Toxic Alcohols

BADR ALDAWOOD, FRCPC

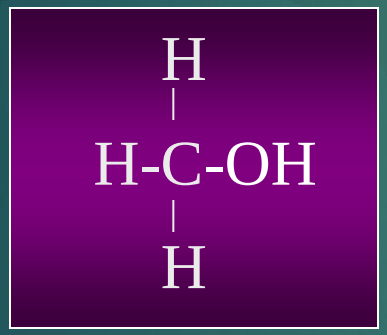
MARCH, 2019

Outline

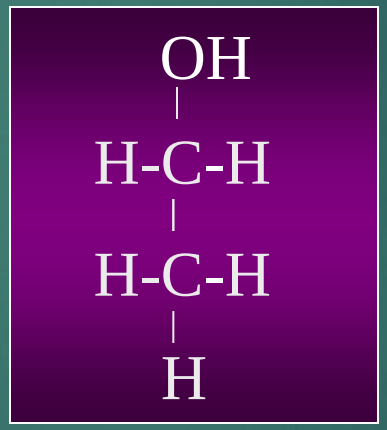
- Biochemistry
- Ethanol
- Methanol
- Ethylene Glycol
- Isopropanol

Alcohols molecular structure?

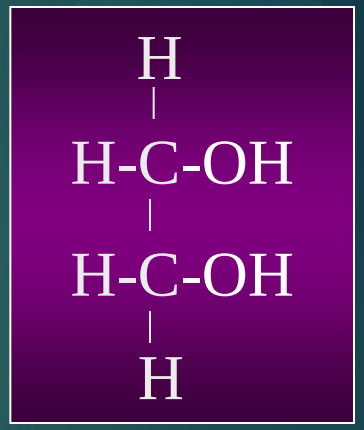
Alcohols: R-OH



Methanol
1C

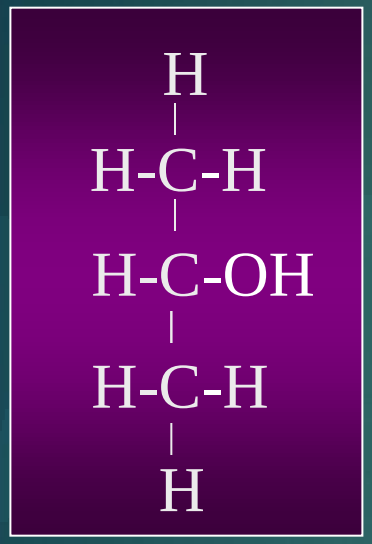


Ethanol
2C

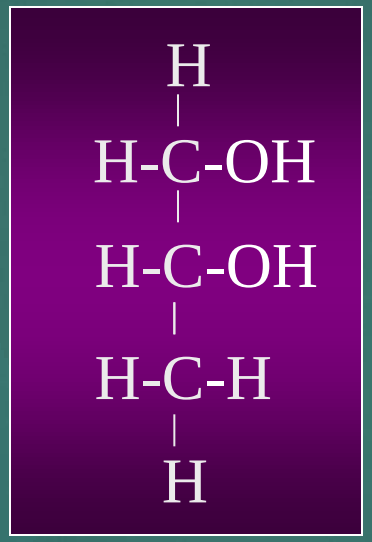


Ethylene Glycol
2C

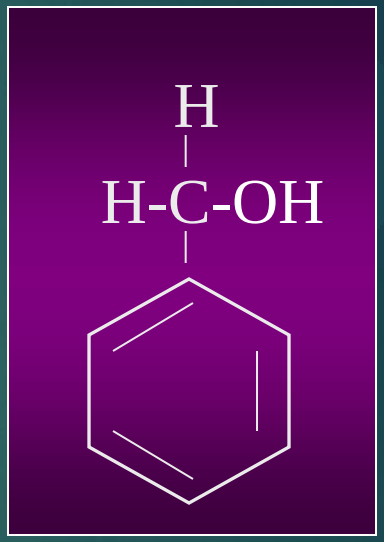
Alcohols: R-OH



Isopropanol
3C



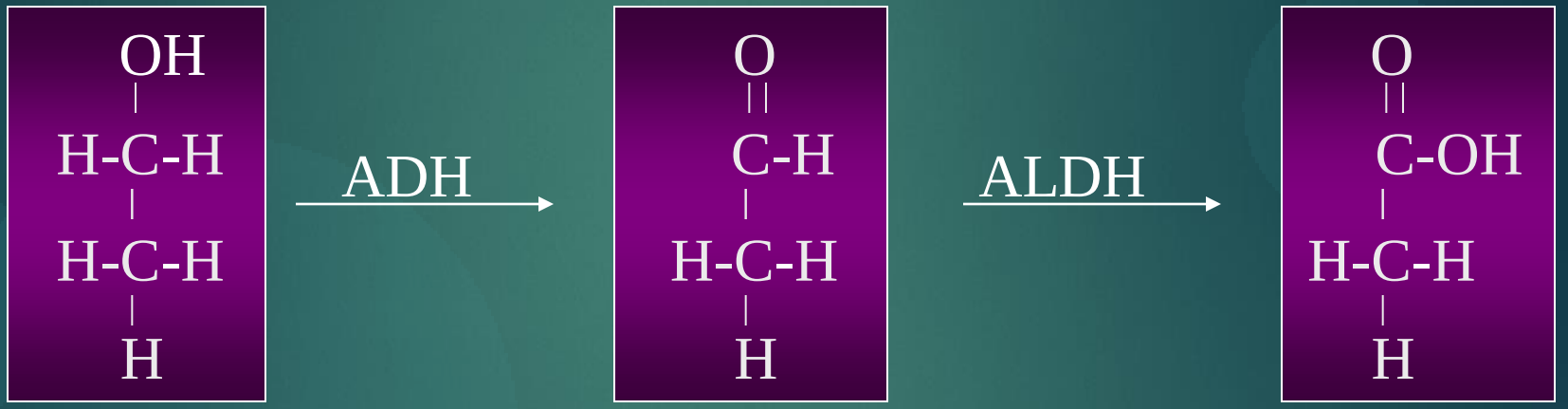
Propylene Glycol
3C



Benzyl Alcohol

Ethanol Metabolism ?

