ALCOHOLS

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Objectives

? Not given (Who said toxicologists need 'em?)

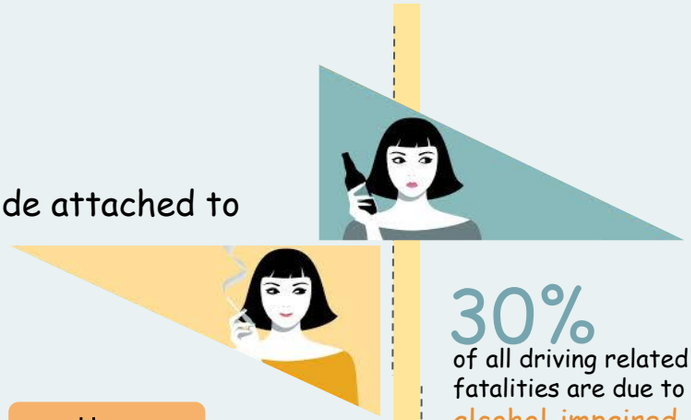
This lecture is EXTREMELY important for your career and your exam >_< AND don't skip any note!

NOTES EXTRA BOOK IMPORTANT GOLDEN NOTES

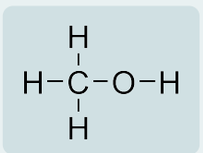
Introducing Alcohol

Alcohol molecular structure:

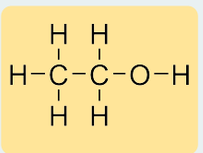
Alcohol is any carbon chain with hydroxide attached to it, also called hydroxyl group (R-OH)



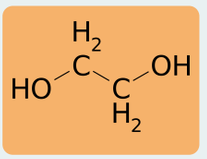
Examples:



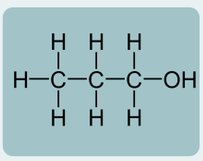
Methanol 1C



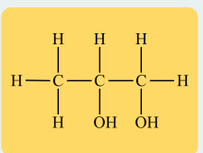
Ethanol 2C



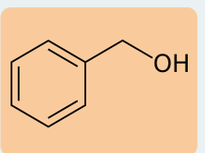
Ethylene Glycol 2C



Isopropanol 3C



Propylene Glycol 3C



Benzyl Alcohol

30% of all driving related fatalities are due to alcohol-impaired driving!

4700 teen dies every year because of alcohol use; that's more than all other illegal drugs combined!

Extra statistics

Metabolism:

Extra but it is good to go through it (:

1st These are the two primary enzymes in any alcohol metabolic pathway; the lack of either will alter this pathway:

- Alcohol dehydrogenase
- Aldehyde dehydrogenase

Occurs in

This is particularly evident in the liver, where the bulk of alcohol metabolism takes place. Some alcohol metabolism also occurs in other tissues, including the pancreas and the brain, causing damage to cells and tissues.

Metabolites

Ethanol	Methanol	Ethylene Glycol	Isopropanol
Acetaldehyde Acetic acid	Formaldehyde Formic acid	Glycolaldehyde Glycolic acid Glyoxylic acid Oxalic acid	Acetone "No acid formation"

Ethanol

Overview:

- Most commonly abused drug in the world. Even in SA.
- Majority of morbidity and mortality is due to trauma owing to impaired cognitive function.
- Rate of metabolism 20 mg/dL/h. They get sober by morning
- Blood ethanol levels correlate poorly with the degree of intoxication (Tolerance) (people who drink regularly will have higher tolerance thus it's harder for them to get intoxicated)

Ethanol Toxicity:

Metabolism (image)

-**Ethanol** (Alcohol) will be metabolized into **acetaldehyde** (aldehyde) by **ADH**[1]
-**Acetaldehyde** will get metabolized into **Acetic acid** (acid) by **ALDH**[2] as final product of Ethanol metabolism

1-Alcohol Dehydrogenase
2-Aldehyde Dehydrogenase

Clinical Presentation

-Disinhibited behavior
-Slurred speech
-Impaired coordination
-Later: Respiratory and (CNS) depression with severe alcohol consumption, it can lead to coma

*Cerebellar symptoms:
-wide-based gait
-ataxia
-incoordination (movement)
-slurred speech

Toxicity Workup

-Ethanol levels
- ABG/VBG because they 1-produce acetic acid, 2-later on respiratory depression CO2 level will increase**, 3-dehydration and hypotension will turn cellular metabolism to anaerobic producing lactic acid. (they get both respiratory and metabolic acidosis).

