



A. Schunk, PU Marburg, 12/2004



Toxic Alcohols

BADR ALDAWOOD, FRCPC

MARCH, 2019



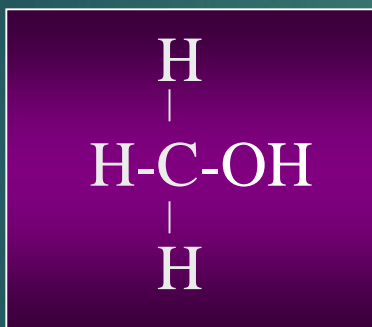
Outline

- ▶ **Biochemistry**
- ▶ **Ethanol**
- ▶ **Methanol**
- ▶ **Ethylene Glycol**
- ▶ **Isopropanol**

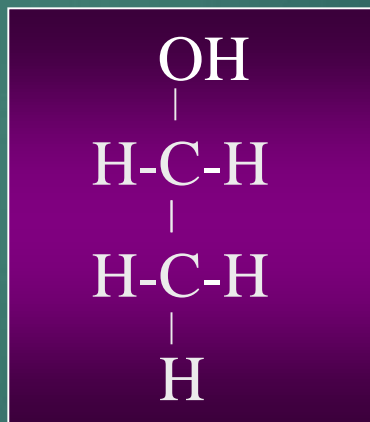
Alcohols molecular structure?



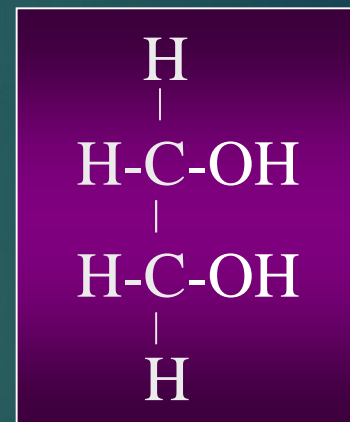
Alcohols: R-OH



Methanol
1C

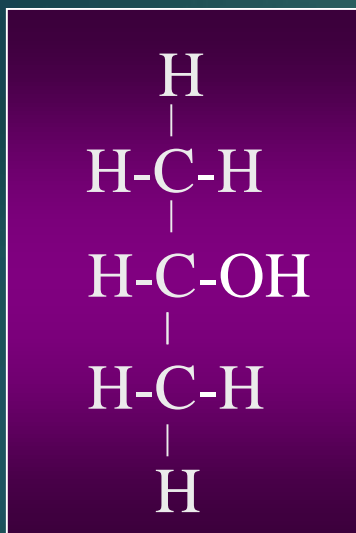


Ethanol
2C

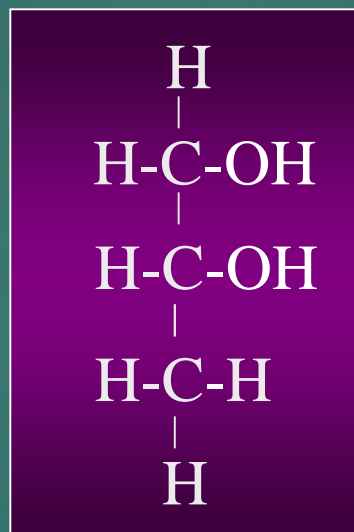


Ethylene Glycol
2C

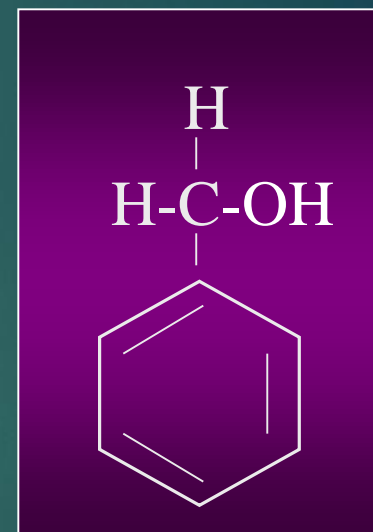
Alcohols: R-OH



Isopropanol
3C

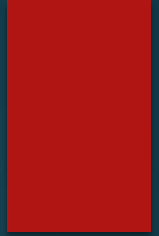


Propylene Glycol
3C

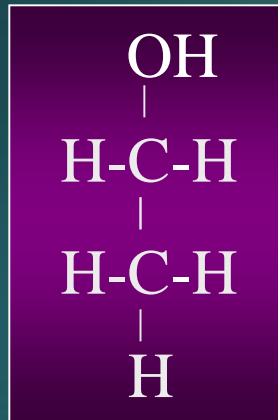


Benzyl Alcohol

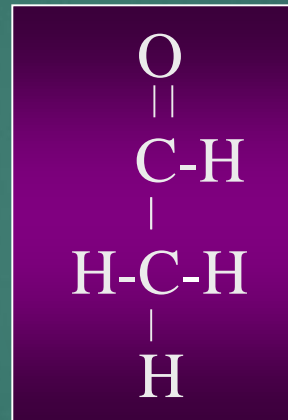
Ethanol Metabolism ?



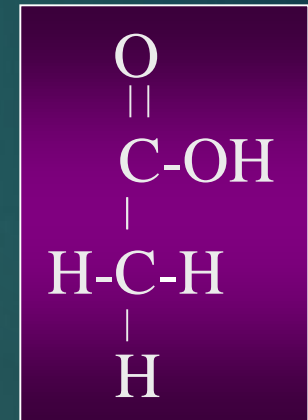
Ethanol Metabolism ?