Ethanol Metabolism ?



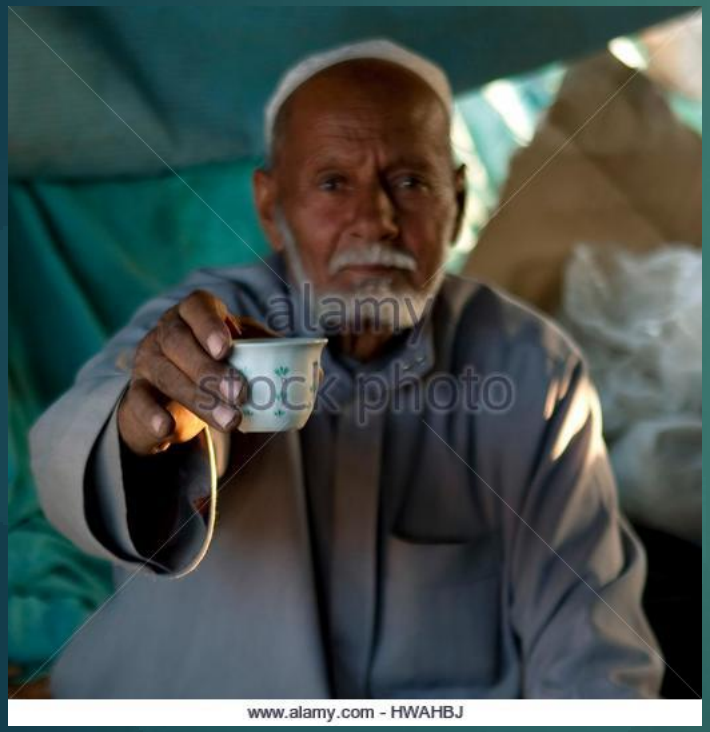
Ethanol **Acetaldehyde** **Acetic Acid**

ADH = Alcohol Dehydrogenase
ALDH = Aldehyde Dehydrogenase

Ethanol Toxicity

- Most commonly abused drug in the world
- Majority of morbidity and mortality is due to trauma owing to impaired cognitive function
- Rate of metabolism 20 mg/dL/h

Which one will get intoxicated from one can of beer?



Blood ethanol levels correlate poorly with the degree of intoxication (Tolerance)

Ethanol Toxicity clinical presentation ?

Ethanol Toxicity clinical presentation ?

- Disinhibited behavior
- Slurred speech
- Impaired coordination
- Later: Respiratory and (CNS) depression

Ethanol Toxicity work up?

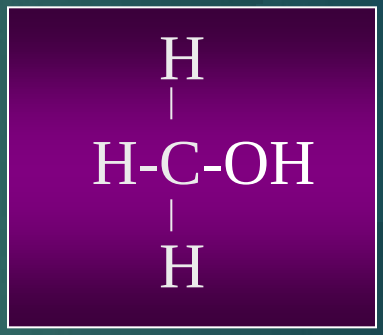
- Ethanol levels
- ABG/VBG
- Renal profile/Lytes
- Don’t miss possible injuries (TRAUMA)

Ethanol Toxicity Treatment?

- Observation
- IV Fluid Hydration (?Alcoholic Ketoacidosis)
- Thiamine ?
- Discharge the patient once sober

Methanol

- Molecular weight 32
- Low freezing point
- Highly volatile



Methanol

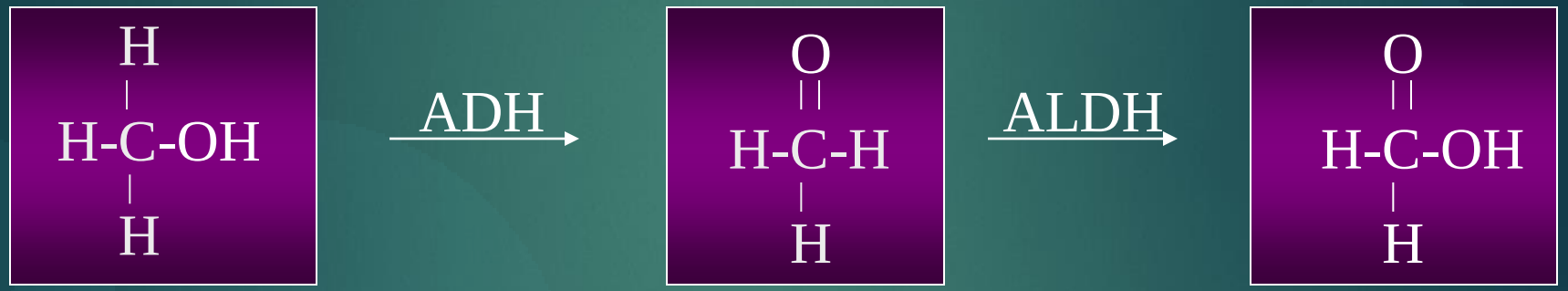
Methanol containing products?

Methanol containing products?

- Gas Line Antifreeze 100%
- Windshield washer fluid 30%
- Varnish removers
- Fuel for food warming 3-70%
- Industrial uses

Methanol Metabolism?

