

Toxic Alcohols

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Case

- 19 male and his 17-year-old girlfriend present to ED at 3am.
- Male is obviously intoxicated, slurring his words and swearing at the triage nurse.
- Presenting complaint.... “my girlfriend can’t see”.
- Couple came from a party. Heavy drinking and marijuana consumption at the party.

Case

- Guy
 - Obnoxious, ongoing slurring and swearing
 - Vitals: T37.9, HR 110, RR 18, BP 120/80
 - O/E
 - Diaphoretic
 - H&N normal
 - CVS, Resp, GI normal
- Labs???

Labs on guy

- Glu: 99
 - Na 138
 - K 4.0,
 - BUN: 7
 - Cr: 0.7
- ABG:
 - PH:7.35
 - PCO2:35
 - PO2:55
 - HCO3:21
 - BE:-4

- Girl
 - Very sedated, vomited at triage
 - Vitals:
 - T: 37.8
 - HR: 112
 - BP: 115/70
 - RR: 28
 - Ph/E:
 - Eye exam: mydriasis, but uncooperative
 - CVS normal, resp normal, abdo tender diffusely
- Labs???

Labs on girl

- Glu: 110
- Na: 142
- K: 4.0
- BUN: 8
- Cr: 0.95
- ABG:
 - PH:7.25
 - PCO2:30
 - PO2:65
 - HCO3:14
 - BE:-10

Labs on girl

- Glu: 110
 - Na: 142
 - K: 4.0
 - BUN: 8
 - Cr: 0.95
- ABG:
 - **PH:7.25**
 - PCO2:30
 - PO2:65
 - **HCO3:14**
 - **BE:-10**

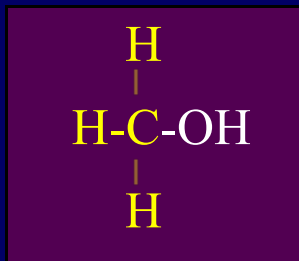
Case

- What's the girl's diagnosis?
- What do you want to do for her?
- What's the guy's diagnosis?
- What do you want to do for him?

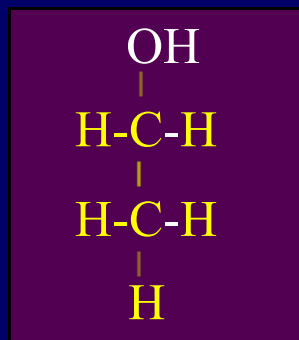
Case

- Further history....girl showed up at the party at 7pm, clearly intoxicated
- Rumours that prior to the party she had experimented with windshield wiper fluid in order to “get drunk fast”, as did another girl
- At the party, she consumed 5 beer
- At 2 am she started to complain of blurred vision.

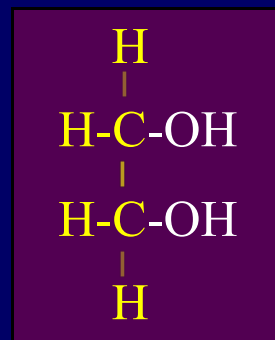
Alcohols: R-OH



Methanol
1C



Ethanol
2C



Ethylene
Glycol
2C

Toxic Alcohols

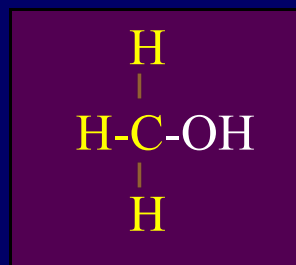
- “Toxic”
 - Generally reserved for any alcohol other than ethanol.
- A few mouthfuls can kill:
 - Average adult mouthful: 0.42cc/kg
 - **Lethal** dose of methanol: 1.2cc/kg
 - **Lethal** dose of ethylene glycol: 1.4-1.6cc/kg

Methanol

- Paint removers, solvents, varnishes, windshield washing fluid
- Well absorbed from the GI tract
- Peak levels 30-90 minutes after ingestion
- Presentation may be delayed 12-18 hours (longer if EtOH co-ingested)
- Toxicity is the result of the metabolites
 - Formaldehyde & formate
 - Cause optic papillitis and retinal edema---> blindness
 - Inhibits mitochondrial respiration---> lactic acidosis