Ethanol



Acetaldehyde



Acetic Acid

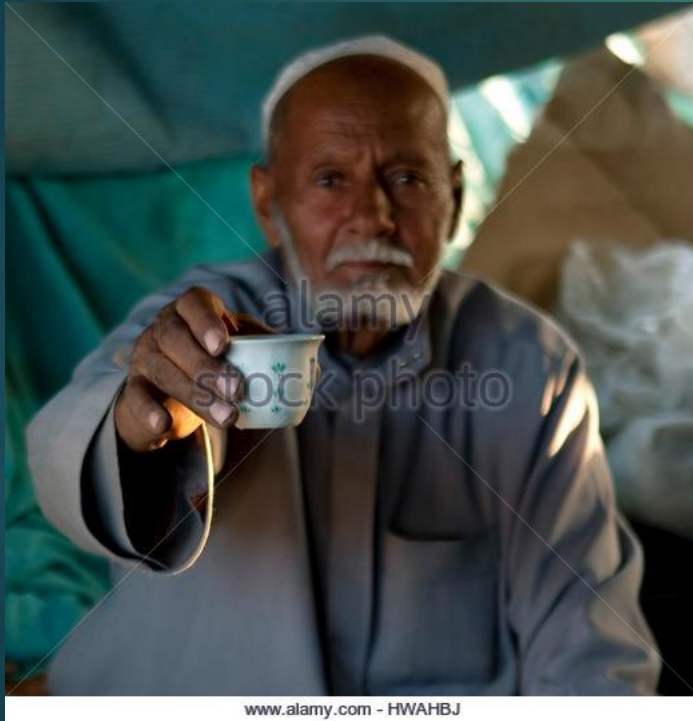
ADH = Alcohol Dehydrogenase

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?



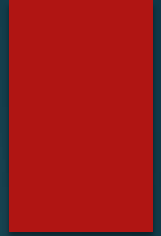
www.alamy.com - HWAHBJ



© Rachel Megawhat / Demotix

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?

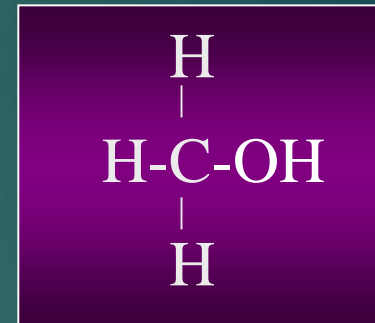
- ▶ Ethanol levels
- ▶ ABG/VBG
- ▶ Renal profile/Lytes
- ▶ Don't miss possible injuries
(TRAUMA)

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?

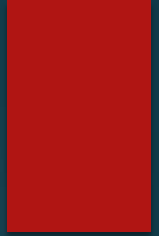


Methanol containing products?

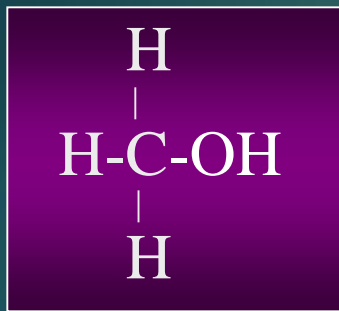
- ▶ Gas Line Antifreeze 100%
- ▶ Windshield washer fluid 30%
- ▶ Varnish removers
- ▶ Fuel for food warming 3-70%
- ▶ Industrial uses



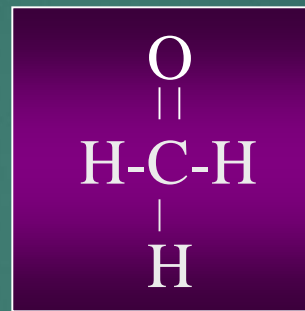
Methanol Metabolism?



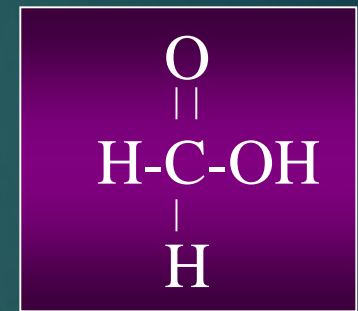
Methanol Metabolism



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?

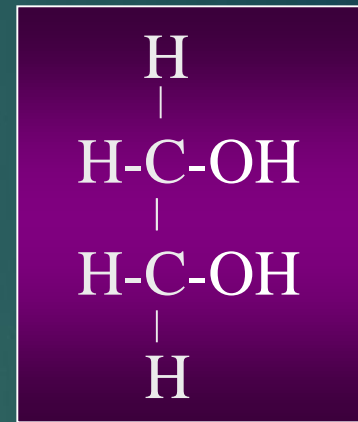


Methanol work up?

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

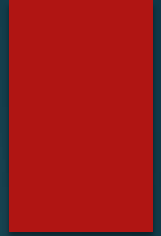
Ethylene Glycol (EG)

- ▶ Low Volatility
- ▶ Low freezing point
- ▶ High boiling point



Ethylene Glycol

Ethylene Glycol containing
products?