-Renal profile/Lytes
-Don't miss possible injuries (TRAUMA)
-Breathing test is a screening test done usually by the police on the street, it is not used in the ER.
-**At first alcoholics will have tachypnea as compensation for acetic acidosis, but later when CNS depression is significant they will have hypopnea or even a respiratory rate of 2-3 per minute
-Most important is to make sure not to miss checking for trauma , most of the time they come unconscious and they can't give a history so it is important to examine them from head to toe when alcohol smell is obvious.

Treatment

-Observation
-IV Fluid Hydration (Alcoholic Ketoacidosis) they get ketone bodies because they don't eat and instead drink alcohol all the time
-Thiamine***
-Discharge the patient once sober usually in the morning
-ABC
-Sodium Bicarb if the VBG is high.
-Most of the time we just give them IV and observe them in the ER, ethanol will get metabolised by the body within 6-8 hours.

***why thiamine?
because of **Wernicke-Korsakoff syndrome** which is associated with chronic alcoholism.
criteria of **Wernicke encephalopathy** include:
-ophthalmoplegia
-memory problems
-slurred speech
criteria of **Korsakoff** include:
-dementia
-confabulation (specific feature of this syndrome): filling the gap of a story not initially
(يبهر القصص بدون ما يدري)

-99% of alcoholics die from trauma
-CNS depression and respiratory arrest are rarely the cause of death UNLESS alcohol is given by IV.

-Why do alcoholics urinate a lot?
Because of the osmotic effect of alcohol; it is like glucose will go to urine pushing the water outside the body that will lead to dehydration, hypotension and tachycardia as a compensatory mechanism.
-Another cause of dehydration is vomiting, which also contributes in hypotension and tachycardia by decreasing intravascular volume.

Methanol

Overview:

Methanol Properties:

Methanol is more toxic than ethanol

Molecular weight 32

Low freezing point That's why they use it in car radiators instead of water especially in cold regions, water will freeze too fast

Highly volatile Toxic by inhalation
You can get drunk without drinking it "just by smelling it

"This tree trunk is not here to add to the design but to remind you of methanol; in the past, methanol had been made by destructive distillation of wood!

Methanol containing products:

-Gas Line Antifreeze 100% as fluid in car radiator
-Windshield washer fluid 30%
-Varnish removers

-Fuel for food warming 3-70%
-Industrial uses
-Copy machine ink

Methanol Toxicity:

Metabolism (image)

-**ADH** will act on **Methanol** to convert it into **Formaldehyde**
-The latter will be metabolized into **Formic Acid** (The bad one " it is the main cause of blindness in Methanol toxicity ") by **ALDH**

Clinical Features

-Delayed onset (8-12 hrs) drink around noon so they can party at 7-8 pm
-CNS depression, Ataxia, Confusion
-Abdominal pain that will induce vomiting causing more dehydration than in ethanol toxicity
-Multisystem organ failure from significant dehydration mainly the kidneys, the CNS and the heart.
-Visual complaints:
1-Retinal damage
2-"Snow storm" it's a classical feature of initial blindness; when the formic acid gets into the eyes they will start to see everything as if there was a snow storm. If they didn't treat this problem early, instead of ending up with partial blindness they will end up with permanent blindness.
-Anion gap acidosis formic acid and lactic acid, NO ketone bodies
-Tachypnea at first then bradypnea and they will have CNS depression and respiratory depression.

Methanol Workup

-ABG/VBG Tells us about the level of formic acid, if anion gap acidosis is significantly high and the PH is significantly low that means there is significant amount of formic acid in the blood.
-Osmolality measures indirectly the main compound. Osmolality will increase before blood PH decrease because it will take time for the methanol to metabolise.
Serum levels
-Lactate with severe dehydration
-Renal profile
-Ethanol level to see if it's mixed alcohol, methanol level is not used because it takes 6-12 hrs to get the result waiting that long time would lead to permanent blindness.

-Its effect is similar to ethanol
-Blindness is one of the complications that seen in methanol but not ethanol toxicity; formic acid gets accumulated in the optic nerve causing optic neuritis and eventually that will cause permanent blindness.
-Because of that issue most of the products try to use ethanol instead of methanol.