Methanol Metabolism



Methanol **Formaldehyde** **Formic Acid**

ADH: Alcohol Dehydrogenase
ALDH: Aldehyde Dehydrogenase

Methanol Toxicity ?

Methanol Toxicity

- Delayed onset (8-12hrs)
- CNS depression, Ataxia, Confusion
- Abdominal pain
- Multisystem organ failure

Methanol Toxicity

- Visual complaints
  - Retinal damage
  - “Snow storm”
- Anion gap acidosis
  - Tachypnea

Yang CS et al Eye 2005;19:806-809

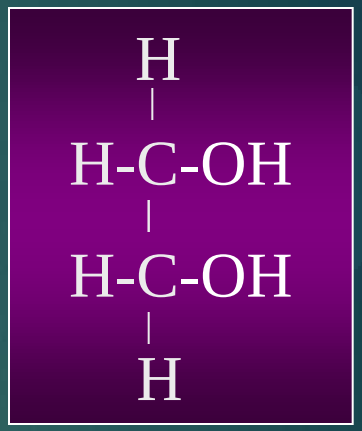
Methanol work up?

Methanol work up?

- ABG/VBG
- Osmolality
- Serum levels
- Lactate
- Renal profile
- Ethanol level

Ethylene Glycol (EG)

- Low Volatility
- Low freezing point
- High boiling point



Ethylene Glycol

Ethylene Glycol containing products?

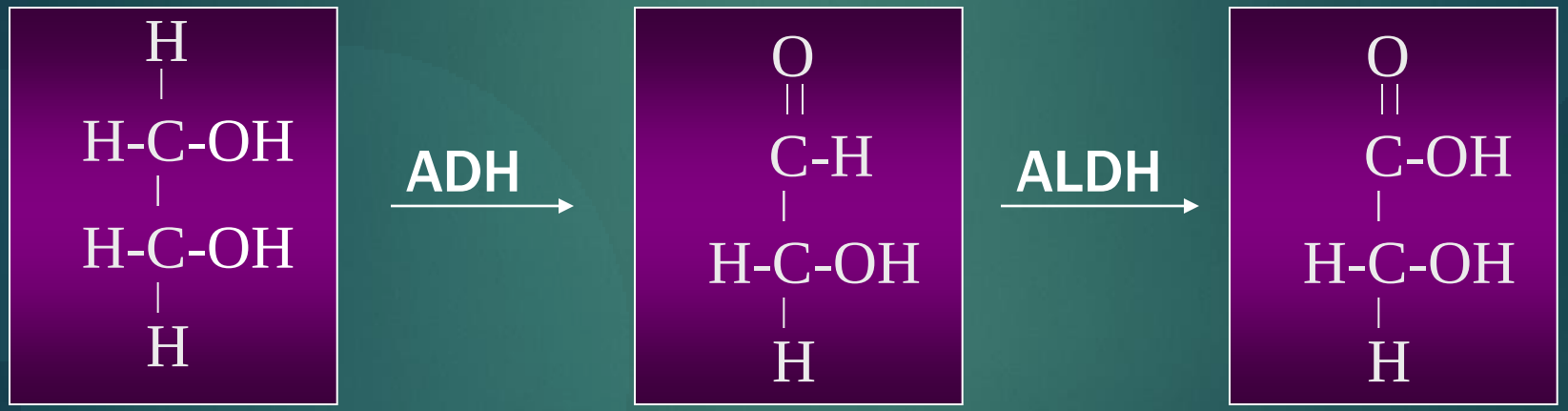
Ethylene Glycol

- Coolant/Antifreeze

- Solvents

Ethylene Glycol Metabolism?