Ethylene Glycol

▶ Coolant/Antifreeze



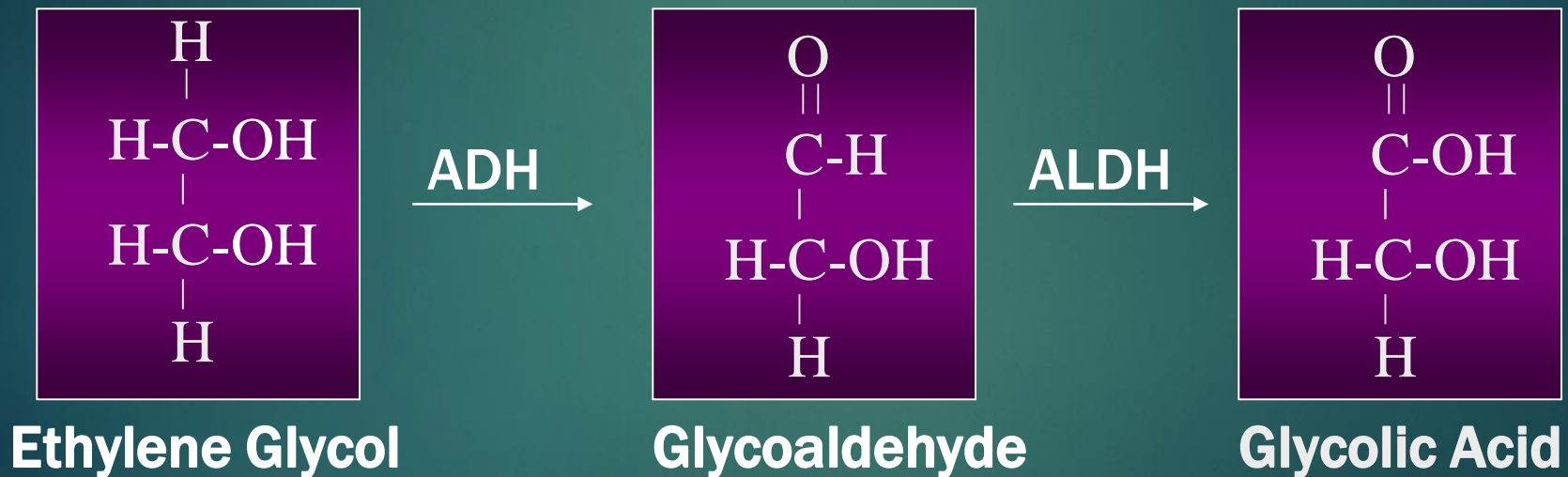
▶ Solvents



Ethylene Glycol Metabolism?