Ethylene Glycol (EG)

Overview:

Ethylene Glycol Properties:

- Low Volatility
- Low freezing point
- High boiling point

Because temperature is high in SA they use it instead of methanol in car radiator.

Ethylene Glycol containing products:

- Solvents
- Coolant\ Antifreeze

Metabolism (image)	Toxicity
-**Ethylene Glycol** will be metabolized into **Glycoaldehyde** by **ADH**. **Glycoaldehyde** then will be metabolized to **Glycolic acid** by the action of **ALDH** -Now, this resulting acid will undergo another metabolic pathway -unlike other alcohols- and it will be converted into **Glyoxylic acid** by **LDH**[1] . The formation of Glyoxylic acid will lead to the production of **Oxalic acid** (the main side product of glyoxylic acid synthesis) -Glyoxylic acid itself will go through another metabolic reaction: 1-**B6** actions will form **Glycine+Benzoic acid** 2-**B1**,**Mg^{2+}** actions will form **α-OH-β Ketoadipic Acid** 1-Lactate dehydrogenase -B1= Thiamine, B6= pyridoxine. They prevent the accumulation of oxalic acid thus prevent the formation of kidney stones and prevent its complications	-Onset 4-6 hours Drink it early to party late at night -Anion gap acidosis Glycolic acid -Tachypnea With CNS depression they end up with bradypnea and hypopnea -Abdominal pain Because of stomach irritation -Hypocalcemia Oxalic acid will attach to calcium that will decrease calcium blood level -Calcium oxalate crystals in urine -Acute Renal failure* (Calcium Oxalate) **Cerebellar symptoms:** -wide-based gait -ataxia -incoordination movement -slurred speech *Oxalic acid combined with calcium get accumulated in renal tubules then they cause renal tubular acidosis or necrosis and patients end up with crystals in the kidney that may lead to kidney failure. Methanol affects the eyes while ethylene glycol affects the kidneys

"Snow White,

she can help us to remember Ethylene Glycol! Well, Snow means cold and EG is found in coolant! Another thing, EG is odorless and colorless so snow and white! Hmm, what about its taste? It has a sweet taste so does the apple! And guess what? EG is toxic and so is Snow white's APPLE!

Methanol & EG

Toxicity Tests for Methanol & Ethylene Glycol (EG)

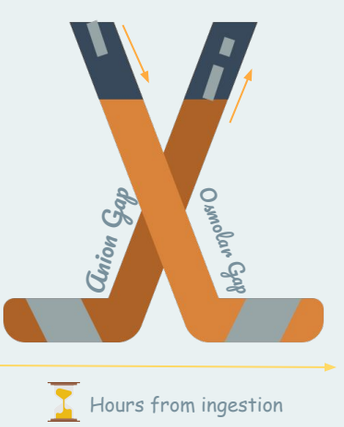
Methanol	Ethylene Glycol
Hyperemic retina or visual complaints	-Limited utility of fluorescence of urine -May note crystals in urine using Wood's lamp -Most of the time doesn't cause visual complaint

fluorescence test is used to look for shiny crystals in the urine under the microscope, BUT only 50% of the patients have the crystals in the urine, finding them confirms the diagnosis but not finding them doesn't exclude EG toxicity

Serum Levels of Alcohol	Limits of Serum Levels: 1-Useful prior to onset of acidosis or in massive overdoses 2-Parent compound not directly toxic it is mainly the metabolite 3-Levels not universally available
Arterial Blood Gas/ Lactate	-Acidosis indicates advanced poisoning -Lactate usually low unless the patient is significantly dehydrated -Patients with acidosis should receive treatment because of the metabolite
Osmol Gap	-Osmol Gap = Measured Osmoles - Calculated Osmoles. If there is a difference that means the measured osmoles has some extra compound, which is probably the EG or methanol. 1-Measured Osmoles: measured in the lab (from blood sample) 2-Calculated Osmoles: 2 Na + BUN + Glucose + 1.25 Ethanol Osmol Gap limitations: -Roughly the gap should be < 10 If it is higher that means there is extra compound (EG or methanol) but keep in mind there are other drugs that could increase the osmol gap like: sorbitol and mannitol (diuretics) -Normal Osmol Gap in setting of poisoning does not rule out a treatable level -Osmol Gap diminishes as parent compound is metabolized

Osmol Gap:

(graphs found in doctor's slides for osmol gap)



-As time goes by the anion gap will go up (causing acidosis) and the alcohol level will go down
-Again, in alcohol intoxication acidosis will go up, osmol gap will go down and the metabolite will increase with time

Methanol & EG

Identifying Patients for Treatment

we need to get the levels of EG and methanol to assess if the patient needs treatment or not

When do we take action and start treating someone based on serum level ?

