study, poor outcomes were associated with coma or seizures on presentation or acidosis with pH less than 7 .

ETHYLENE GLYCOL

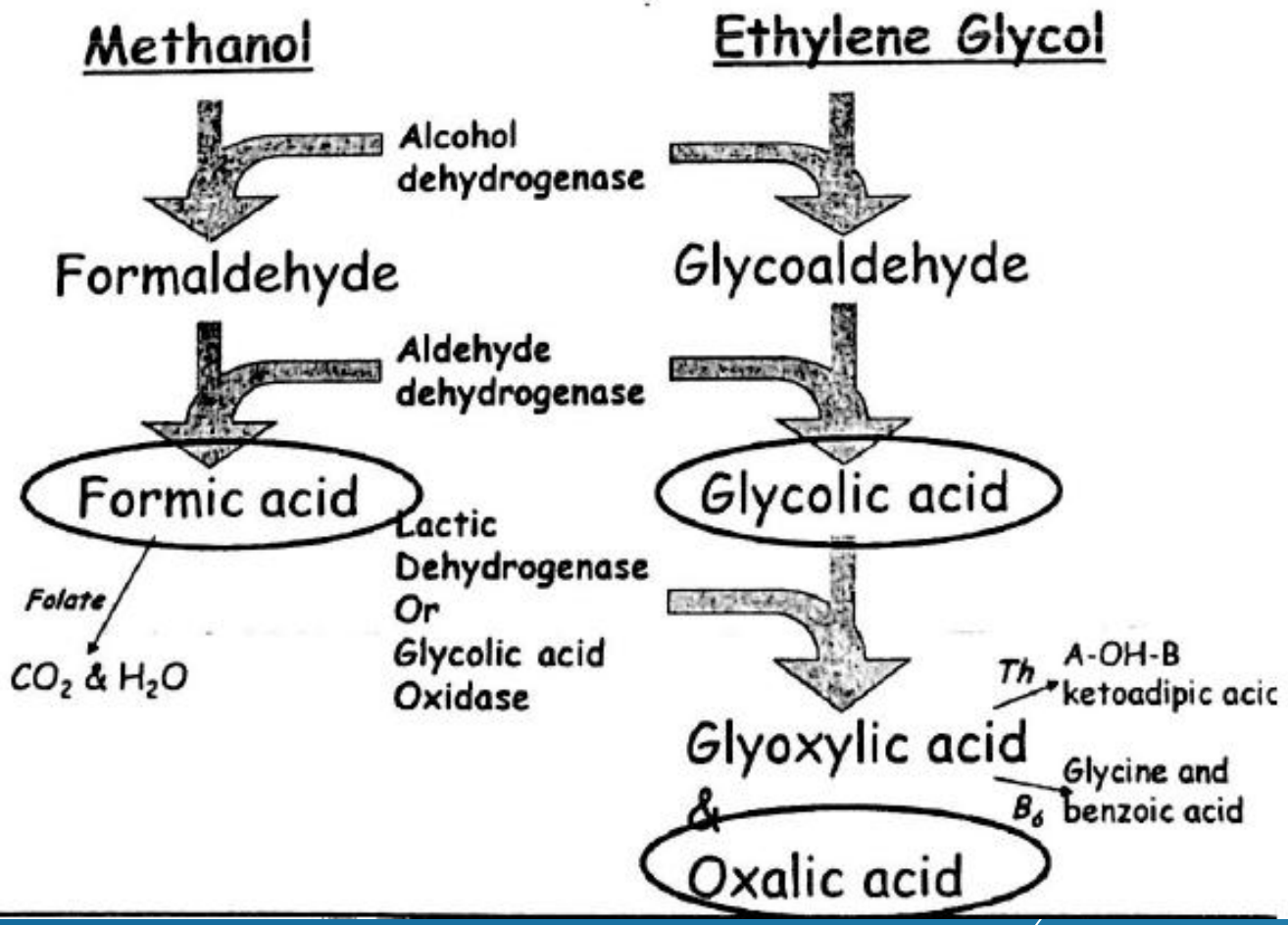
Overview

- The most common sources of ethylene glycol are **automotive antifreeze** , engine coolants and hydraulic brake fluids.
- In ethylene glycol poisoning, the clinical course is initially characterized by **mild symptoms that may gradually develop to produce serious or even fatal toxicity.**
- Ethylene glycol poisoning presents many challenges in making a definitive diagnosis. If treatment is initiated **early**, prognosis is **excellent**; however, a disturbing proportion of patients are admitted at a late stage to hospitals that are not capable of performing analysis which identifies ethylene glycol toxicity on a 24-hour basis.
- Therefore, rapid treatment is often prevented because of a **delayed diagnosis**, which may result in **fatal consequences** .
- The lethal dose of ethylene glycol is usually **1.4-1.6 mL/kg** (about 100 mL in an adult), but as little as **30 mL may be fatal .**