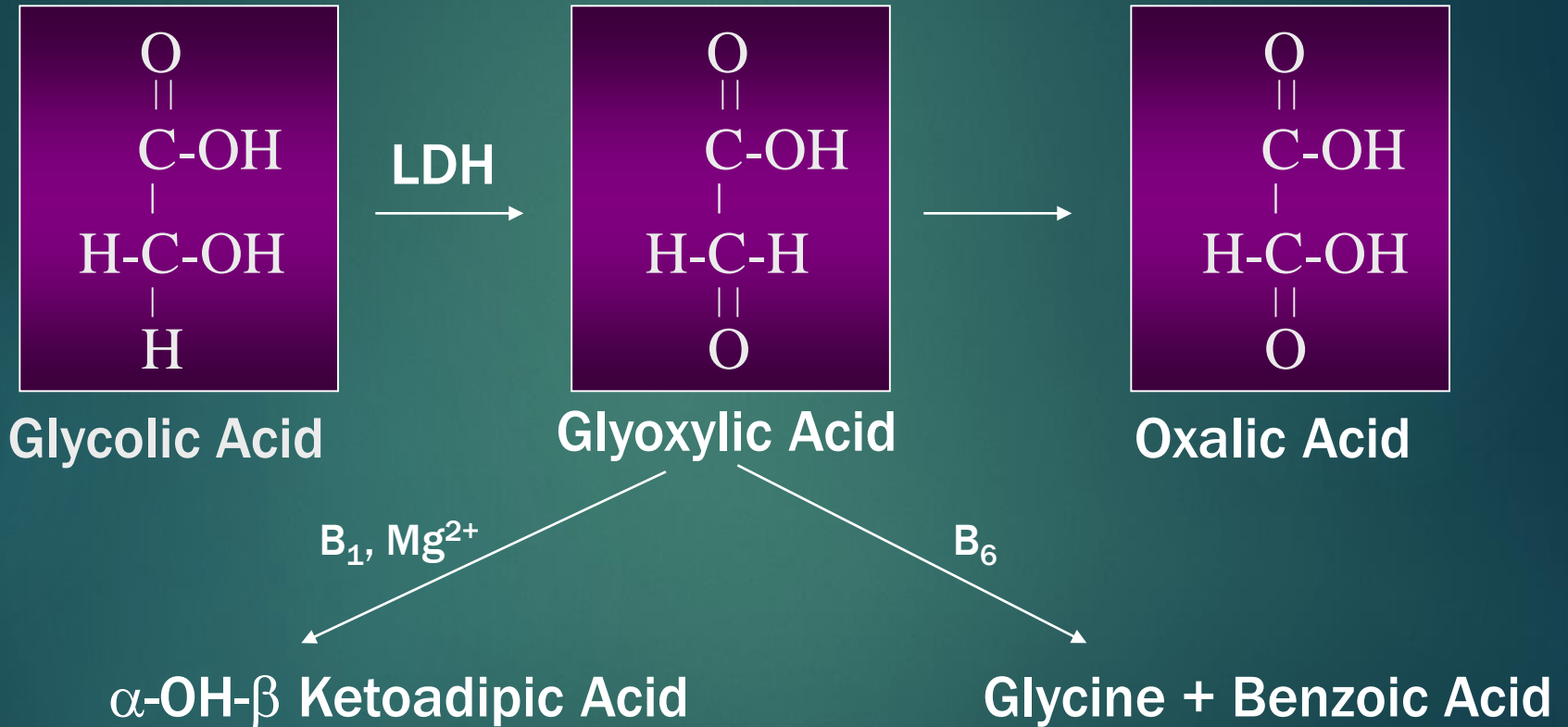
Ethylene Glycol Metabolism



ADH = Alcohol dehydrogenase

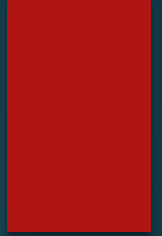
ALDH = Aldehyde dehydrogenase

Ethylene Glycol Metabolism



LDH = Lactate dehydrogenase

Ethylene Glycol Toxicity ?

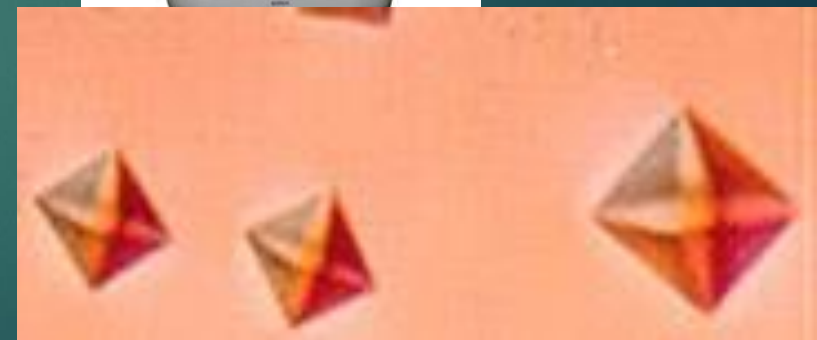


Ethylene Glycol Toxicity

- ▶ 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

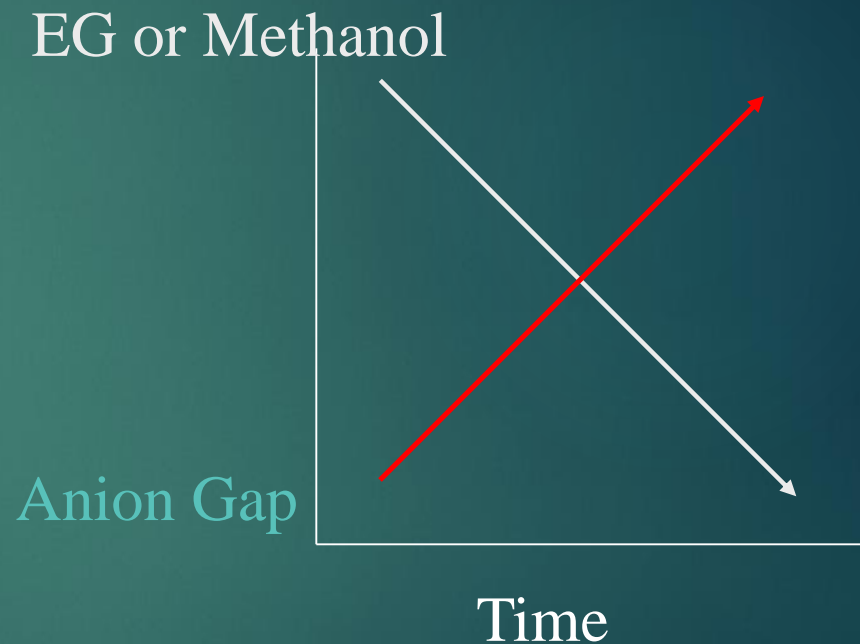


Identifying Patients for Treatment: Methanol/EG

- ▶ Serum ethylene glycol or methanol level
- ▶ Action level for treatment:
 - ▶ Methanol / EG > 25 mg/dL
 - ▶ Any level with acidosis

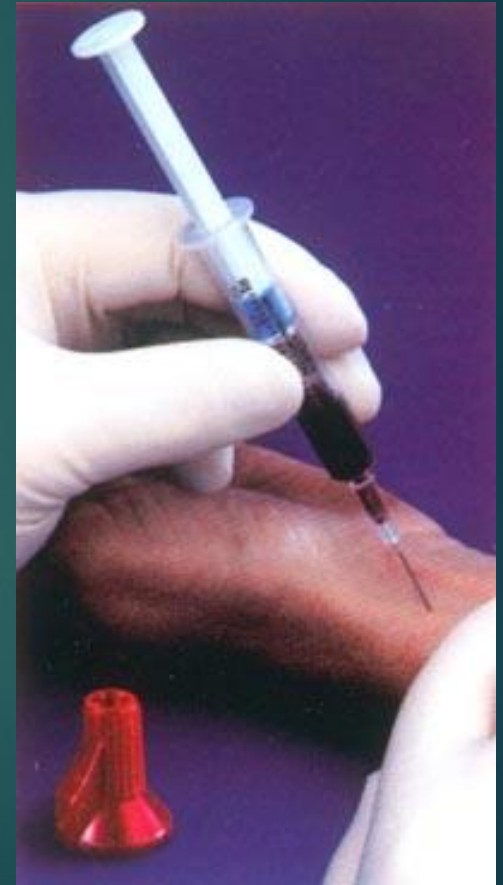
Limits of Serum Levels

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

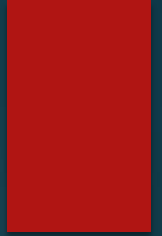


Arterial Blood Gas/Lactate

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



Osmol Gap ?