If

- Methanol / EG serum level > 25 mg/dL*
- Any serum level with acidosis

*this level will decrease with time to 0 because of the metabolism but that doesn't mean that the patient doesn't have nothing at all! Because if we do blood Gas we're gonna see the acidosis super high.
-the problem is not with parent compound, the problem is with the metabolites, they are the ones causing the complaints so patients will get sicker with time

Aims of the treatment: (Main treatment)

1-Limit absorption

- NG Tube Suction to limit the absorption, used within first hour

2-Prevent metabolism of parent compound to toxic metabolite

- ADH Inhibition (most important one)
  - Ethanol
  - Fomepizole

How would ethanol inhibit ADH?
It Competes for the enzymes and because it has higher affinity to the enzymes it will get metabolized instead of other alcohols (EG and methanol)

3-Enhance elimination of Parent and its Metabolites & Correct Derangements*

- Hemodialysis if the patient has significant acidosis

*Mainly electrolytes and dehydration; we give them fluid and HCO3 to decrease the acidosis

Adjunct Therapy: (This type of therapy is added to the main therapy; you can't use it alone)

Methanol Toxicity

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
With methanol toxicity

Ethylene Glycol Toxicity

To enhance metabolism away from oxalates:
-Thiamine (B1)
-Pyridoxine (B6) With EG toxicity

Next slide for more explanation for main therapy

Methanol & EG

Alcohol Dehydrogenase (ADH) Inhibition

Ethanol
(Image)
It has to be done in the ICU

-Serum Ethanol inhibits the metabolism of both Methanol and EG.
-Onset of toxicity of Methanol\EG may be delayed.
-Ethanol is more avid for ADH:
A)6-8x more avid than Ethylene Glycol
B)4x more avid than Methanol
-And that's why giving ethanol is considered a good treatment for other kinds of alcohol toxicity.

In short:
We give them less harmful alcohol to compete with the more harmful alcohol :)

Ethanol Infusion Management

Serial ethanol levels to make sure it's not too high

Watch glucose and sodium* Children may develop hypoglycemia and sodium level may go up and down

Observe for respiratory status* Watch for respiratory arrest

* Especially in children

Fomepizole

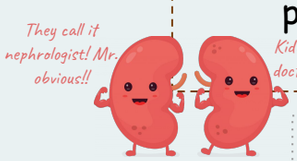
-First line antidote
-A blocker of alcohol dehydrogenase(ADH)
-Has replaced ethanol as the agent of choice in known or suspected exposures
-Minimal adverse effects

What to consider!

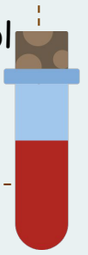
Ethanol	Fomepizole
-Pancreatitis -Hypoglycemia -Hypotension -Respiratory depression Used in poor countries because it is cheap and easy to use	Cost(1000$/dose) is the only downside -used in SA

Hemodialysis

Consult nephrology early in acidemic patients



Levels toxic alcohol 25 mg/dL
with methanol or EG



Indications for hemodialysis:
-Severe acidosis (PH<7.1)
-Signs of renal injury with EG
-Any signs of visual changes with methanol
-High level of alcohol 25 mg/dL

Isopropanol

Overview:

Metabolized to : Acetone

NO Acidosis
No acid as a metabolite

Osmol Gap: YES

Treated by: Supportive care

I'm Isopropanol and I am flammable so you should not be playing with me!

-Most commonly found in alcohol swabs
-It is more toxic than the others in terms of the CNS effect
-It is not used any more in alcohol swabs

Summary from SLIDES:

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.