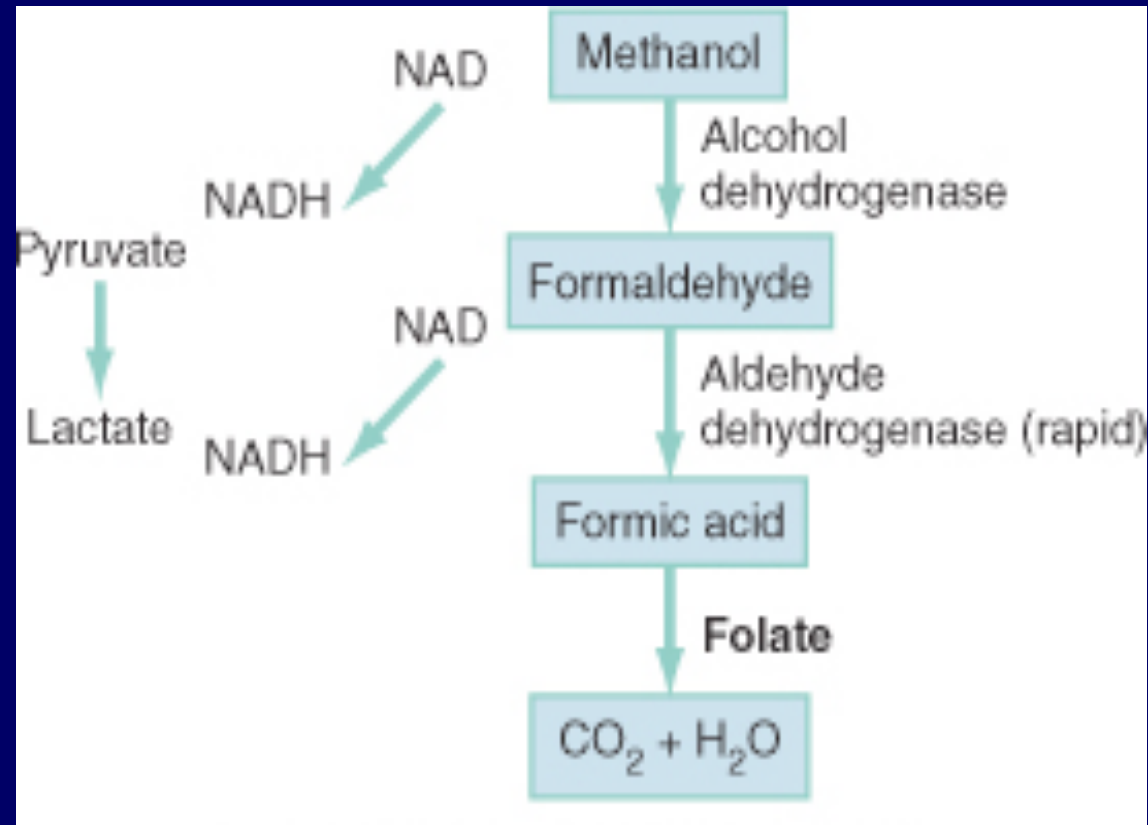
Methanol

- Molecular weight 32
- Low freezing point
- Highly volatility

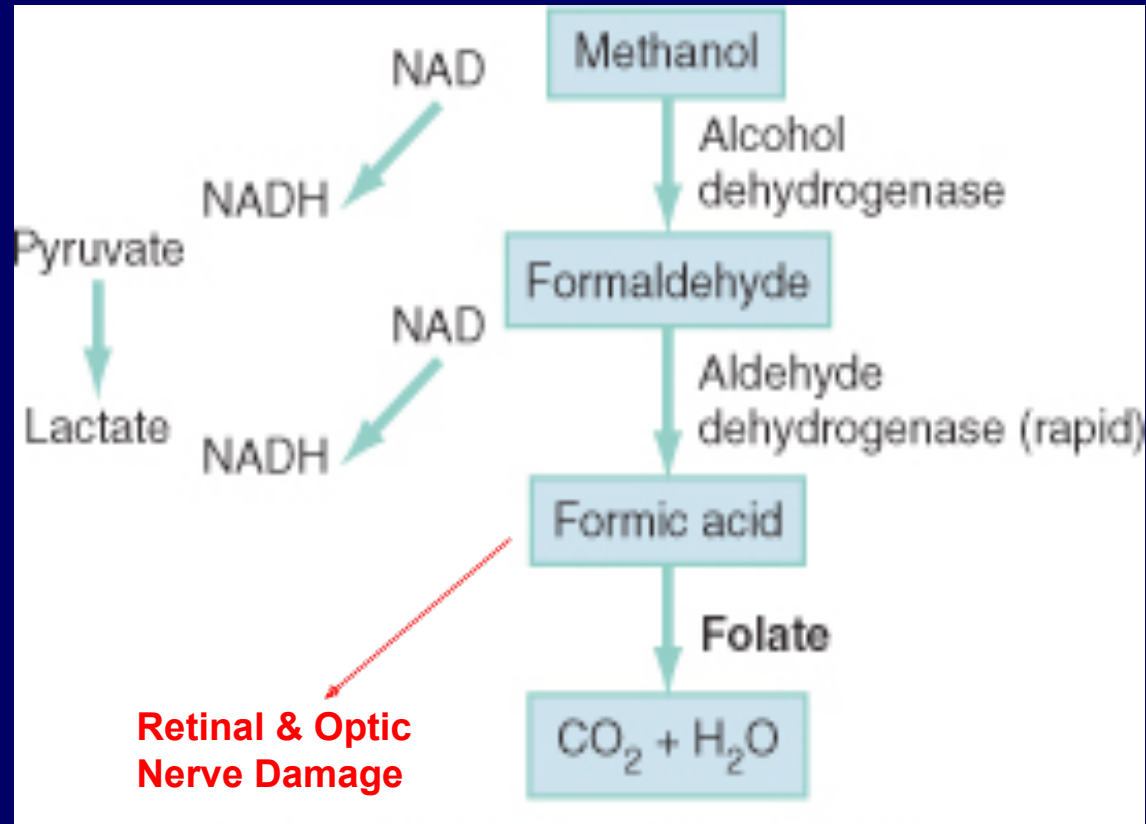


Methanol

Methanol Metabolism

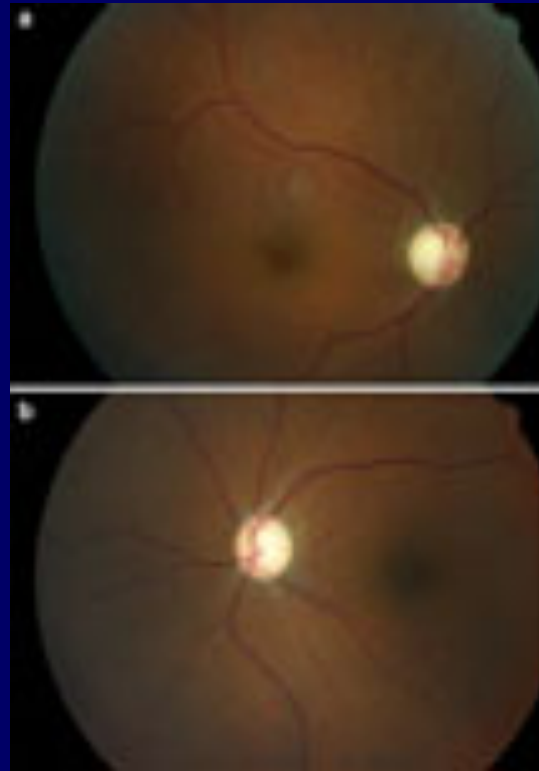


Methanol Metabolism



Methanol

- Clinical presentation
 - CNS Depression
 - Seizures
 - Visual Disturbances
 - Abdominal Pain
 - Nausea
 - Vomiting
 - AG Metabolic Acidosis
 - Osmolar Gap



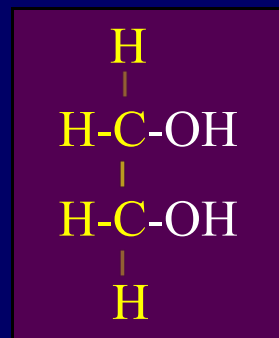
Methanol Toxicity

- CNS depression
 - Bilateral hemorrhage putamen
- Abdominal pain
- Multisystem organ failure