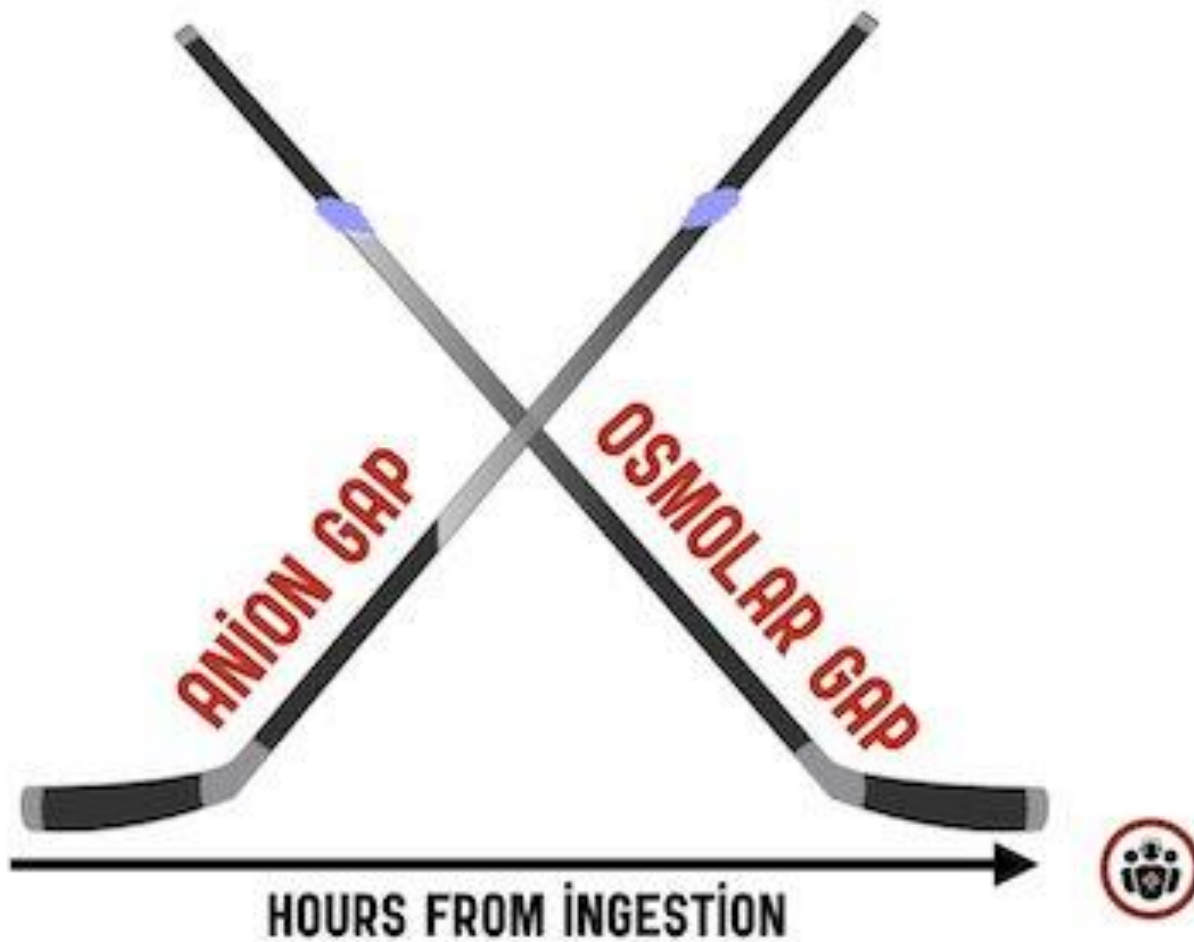
Osmol Gap ?

▶ Osmol Gap = Measured Osmols - Calculated Osmols

▶ Calculated:

2 Na + BUN + Glucose + 1.25 Ethanol

▶ Lab Measurement



METABOLISM

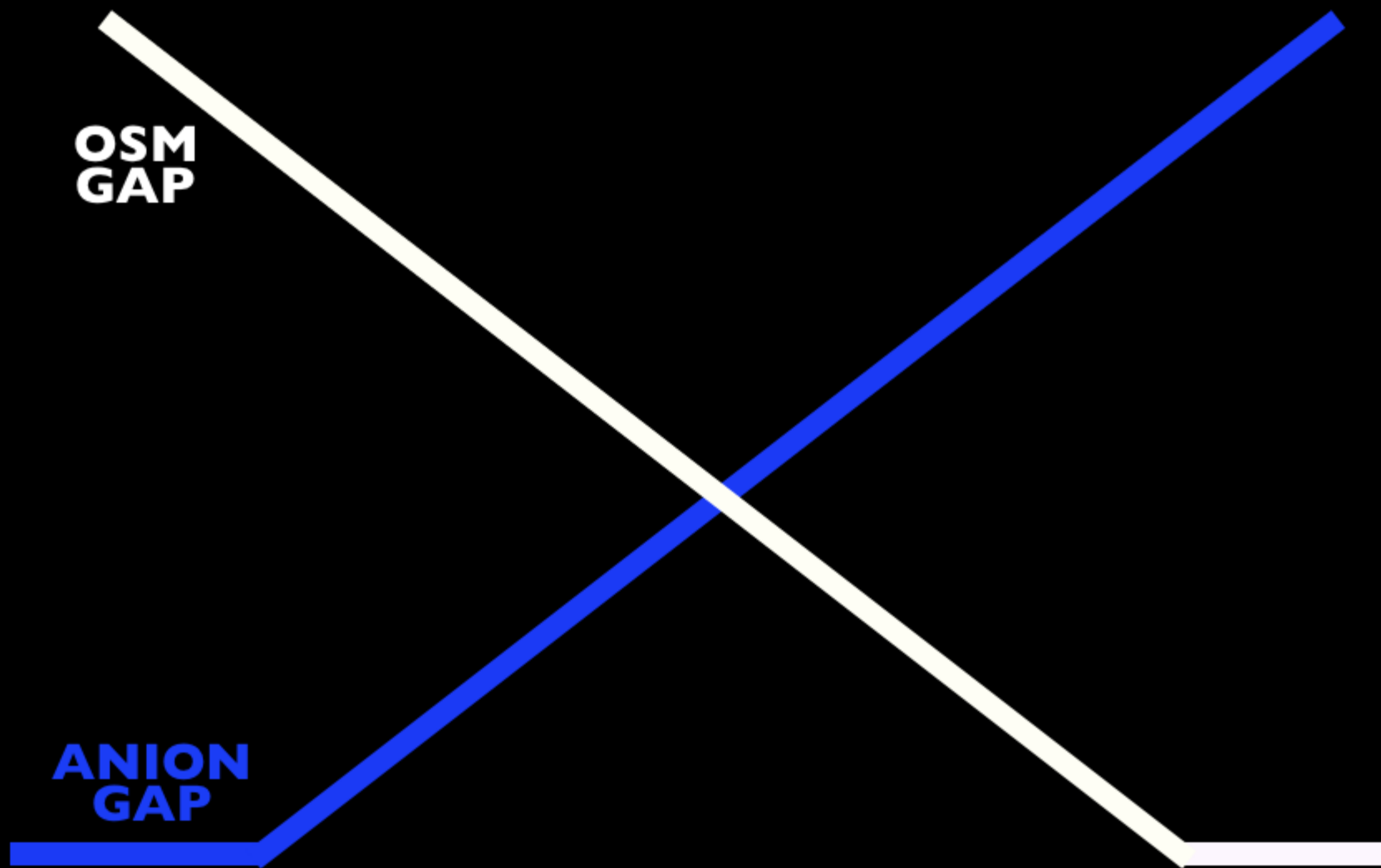


**OSM
GAP**

**ANION
GAP**

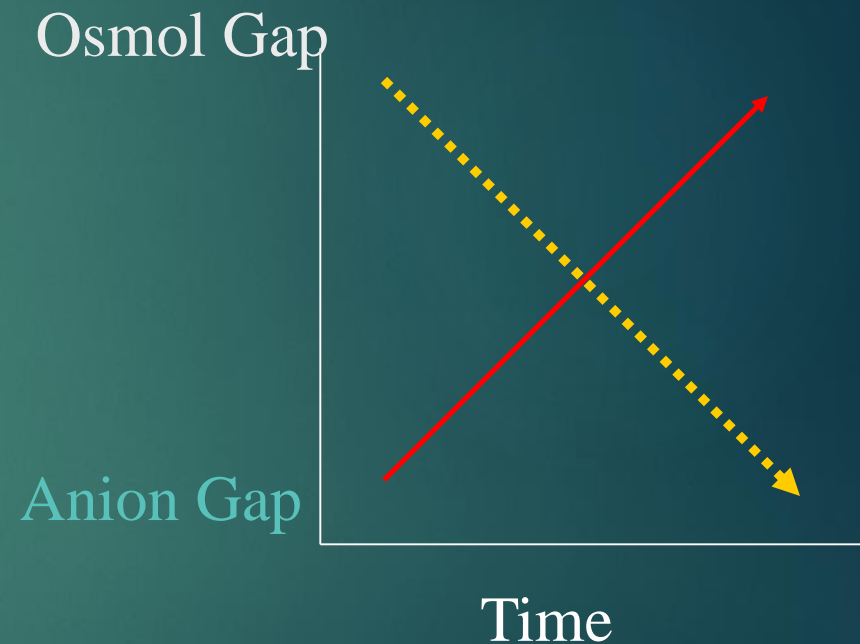
↑ TOXIC ALCOHOL
(METHANOL/ETHYLENE GLYCOL)

↑ METABOLITES
(FORMIC ACID/OXALIC ACID)