A nice diagram that summarizes all alcohol metabolism that was mentioned in this lecture and yup, you finished the lecture (;

Summary

Alcohol	General	Toxicity clinical presentation	Work up	Treatment	Adjuncts for Poisoning
Ethanol	-Most commonly abused drug -Rate of metabolism 20 mg/dL/h. -Blood ethanol levels correlate poorly with the degree of intoxication (Tolerance)	-Disinhibited behavior -Slurred speech -Impaired coordination -Later: Respiratory and (CNS) depression	-Ethanol levels -ABG/VBG -Renal profile/Lytes	-Observation -IV Fluid Hydration -Thiamine -Discharge the patient once sober -ABC	Fomepizole
Methanol	-Molecular weight 32 -Low freezing point -Highly volatile	-Delayed onset (8-12 hrs) -CNS depression, Ataxia, Confusion -Abdominal pain -Multisystem organ failure -Visual complaints: 1-Retinal damage 2-"Snow storm" -Anion gap acidosis -Tachypnea	-ABG/VBG -Osmolality -Serum levels -Lactate -Renal profile -Ethanol level	-Limit absorption: NG Tube Suction. -Prevent metabolism of parent compound to toxic metabolite: ADH Inhibition. -Enhance elimination of Parent and its Metabolites & Correct Derangements: Hemodialysis	-Sodium bicarbonate -Folate administration
Ethylene Glycol	-Low Volatility -Low freezing point -High boiling point	-Onset 4-6 hours -Anion gap acidosis -Tachypnea -Abdominal pain -Hypocalcemia -Calcium oxalate crystals in urine -Renal failure (Calcium Oxalate)	-Limited utility of fluorescence of urine -May note crystals in urine using Wood's lamp		-Thiamine (B1) -Pyridoxine (B6)

How toxic is your knowledge

Q1: Hypothermia may be seen as a complication of which of the following:

A. Cocaine
B. Amphetamine
C. Ethanol
D. Iron

Q2 A 25-year-old man presents to the ED with nausea and abdominal pain after drinking some "bitter liquid" at his friend's house. His BP is 130/70 mmHg, HR is90b/m, RR is 18 breaths per minute, temperature 37°C, and oxygen saturation is 98% on room air. Physical examination is unremarkable, except for slurred speech and smell of acetone on the patient breath. Laboratory results reveal serum sodium 138 mmol/L, potassium 3.5mmol/L,chloride 105 mmol/L, bicarbonate 23 mmol/L, glucose 5 mmol/L, arterial blood pH 7.37, and lactate 1.5 mmol/L. Urinalysis shows moderate ketones. Which one of the following is the most likely diagnosis?

A. Ethanol poisoning
B. Methanol poisoning
C. Isopropyl alcohol poisoning
D. Ethylene glycol poisoning

Q3: A 40-year-old man is brought to the ED by the ambulance who state that the man is an engineer and was found lying on the floor of an aircraft hangar. He is drowsy, speaks with slurred speech, and is vomiting. His BP is 140/85 mmHg, HR is 94 bpm, and temperature is 36.80°C, RR is 18 per minute. Laboratory results reveal serum sodium 139 mmol/L, potassium 3.5 mmol/L, chloride 101 mmol/L, bicarbonate 14 mmol/L, glucose 5.5 mmol/L, arterial blood pH 7.27 and lactate 2 mmol/L. Urinalysis shows multiple calcium oxalate crystals. Which one of the following would best explain the metabolic state of this man?

A. Ethylene glycol poisoning
B. Diabetic ketoacidosis
C. Lactic acidosis
D. Isopropyl alcohol poisoning

Q4: The hemodialysis is useful for the removal of which of the following poisons?

A. Methanol
B. Caustics
C. Cyanide
D. Organophosphorus

Q5: A 29-year-old male is brought to the emergency department after methanol ingestion. Which of the following treatments are proven to be beneficial in the management?

A. Activated charcoal
B. Sodium bicarbonate
C. Flumazenil
D. Plasmapheresis

Q6: An ambulance brings a 37-year-old man to the emergency department with altered mental state. His BP is 130/80, HR 93 bpm, temperature is 36.8°C, RR is 18, and oxygen saturation is 99% on room air. Physical examination reveals a strong odor of alcohol on his breath. Laboratory result reveals high anion gap metabolic acidosis and high osmolar gap. Which one of the following is the antidote for this poisoning?