ETHYLENE GLYCOL

- Ethylene glycol has many commercial uses as a coolant (antifreeze), preservative, and glycerine substitute; it has also been used in polishes, and detergents.
- It may be ingested as an alcohol substitute by alcoholics, in suicide attempts, and accidentally by children.
- Poorman's substitute for alcohol

Methanol/ Ethylene Glycol



- **Main risks and target organs**

The main risk is severe metabolic acidosis with **CNS depression, cardio-pulmonary failure and acute renal failure.**

- Lethal dose as little as **1 mL/kg**.
- **Summary of clinical effects**

Within 4 to 12 hours CNS-depression (like ethanol) and increasing metabolic acidosis. Later stages (>12 hours) severe metabolic acidosis with electrolyte disturbances, elevated blood pressure, cardiopulmonary failure. Decreasing diuresis (>24 hours) with development of acute oliguric renal failure.

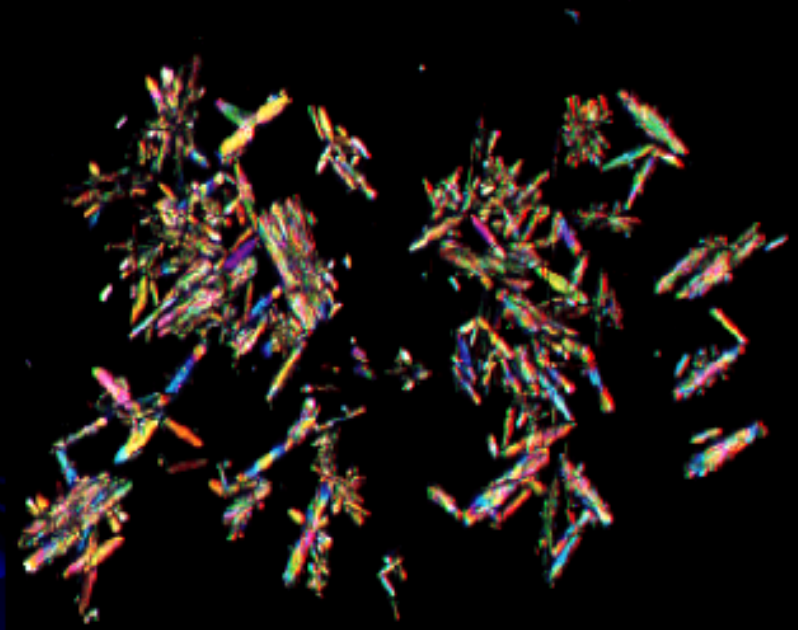
- .

The diagnosis is based on history of exposure, clinical features and laboratory findings.