Ethylene Glycol

- Molecular Weight 62
- Low Volatility
- High boiling point



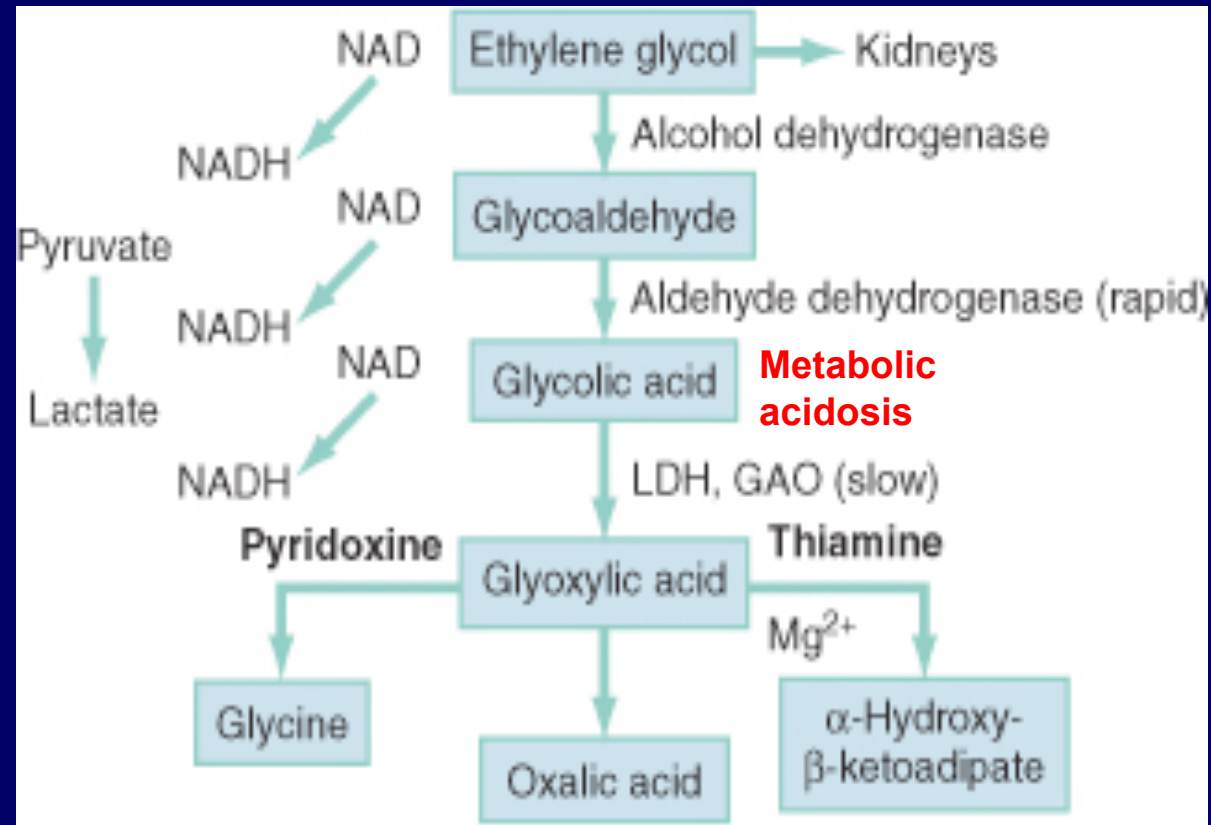
Ethylene
Glycol

Ethylene Glycol

- Coolant/Antifreeze
- Solvents
- De-Icer



Ethylene Glycol Metabolism



Stages of EG toxicity

- Phase 1 (1-12 hours post ingestion)
 - CNS depression (inebriation, hallucinations, coma, seizures)
- Phase 2 (12-24 hours post ingestion)
 - Cardiopulmonary phase (tachycardia, tachypnea, mild hypertension, CHF, ARDS, cardiomegaly, circulatory collapse)
- Phase 3 (24-72 hours post ingestion)
 - Nephrotoxicity (CVA tenderness, oliguria, ATN)
- Phase 4 (6-12 days)
 - Delayed CNS (Cranial neuropathies, motor deficits, cognitive deficits)

EG & Methanol Tx Approach

- ADH blockage.
- Alkalinization.
- Accelerate Elimination.
- Adjuncts:
 - Folic/Folinic Acid
 - Thiamine
 - Pyridoxine.
- Supportive treatment:
 - Seizures.
 - IV Calcium for Symptomatic Hypocalcemia

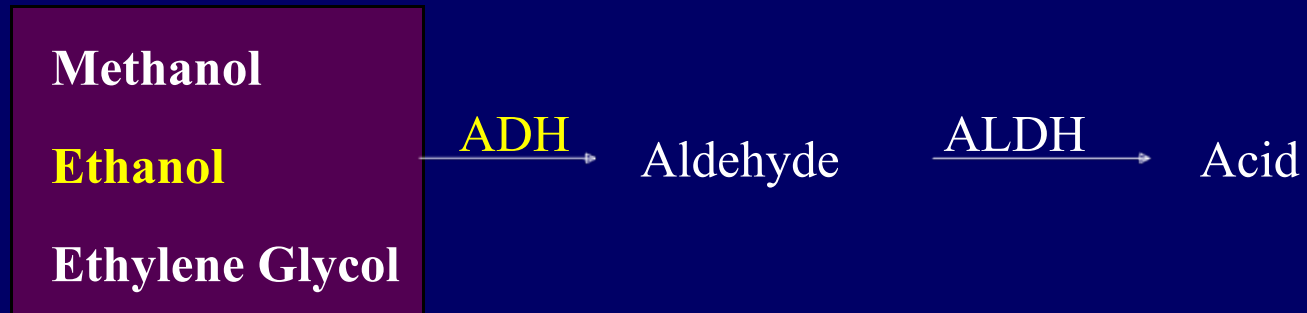
GI decontamination

- EG/Methanol are very Rapidly Absorbed.
- AC ---NO Role / Except in Concomitant ingestion.