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

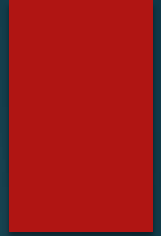
▶ Metabolites



→ 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

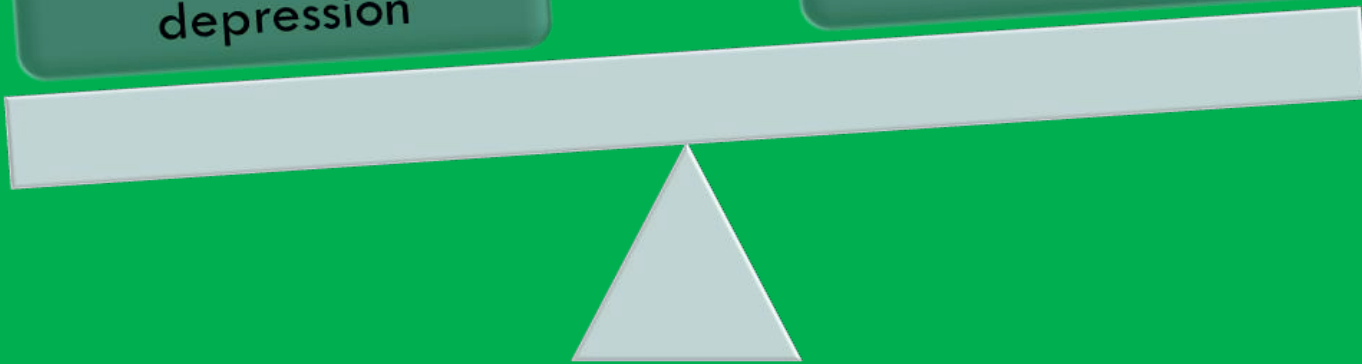
Pancreatitis

Hypoglycemia

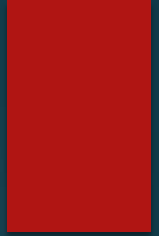
Hypotension

Respiratory
depression

Cost (~\$1000/
dose)



Hemodialysis ??



Hemodialysis

- ▶ Consult nephrology early in acidemic patients
- ▶ Levels toxic alcohol ≥ 25 mg/dL