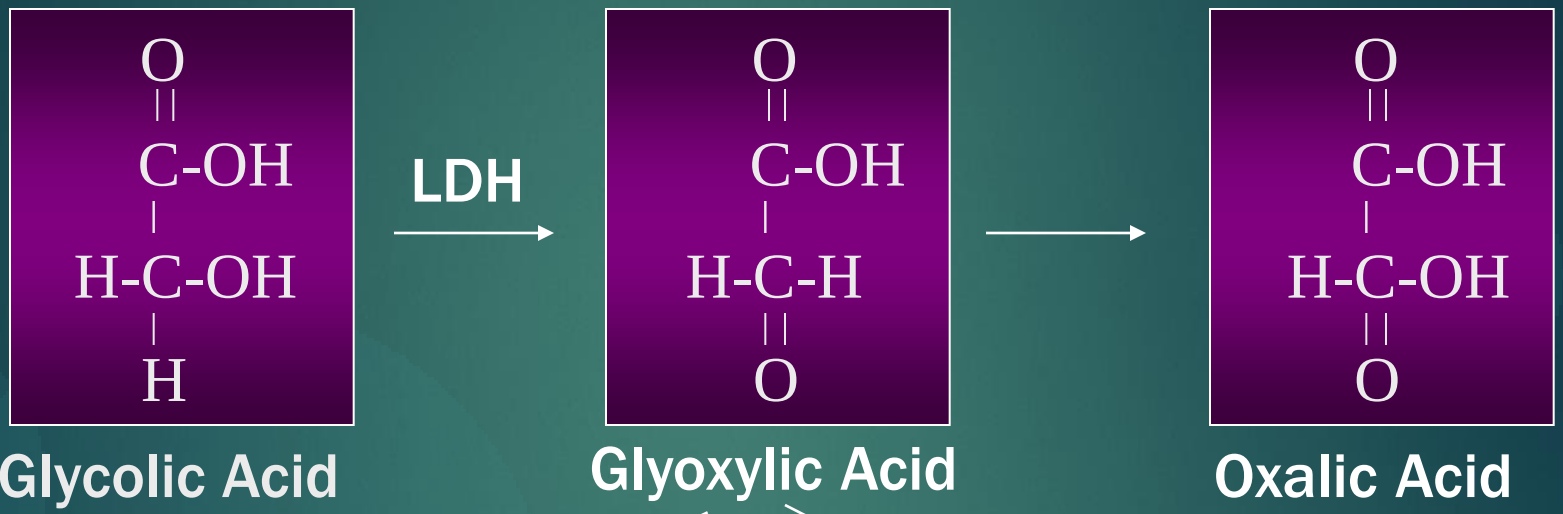
Ethylene Glycol Metabolism



Ethylene Glycol **Glycoaldehyde** **Glycolic Acid**

ADH = Alcohol dehydrogenase
ALDH = Aldehyde dehydrogenase

Ethylene Glycol Metabolism



LDH = Lactate dehydrogenase

Ethylene Glycol Toxicity ?

Ethylene Glycol Toxicity

- Onset 4-6 hours
- Anion gap acidosis
  - Tachypnea

Ethylene Glycol Toxicity

- Abdominal pain
- Hypocalcemia ?
- Calcium oxalate crystals in urine
- Renal failure (Calcium Oxalate)

Toxicity tests Methanol/EG

- Ethylene glycol:
  - Limited utility of fluorescence of urine
  - May note crystals in urine using Woods lamp
- Methanol
  - Hyperemic retina or visual complaints

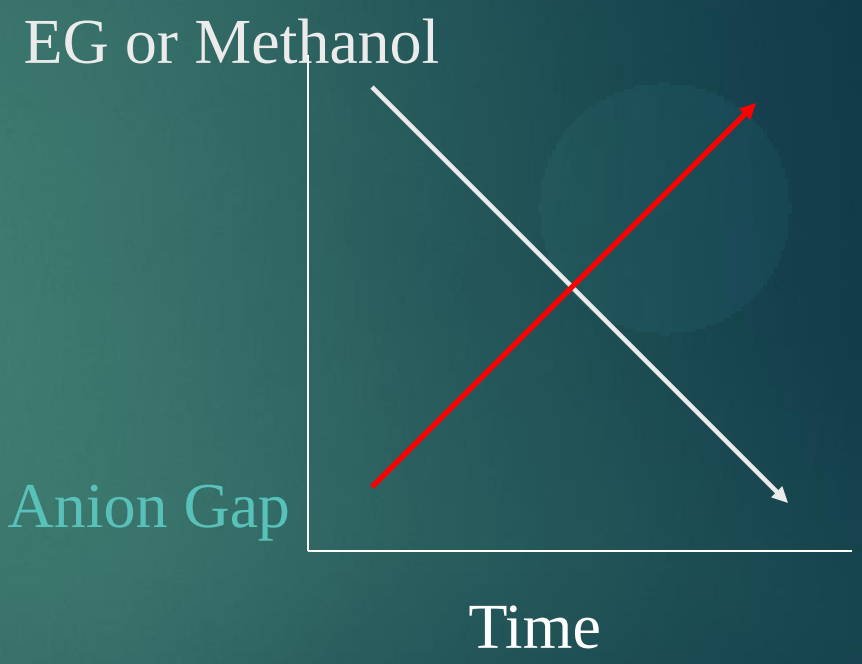
Identifying Patients for Treatment: Methanol/EG

- Serum ethylene glycol or methanol level

- Action level for treatment:
  - Methanol / EG > 25 mg/dL
  - Any level with acidosis

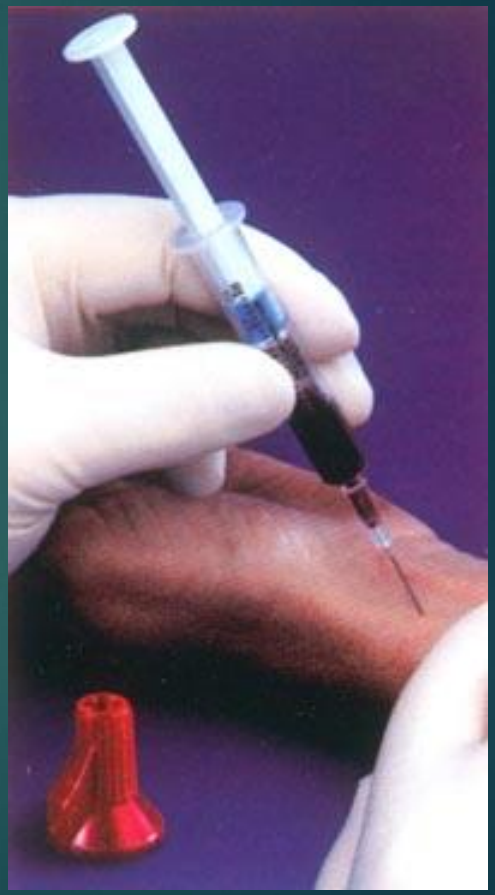
Limits of Serum Levels

- Useful prior to onset of acidosis or in massive overdoses
- Parent compound not directly toxic
- Levels not universally available



Arterial Blood Gas/Lactate

- Acidosis indicates advanced poisoning
- Lactate usually low*
- Patients with acidosis should receive treatment