ADH Inhibition

- Prevents conversion of parent alcohol to its toxic metabolites.
- ADH inhibition doesn't help once the toxic metabolites are formed.
- 2 options
 - **EtOH**
 - 65X more affinity for ADH than EG
 - 10-20X more affinity for ADH than methanol
 - **Fomepizole**
 - 500-1000 X more affinity for ADH than EtOH

Treatment



- Ethanol more avid for ADH
 - 65X more avid than Ethylene Glycol
 - 10-20X more avid than Methanol

EtOH

- Load
 - 8-10ml/kg of **10%** solution IV in D5W over 30 min.
 - Patients receiving IV ethanol require ICU monitoring.
- Maintenance
 - 0.8- 2 ml/kg/h
 - With dialysis: 3 mL/kg/h
- Monitor levels q1h
- Goal: 100-120mg/L EtOH Serum level
- Continue until EG/Methanol levels are undetectable
 - T1/2 is increased with ethanol
 - EG 11-18h, Methanol 30-52 h

EtOH

- Complications of infusion

- Hypotension.

- Respiratory depression.

- Flushing.

- Hypoglycemia.

- Hyponatremia.

- Pancreatitis.

- Gastritis.

- Inebriation.

- Patients receiving IV Ethanol require ICU monitoring

- Orally administered ethanol is effective, and may be considered when ICU is unavailable.

- Rural areas where there may be a significant delay in getting the patient to another hospital.

- IV and Oral dose are same but in oral route can give 20% preparation and should be consider GI prophylaxis.

Fomepizole (4-methylpyrazole)

- Load
 - 15mg/kg IV in 250 cc NS or D5W over 30 min
- Maintenance
 - 10mg/kg IV q12h X 4 doses
 - Then 15mg/kg q12h until EG/methanol levels <3.2mmol/L
- Don't need to monitor levels & no ICU monitoring
- Expensive (~\$1000 per 1.5g vial)
 - Average 4 vials per patient
- Previous EtOH intake does not decrease efficacy
- T1/2 is increased
 - EG 20h; methanol 54h

Ethanol

Fomepizole

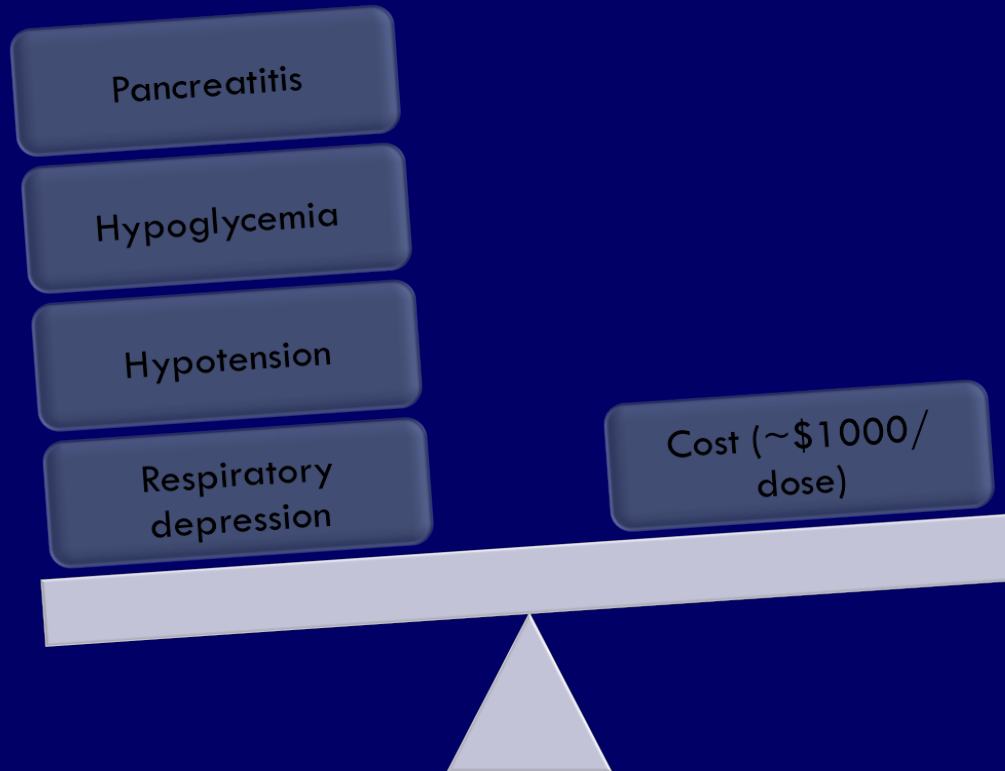
Pancreatitis

Hypoglycemia

Hypotension

Respiratory
depression

Cost (~\$1000/
dose)