A. Flumazenil
B. Physostigmine
C. Desferrioxamine
D. Fomepizole

Q7: Which ONE of the following is the antidote for Methanol?

A. n-acetylcysteine
B. Ethanol/fomepizole
C. Oxygen/hyperbarics
D. Naloxone/nalmefene

1-C
2-D
3-A
4-A
5-B
6-D
7-B

How toxic is your knowledge

Q8: Which one of the following is a consequence of vitamin and mineral deficiencies that may lead to dementia and memory disorder in alcohol abuse?

A. Seminoff's syndrome
B. Korsakoff's syndrome
C. Hemert syndrome
D. Huynh-feldt syndrome

Q9: which one of the following can cause high anion gap metabolic acidosis?

A. Methanol
B. Mannitol
C. Isopropanol

Q10: what is the treatment of choice for alcoholic toxicity?

A. Ethanol
B. Sodium bicarbonate
C. Aspirin
D. Hydroxocobalamin

Q11: a 30-year-old male presents with methyl alcohol poisoning. There is CNS depression, cardiac depression and optic nerve atrophy. What is the cause?

A. Formaldehyde and formic acid.
B. Acetaldehyde
C. Pyridine
D. Acetic acid

Q12: Calcium oxalate is found in toxication of what type of alcohol intoxication?

A. Ethanol
B. Ethylene glycol
C. Methanol
D. Cyanide

Q13: 4-year-old boy drinks the windshield washer fluid and after few hours he became drowsy and comatose. What did he drink?

A. Ethanol
B. Iron
C. Methanol
D. TCA

Q14: Which of the following is considered a non-toxic alcohol?

A. Ethylene glycol
B. Ethanol
C. Methanol
D. Isopropyl alcohol

Q15: A 33-year-old man is brought to the ED with altered mental status ,flank pain, the man works in an airport and has an access to ethylene glycol, toxicity with ethylene glycol is suspected , how would you approach this patient "first step" ?

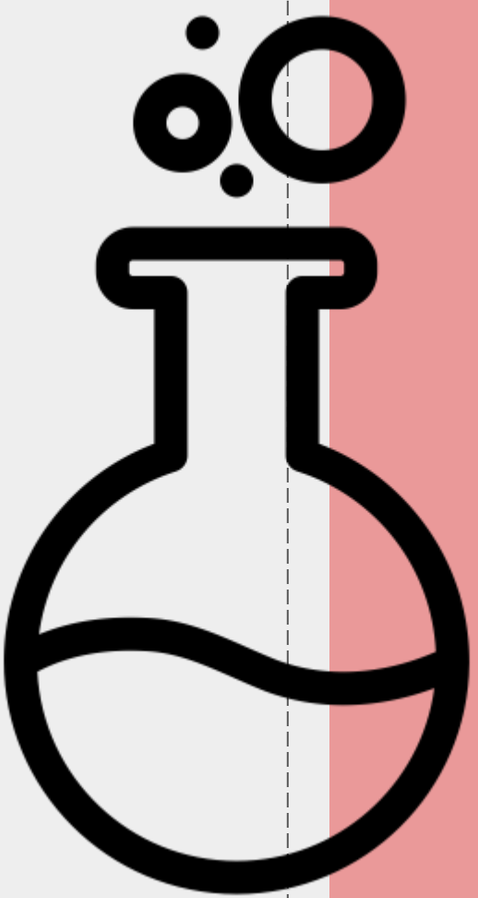
A. ECG
B. Urinalysis
C. ABC
D. Hemodialysis

Q16: The difference between (methanol/ethylene glycol) and (isopropanol) intoxication is the:

A. Presence of CNS symptoms.
B. Metabolic alkalosis.
C. Ketosis without acidosis
D. Increased osmolar gap.

8-B
9-A
10-A
11-A
12-B
13-C
14-B
15-C
16-C

Thank you and good luck!



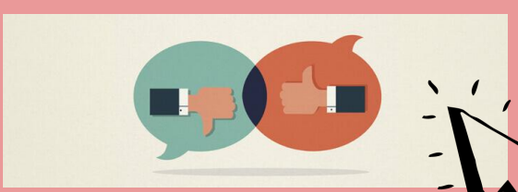
Very Toxic but you are gonna do it!

A+ is yours (:

- Email us at:

436toxicology@gmail.com

How well do you think we have done? We are waiting for your feedback!



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