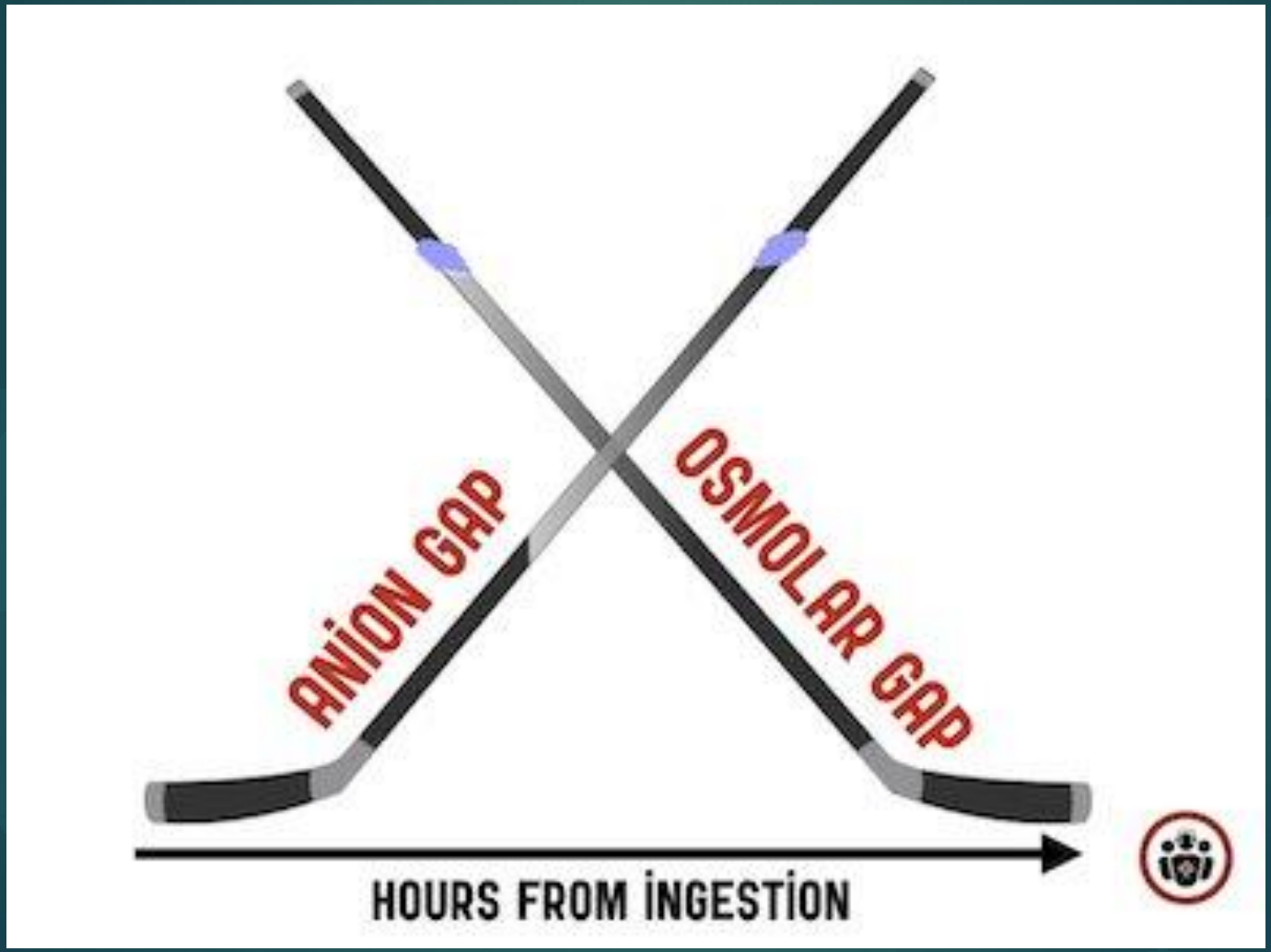
Osmol Gap ?