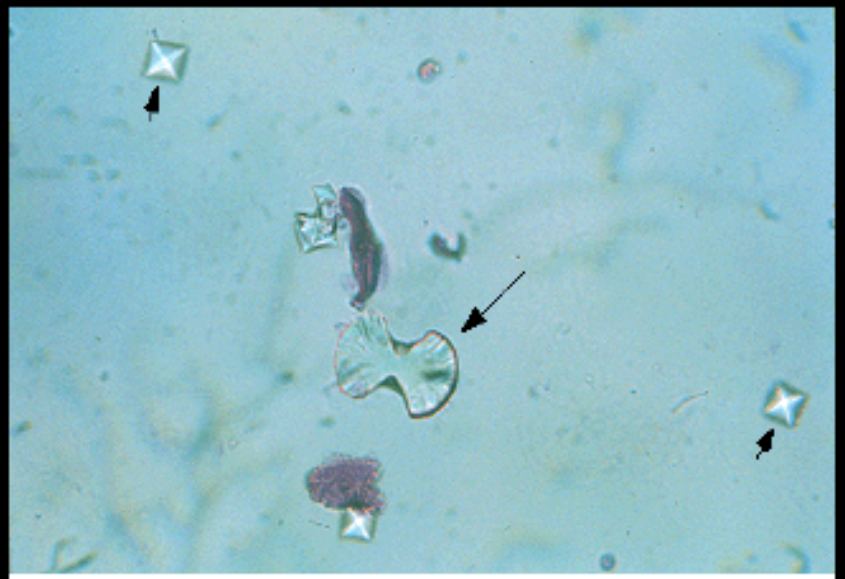
Drowsiness, coma, elevated blood pressure, tachycardia and hyperventilation are the typical clinical features of ethylene glycol poisoning.

Severe metabolic acidosis with elevated anion and osmolal gap is typical. The degree of metabolic acidosis is related to the severity of poisoning. Urine microscopy may reveal presence of **needle or envelope shaped calcium oxalate crystals** (oxalate is one of the metabolites from ethylene glycol metabolism).

Concentrations of both ethylene glycol and the major acidic metabolite, glycolate, are best determined by gas-chromatography or HPLC.



Calcium oxalate monohydrate crystals Urine sediment viewed under polarized light showing coarse, needle-shaped calcium oxalate monohydrate crystals. These crystals have a similar appearance to hippurate crystals. Courtesy of W Merrill Hicks, MD.



Calcium oxalate crystals Urine sediment showing both dumbbell-shaped calcium oxalate monohydrate (long arrow) and envelope-shaped calcium oxalate dihydrate (short arrows) crystals. Although not shown, the monohydrate crystals may also have a needle-shaped appearance. The formation of calcium oxalate crystals is independent of the urine pH. Courtesy of Frances Andrus, BA, Victoria Hospital, London, Ontario.

TABLE 32B-3 Ethylene Glycol Poisoning

MAJOR SYMPTOMS AND SIGNS	LABORATORY FINDINGS
Early	
Inebriation, drowsiness	Elevated osmolal gap
Coma, ataxia, CNS depression	Detectable ethylene glycol
Vomiting, nausea	
Delayed	
Dyspnea, hyperventilation, tachypnea	Acidosis with elevated anion gap
Kussmaul's respiration	Detectable ethylene glycol and metabolites
Coma, seizure, cerebral edema	Elevation of serum creatinine
Tetany, muscle paralysis, myoclonus	Elevation of blood urea nitrogen
Tachycardia, hypertension, dysrhythmias, myocarditis	Hypocalcemia
Acute renal failure	Elevation of creatine phosphokinase
Respiratory distress, noncardiogenic pulmonary edema	Hematuria, proteinuria, leukocyturia
Multiorgan failure	Calcium oxalate crystals in urine
Very Delayed (rare)	
Persistent renal insufficiency	
Cranial nerves deficiencies (including bilateral facial paralysis and ophthalmoplegia)	

Clinical Features

- Ethylene glycol poisoning often exhibits three distinct clinical phases, the severity and progression of which depends on the amount ingested:

1)The initial phase (CNS depression) 1 to 12 h after ingestion.

2)The second phase (cardiopulmonary phase) develops 12 to 24 h after ingestion.

3)The third phase (nephrotoxicity) occurs 24 to 72 h after ingestion.

The initial phase

- Patients may appear inebriated, with slurred speech and ataxia but without the odor of ethanol on their breath.
- Hallucinations, coma, seizures, and death may also occur during this initial phase.
- The optic fundus is usually normal, differentiating the syndrome from methanol poisoning, although nystagmus and ophthalmoplegia may be observed.
- Lumbar puncture may demonstrate elevated CSF pressure and protein and a few polymorphonuclear cells.