NaHCO₃

- Rationale

- EG metabolized to glycolate, glyoxalate & oxalate.
- Methanol metabolized to formate.
- Acidemia leads to protonation of these metabolites & makes them more likely to penetrate end-organ tissues
- **Bicarb Deprotonates them, making them Less Toxic.**

- Issues

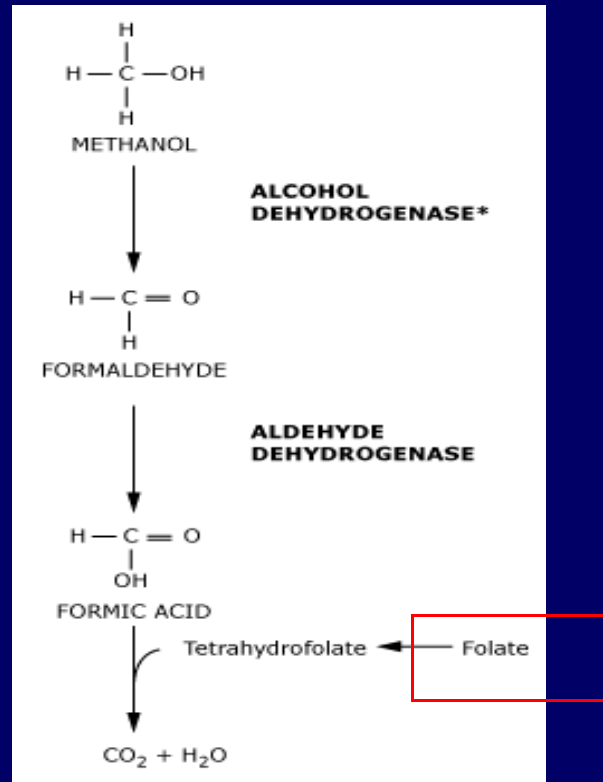
- No clear evidence for how bicarb should be given

NaHCO₃

- 1-2 mEq/kg bolus for pH < 7.3,
- Then infusion (133meq /3Vials NaHCO₃ in 1L D5W) to maintain pH >7.35
- American Academy of Clinical Toxicology Practice Guidelines on the treatment of Methanol Poisoning. J Toxicol Clin Toxicol 2002

Adjuncts

- Folinic acid
 - 50mg IV
- Folic acid
 - 50mg IV q6h for methanol
- How about for EG?
- Perhaps a better question is....Does ethylene glycol metabolism produce formate?



Adjuncts

- Thiamine & Pyridoxine
 - MOA: involved in the metabolism of glyoxylic acid to non-toxic substrates

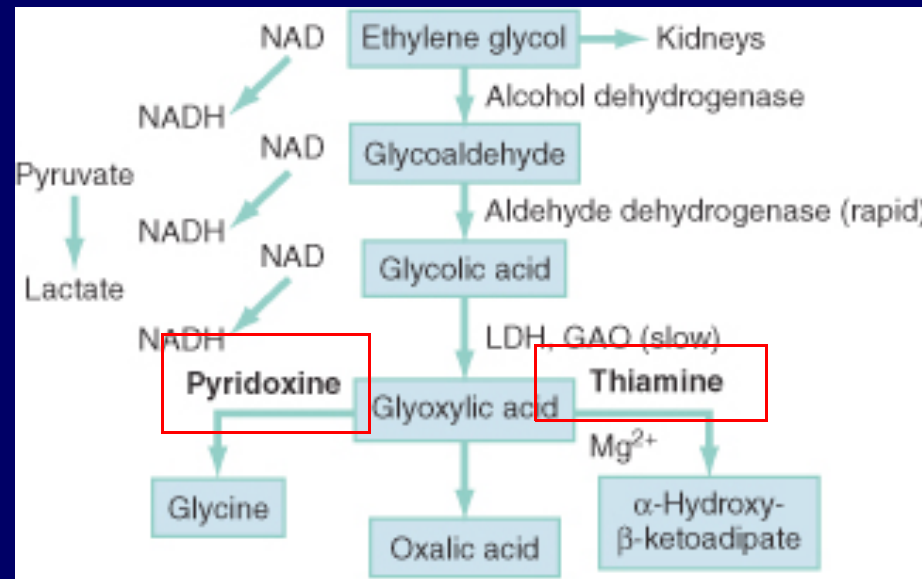
Theoretical benefit with
some indirect evidence

Cheap! So use them!