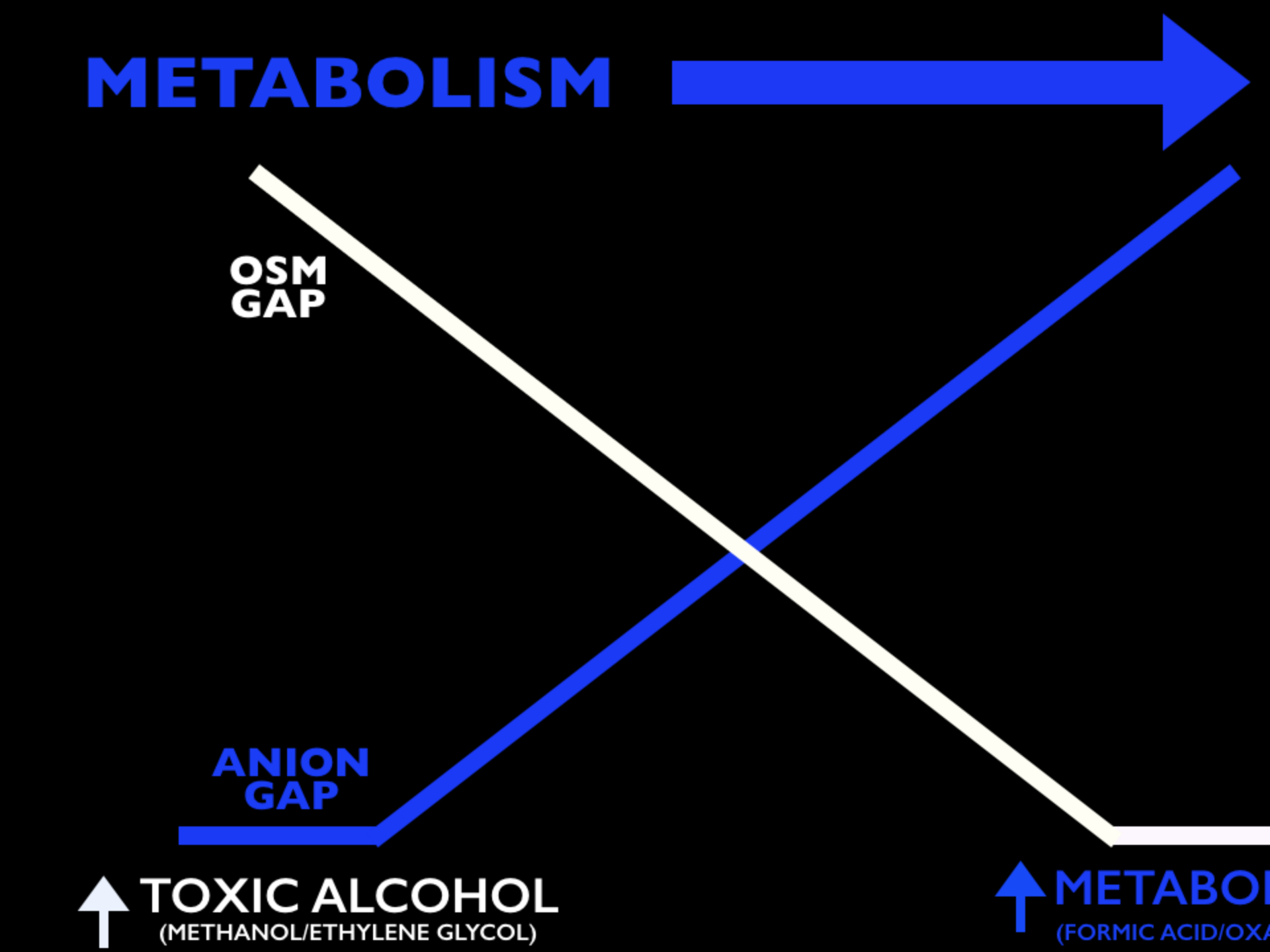
Osmol Gap ?

- Osmol Gap = Measured Osmols - Calculated Osmols
- Calculated:

  2 Na + BUN + Glucose + 1.25 Ethanol

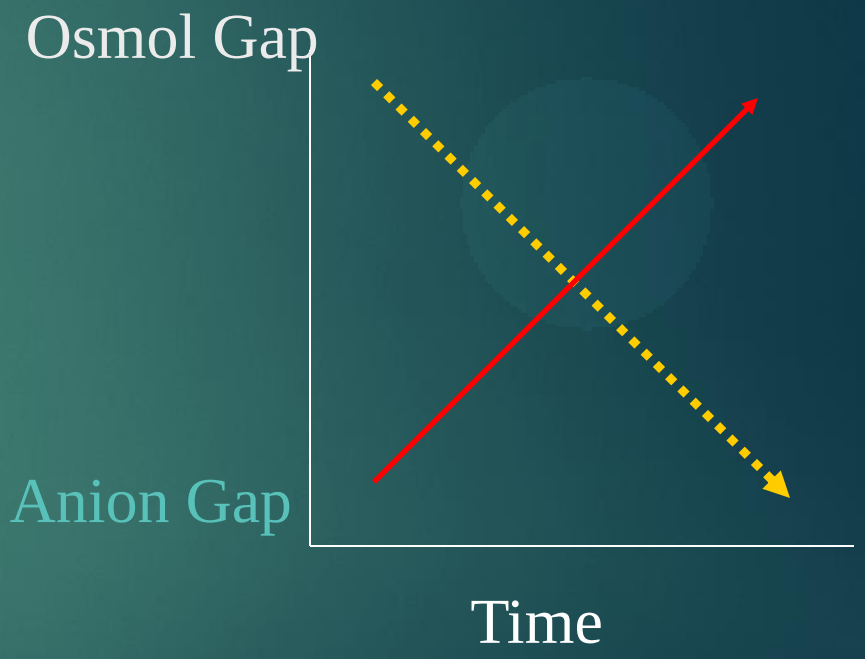
- Lab Measurement


ANION GAP
OSMOLAR GAP
HOURS FROM INGESTION


METABOLISM
OSM GAP
ANION GAP
TOXIC ALCOHOL
(METHANOL/ETHYLENE GLYCOL)
METABOL
(FORMIC ACID/OXA

Osmol Gap: Limitations

- **Roughly the gap should be < 10**
- Normal Osmol Gap in setting of poisoning **does not rule out a treatable level**
- Osmol Gap diminishes as parent compound is metabolized



Treatment

Treatment

- Limit absorption: → NG Tube Suction
- Prevent metabolism of parent compound to toxic metabolite → ADH Inhibition
- Enhance elimination → Substrates/Other
  - Parent
  - Metabolites

  → Hemodialysis
- Correct Derangements

Antidotal Therapy

Antidotal Therapy: Ethanol

- Serum ethanol inhibits metabolism:
  - EG
  - Methanol
- Onset of toxicity EG/Methanol may be delayed

Treatment

- Ethanol more avid for ADH
  - 6-8 X more avid than ethylene glycol
  - 4 X more avid than methanol