The second phase

- The second, cardiopulmonary phase develops 12 to 24 h after ingestion. Tachycardia, mild hypertension, and tachypnea are the most common symptoms;

- Congestive heart failure, acute respiratory distress syndrome, cardiomegaly, and circulatory collapse are also observed.

- Myositis has also been reported less commonly during this phase.

The third phase

- Early symptoms consist of flank pain. Oliguric renal failure and acute tubular necrosis.
- Complete anuria may occur, but most patients recover without renal damage if they receive appropriate therapy.

- Nephrotoxicity is caused by aldehyde metabolites and oxalic acid.

Clinical Features

- Hypocalcemia may develop secondary to precipitation of calcium as calcium oxalate and may be severe enough to cause tetany and prolongation of the QT interval.

- Elevated serum creatine phosphokinase levels may accompany and explain the generalized myalgias experienced by some patients.

Treatment Objectives

- Treatment of ethylene glycol poisoning involves three primary goals:
- **Correction of the patient's metabolic acidosis,**
- **Prevention of metabolism of the compound to its toxic metabolites,**
- **Removal of ethylene glycol and its toxic metabolites with hemodialysis, if necessary.**

Treatment Objectives

- Gastric lavage may be indicated if performed soon after ingestion, or in patients who are comatose or at risk of convulsions.
- Ipecac is considered contraindicated
- Charcoal is of little benefit as ethylene glycol is not significantly absorbed by activated charcoal; in cases of multiple chemical ingestions, however, it would be used for the co-ingestant(s)
- Because of the potential for CNS depression, airway protection may be indicated and respiratory support provided as needed. Intravenous (IV) fluids may be needed to correct electrolyte imbalance and to maintain adequate urine output.
- Urine output needs to be carefully monitored; however, if renal failure develops, IV fluids may need to be withdrawn to avoid fluid overload.

- **Pyridoxine and thiamine** may be administered to patients with ethylene glycol poisoning to promote alternate metabolism or conversion to nontoxic metabolites **glycine and alpha-hydroxy-beta-ketoadipate**; although, data supporting a beneficial effect of **pyridoxine and thiamine** is sparse.
- Calcium should not be given for hypocalcemia, as this may increase precipitation of calcium oxalate crystals in the tissues . However, in ethylene glycol poisoned patients, tetany and seizures may require treatment with IV calcium gluconate/chloride, as hypocalcemia is an important cause of these complications.

Treatment Objectives

- The dialysance of ethylene glycol and its major metabolite glycolate has been well established. **According to the traditional toxicology literature, hemodialysis should be considered in cases with a serum ethylene glycol concentration greater than 50 mg/dL .**
- Unfortunately, hemodialysis is not available in all hospitals. In the event of a serious poisoning where extracorporeal removal of ethylene glycol may be indicated, transferring the patient to a facility with renal dialysis capabilities should be considered.

- **Fomepizole**
- Fomepizole (4-methylpyrazole, Antizol®) rapidly and competitively inhibits alcohol dehydrogenase more potently than ethanol, and is now the antidote of choice in cases of methanol and ethylene glycol intoxication .

- Small studies or case series have documented dramatic improvements in acidemia and prevention of renal injury when fomepizole is used to treat methanol or ethylene glycol intoxication .

- Fomepizole also prolongs the half-life of ethanol; the simultaneous use of both agents therefore is **not** recommended. Preliminary data suggest that fomepizole is usually well tolerated but occasionally produces headache, nausea, bradycardia, dizziness, eosinophilia, or mild, transient elevation of liver enzymes.

Ethylene glycol (EG)	EG >20 mg/dL Suspicion of ingestion Suspicion and anion gap acidosis	Ethanol Loading dose: 10% ethanol in D5W at 10 mL/kg over 30 min* Infusion: 10% ethanol in D5W at 1.5 mL/kg per h to maintain ethanol level at 100–150 mg/dL† *or* Fomepizole 15 mg/kg over 30 min, then 10 mg/kg q12h‡ × 4 doses *and* Thiamine 100 mg IV Pyridoxine 100 mg IV 10% Calcium gluconate 10 mL IV for hypocalcemia $NaHCO_3$ 1 mEq/kg IV for severe acidosis