Dose:

Thiamine 100mg IV

Pyridoxine 100 mg IV



Hemodialysis

- Intensive Care Med (2005) 31: 189-195

Ethylene glycol poisoning:

Arterial pH $<7.10^9$ or 7.25–7.30 [16]

Drop in arterial pH >0.05 resulting in a pH outside the normal range despite bicarbonate infusion

Inability to maintain arterial pH >7.3 despite bicarbonate therapy

Decrease in bicarbonate concentration >5 mmol/l, despite bicarbonate therapy

Renal failure (serum creatinine concentration >265 $\mu\text{mol/l}$ or rise in the serum creatinine by >90 $\mu\text{mol/l}$ [10])

Deteriorating vital signs despite intensive supportive care

Initial plasma e.g., concentration ≥ 0.5 g/l (8.1 mmol/l) unless fomepizole is administered in the absence of both renal dysfunction and significant acidosis^a

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Visual impairment

Renal failure

Deteriorating vital signs despite intensive supportive care

Initial plasma methanol concentration ≥ 0.5 g/l (15.6 mmol/l)^a

Rate of methanol decline <0.1 g/l (3.1 mmol/l) per 24 h

^a The recommendation for routine hemodialysis on the basis of serum concentrations alone has been recently called into question

Hemodialysis

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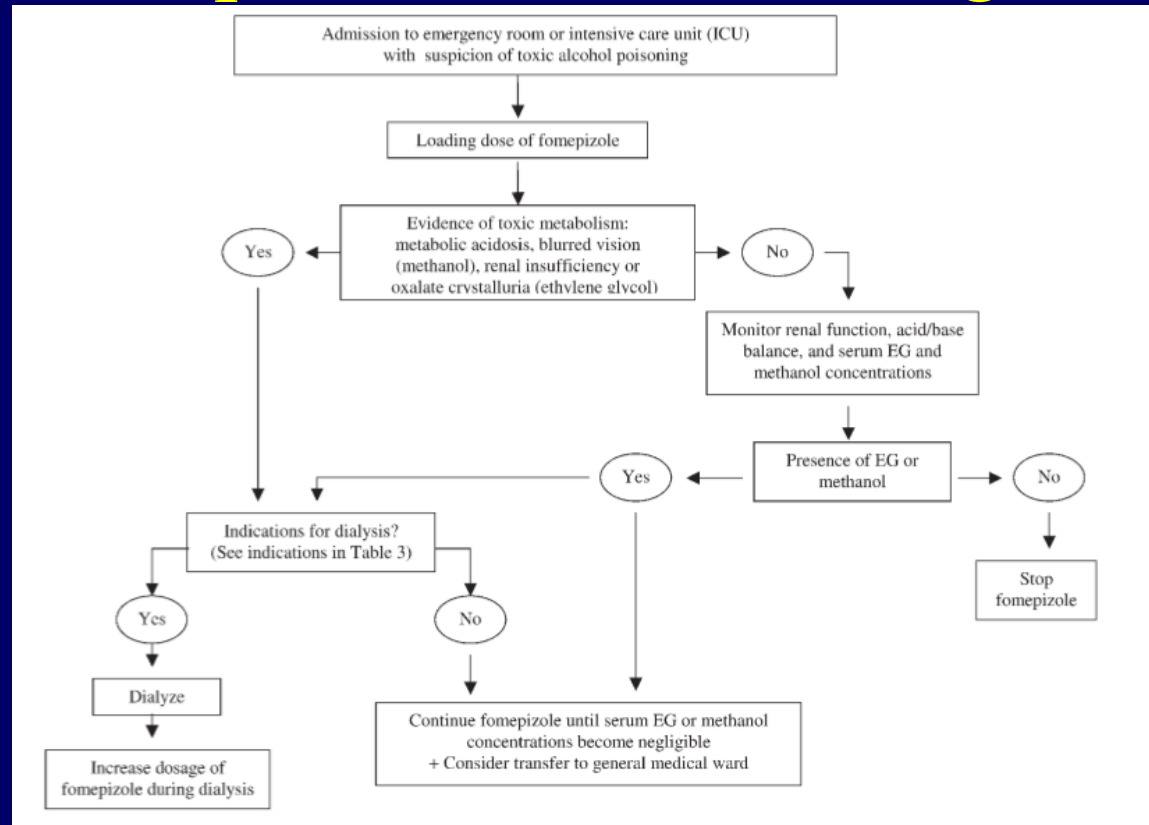
Indications of Hemodialysis