Adjuncts for Methanol Poisoning

- ▶ **Sodium bicarbonate**

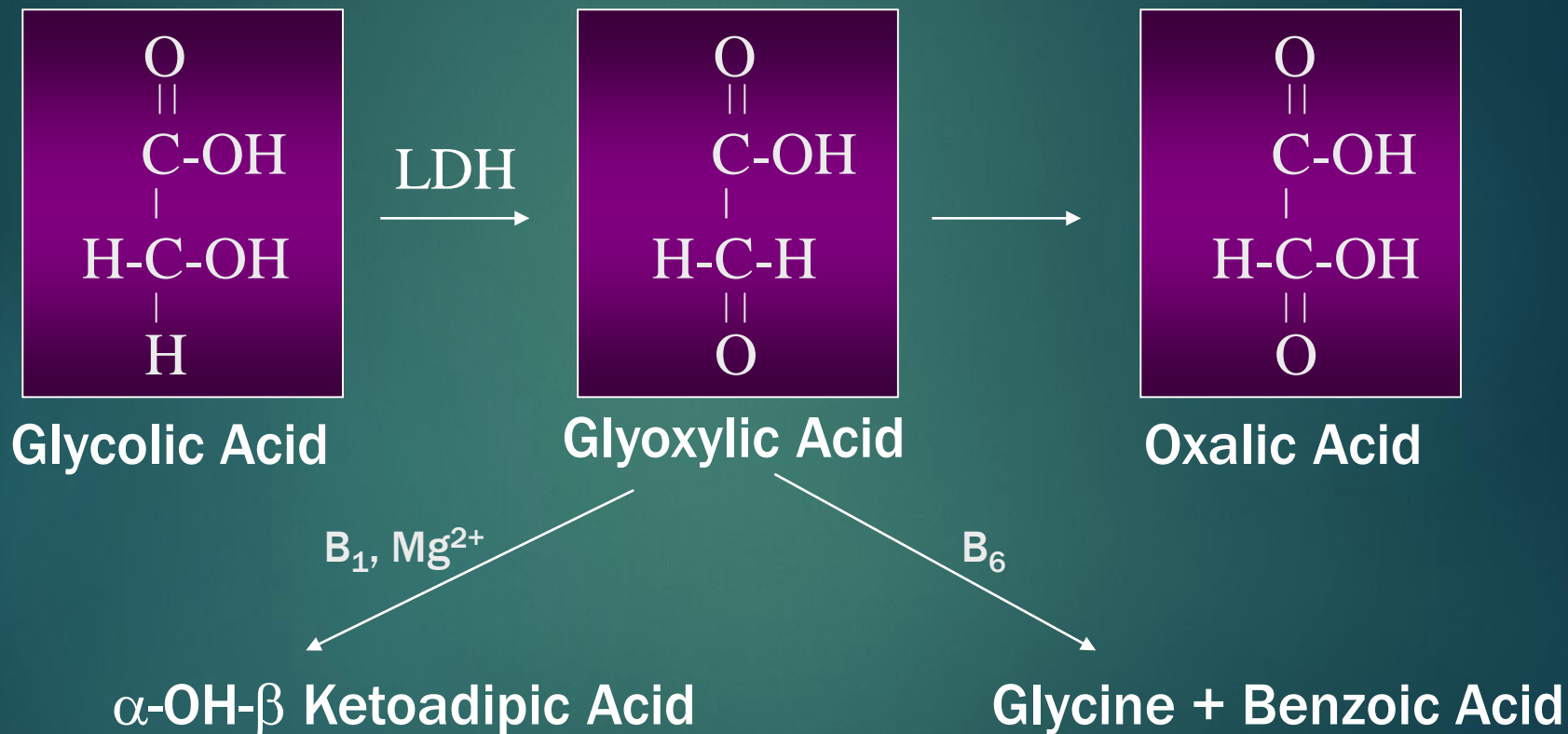
- ▶ pH < 7.30

- ▶ Can ion trap formic acid in urine and enhance elimination

- ▶ **Folate administration**

- ▶ Facilitates conversion of one carbon fragments to CO₂

Adjuncts for Ethylene Glycol Poisoning



LDH = Lactate dehydrogenase

Adjuncts for Ethylene Glycol Poisoning

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

Isopropanol

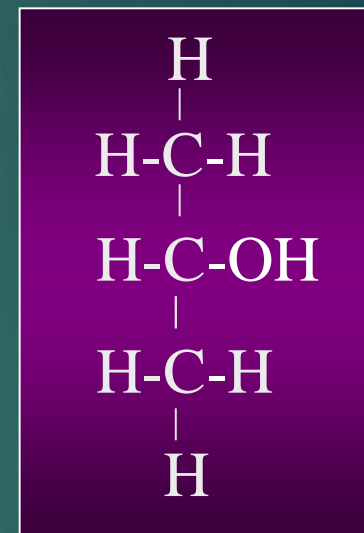
▶ Metabolized to :

▶ Acetone

▶ Acidosis: **NO**

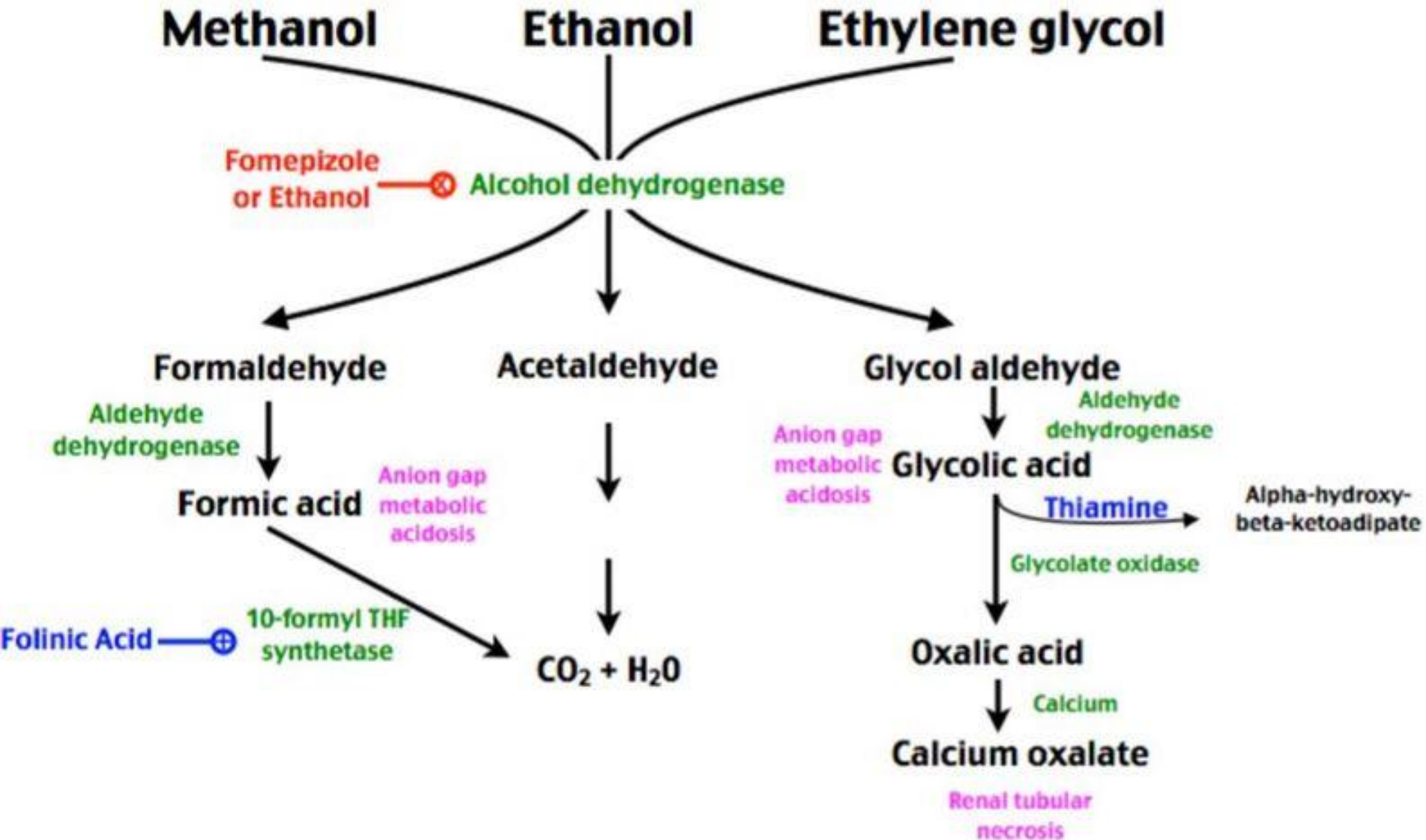
▶ Osmol Gap: **YES**

▶ 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.