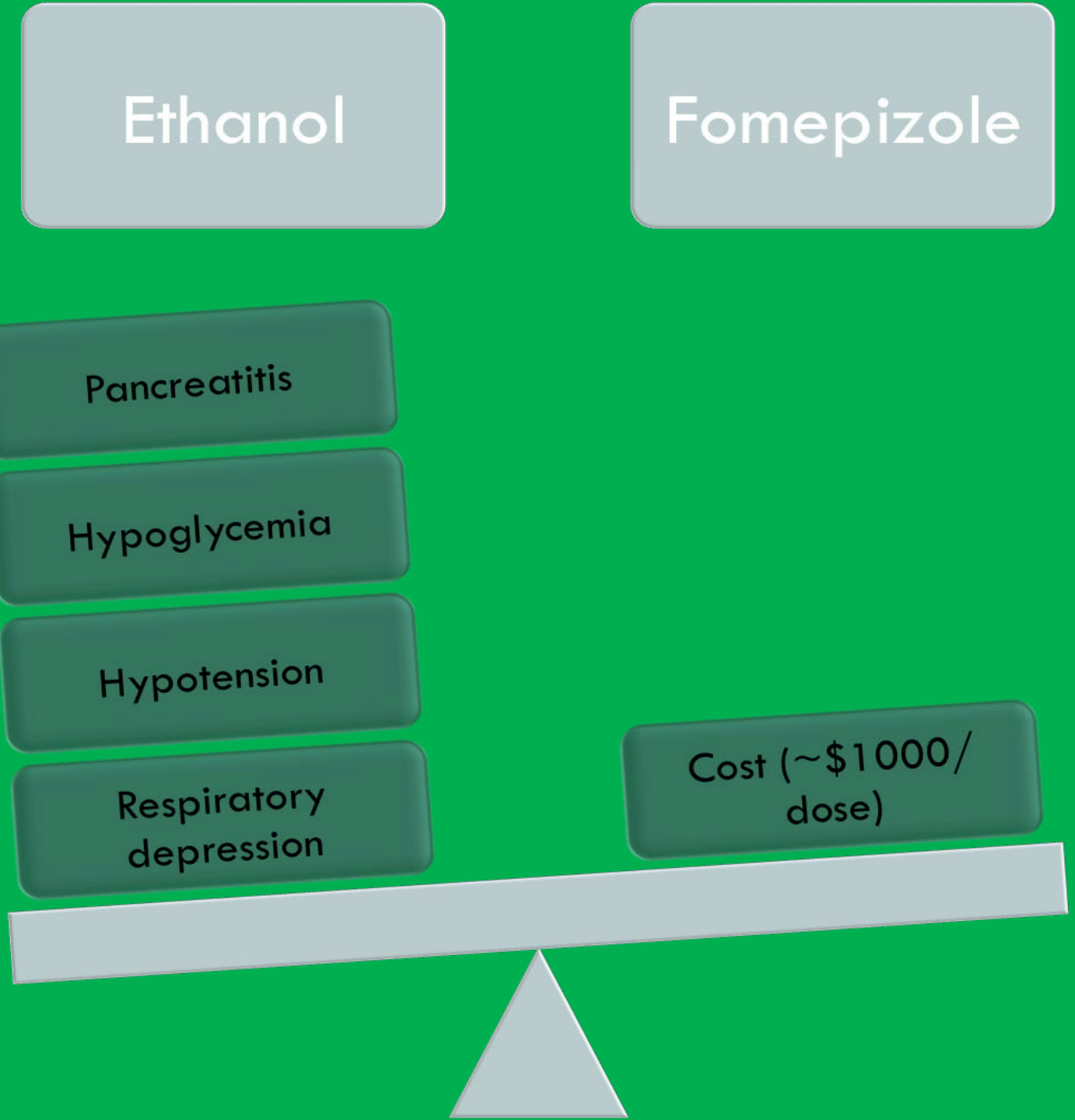
Ethanol Infusion: Management

- Serial ethanol levels
- Watch glucose* and sodium*
- Observe for respiratory status*

* Especially in children

1st line Antidote Fomepizole

- A blocker of alcohol dehydrogenase
- Has replaced ethanol as the agent of choice in known or suspected exposures
- Minimal adverse effects


Ethanol
Fomepizole
Pancreatitis
Hypoglycemia
Hypotension
Respiratory depression
Cost (~$1000/ dose)

Hemodialysis ??

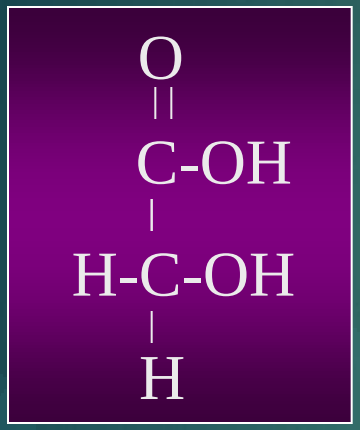
Hemodialysis

- Consult nephrology early in acidemic patients
- Levels toxic alcohol $\geq$ 25 mg/dL

Adjuncts for Methanol Poisoning

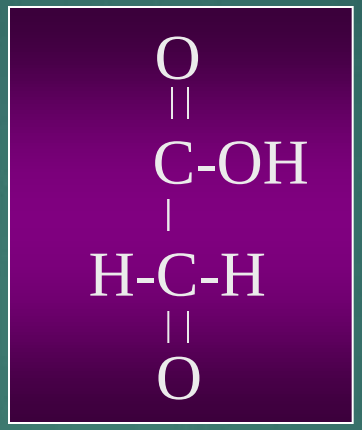
- **Sodium bicarbonate**
  - pH < 7.30
  - Can ion trap formic acid in urine and enhance elimination
- **Folate administration**
  - Facilitates conversion of one carbon fragments to CO_2