- Refractory metabolic acidosis:
 - $\text{PH} < 7.25$
 - $\text{AG} > 30 \text{ mEq/L}$
 - $\text{Base Deficit} < -15$
- *Visual abnormality*
- Renal insufficiency
- Deteriorating VS despite aggressive therapy
- Refractory Electrolyte abnormality
- Serum methanol or EG $> 50 \text{ mg/dl}$

Hemodialysis

- Special considerations
 - Fomepizole is dialyzable
 - European recommendation: continuous infusion 1mg/kg/h
 - USA manufacturer recommends q4h administration
- Endpoints
 - Serum pH normal
 - Parent alcohol concentration $<3.2\text{mmol/L}$
 - Resolution of the osmolar gap

Proposed Treatment Algorithm



Care Med

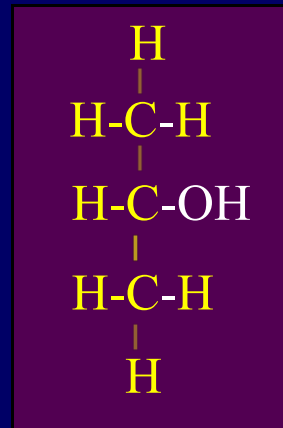
(2005) 31:189–195

Isopropyl Alcohol

- Disinfectant, solvent.
- Typically comprises 70% “rubbing alcohol”.
- When ingested, functions as a CNS depressant and inebriant.
- Fatality is rare.
- Does NOT cause:
 - High Anion Gap Acidosis
 - Retinal Toxicity (as does Methanol)
 - Renal Failure (as does EG)

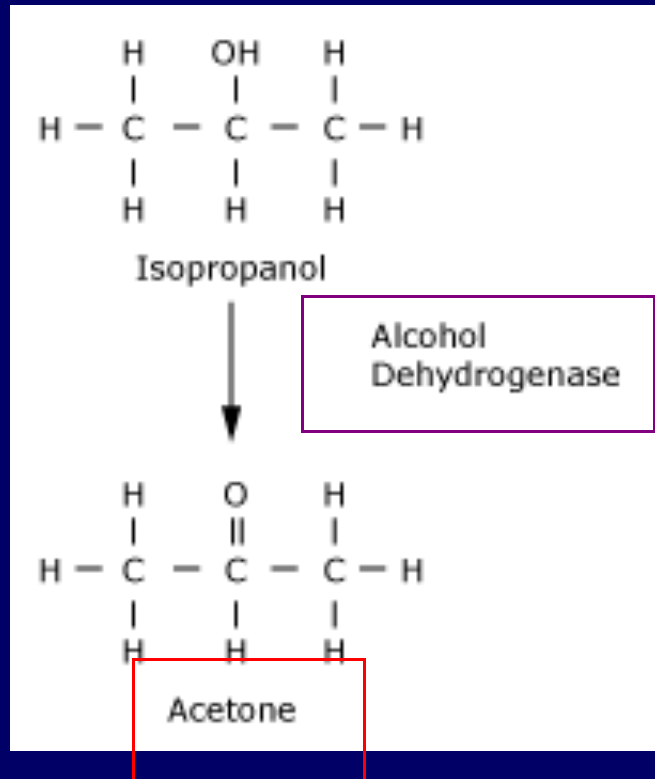
Isopropanol

- Metabolized to Acetone
- No acidosis
- Supportive care



Isopropanol
3C

Isopropyl Alcohol



- Acetone
 - Mild CNS Depressant
 - Responsible for marked Ketosis

Isopropyl Alcohol

- Clinical (Symptoms peak at 1 hour)
 - Inebriation w/ disinhibition--->sedation--->stupor--->coma
 - Nausea, vomiting, abdominal pain
 - Hemorrhagic Gastritis
 - Fruity breath (acetone)
- The metabolite (acetone) causes much less sedation therefore expect clinical improvement with time

Laboratory

- Serum isopropyl alcohol levels & Acetone
- Elevated Osmolar Gap
- Urine & Serum Ketones
- Lytes, BUN, Cr, Blood Gas

Treatment

- Supportive (ABC's)
 - Consider intubation if patient unable to protect airway
 - GI prophylaxis
- Decontamination: no real role
- ADH inhibition: no indication