Adjuncts for Ethylene Glycol Poisoning

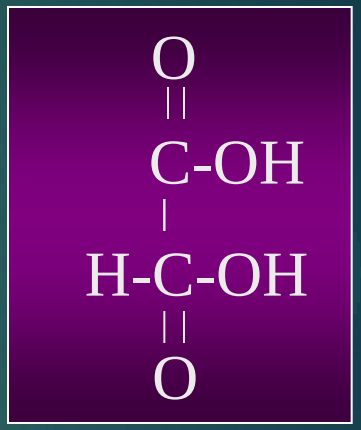


Glycolic Acid

LDH



Glyoxylic Acid



Oxalic Acid

B_1, Mg^{2+}

B_6

α-OH-β Ketoadipic Acid

Glycine + Benzoic Acid

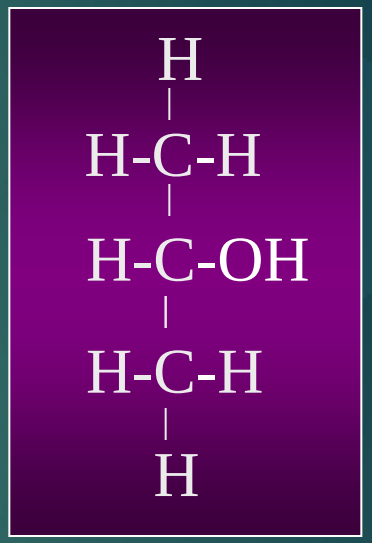
LDH = Lactate dehydrogenase

Adjuncts for Ethylene Glycol Poisoning

- To enhance metabolism away from oxalates*
  - Thiamine (B1)
  - Pyridoxine (B6)

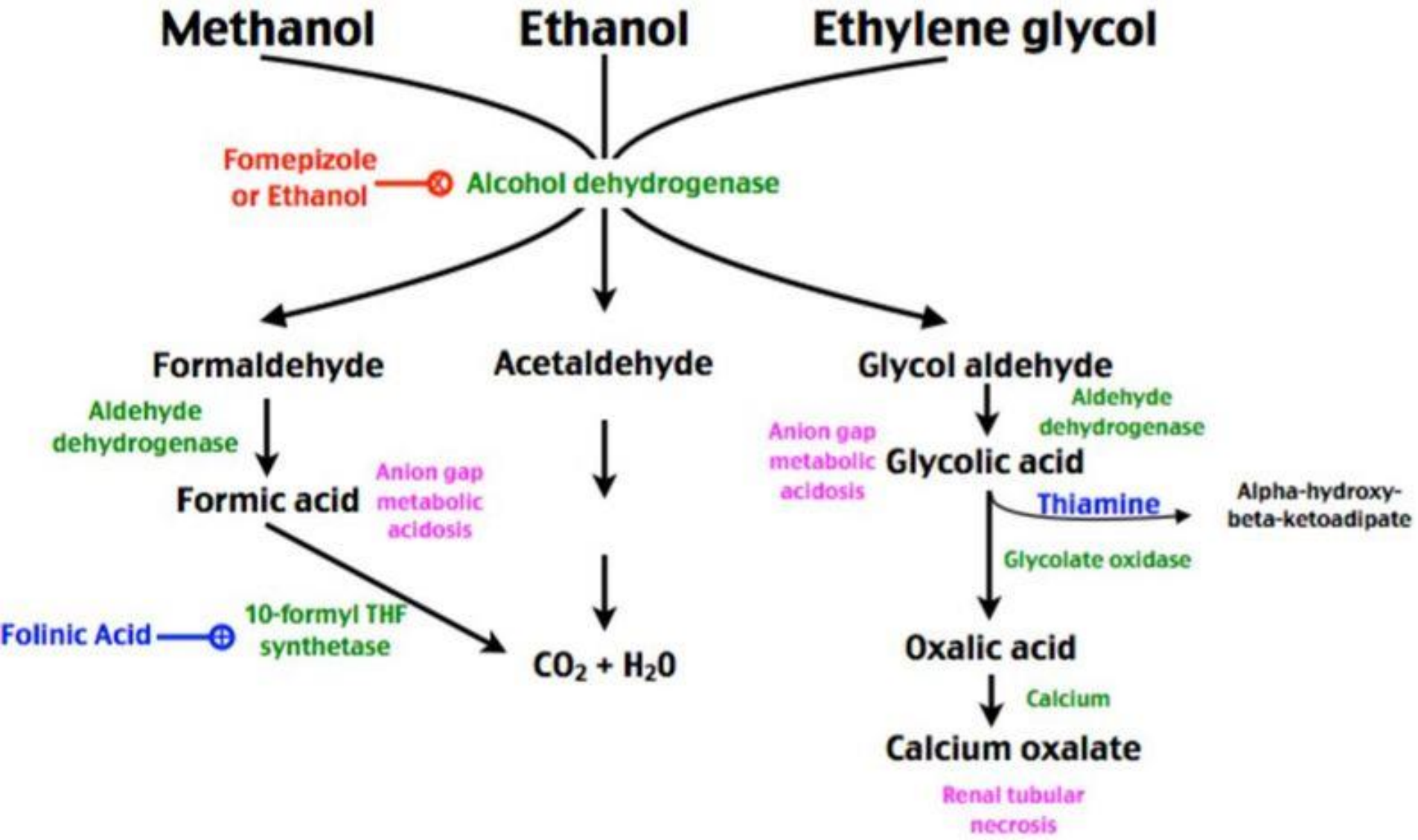
Isopropanol

- Metabolized to :
  - Acetone
- **Acidosis: NO**
- **Osmol Gap: YES**
- Supportive care



Isopropanol
3C

Toxic Alcohol Metabolism



Summary

- For Methanol&EG Poisoning
  - Get early Level, VBG, Lactate, Ethanol level
  - Caution when using osmol gap
  - Antidote: 1st line Fomepizole
  - Hemodialysis is very useful in elimination.