THE ALCOHOLS

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Alcohol = Something White

- **1) Monohydroxy :-** Methyl alcohol (Methanol) ; Ethyl alcohol (Ethanol)
- **2) Dihydroxy :-** Ethylene Glycol
- **3) Trihydroxy :-** Glycerine (Glycerol)
- **4) Polyhydroxy :-** Mannitol

- **Ethanol, Glycerine, Mannitol à** Clinical Importance
- **Methanol, Ethylene Glycol à** Toxicological Importance

Types of Alcohol

1) **Malted Liquors :-** **Beers (3-10% alcohol). Prepared by fermentation of germinated cereals.**

2) **Wines :-** **Fermentation of natural sugars in grapes.**
   (i) Light Wines (9-15%)
   (ii) Effervescent wines (13-16%) **eg. Champagne.**
   (iii) Fortified Wines (16-22%).

1) **Spirits :-** **Distilled after fermentation (43-55%). Eg. Rum, Gin, Whisky, Brandy, Vodka.**

2) **Absolute (Dehydrated) Alcohol :-** **99% w/w Ethanol**

3) **Rectified spirit :-** **90% w/w from mollases by distillation.**

4) **Proof spirit :-** **Whisky poured on Gun powder. 100% Proof spirit contains 49.29 % w/w alcohol.**

ETHYL ALCOHOL (ETHANOL)

- 1) Local Action :- When rubbed on skinà Mild rubifacient, counter-irritant à cooling, irritation & burning sensation.
- Astringent effectà precipitates surface proteins (antiseptic action) and hardens skin.
- 2) CNS :- Depressant effect.
- (i) Pl. Conc. (30-100mg/dl) :- hesitation, caution, self critism, mood & feelings altered, anxiety may be allayed.
- (ii) Pl. Conc. (100-150 mg/dl) :- Mental clouding, thought disorganization, impairment of memory, alteration of perception and drowsiness supervines.
- (iii) Pl. Conc. (150-200 mg/dl) :- sloppy, ataxic, drunk.
- (iv) Pl. conc. (> 200 mg/dl) :- Stupor, slowing of reflexes, driving is dangerous, impaired performance, precise movements obliterated, errors increases and unconsciousness may occur with Pl.conc > 300 mg/dl.

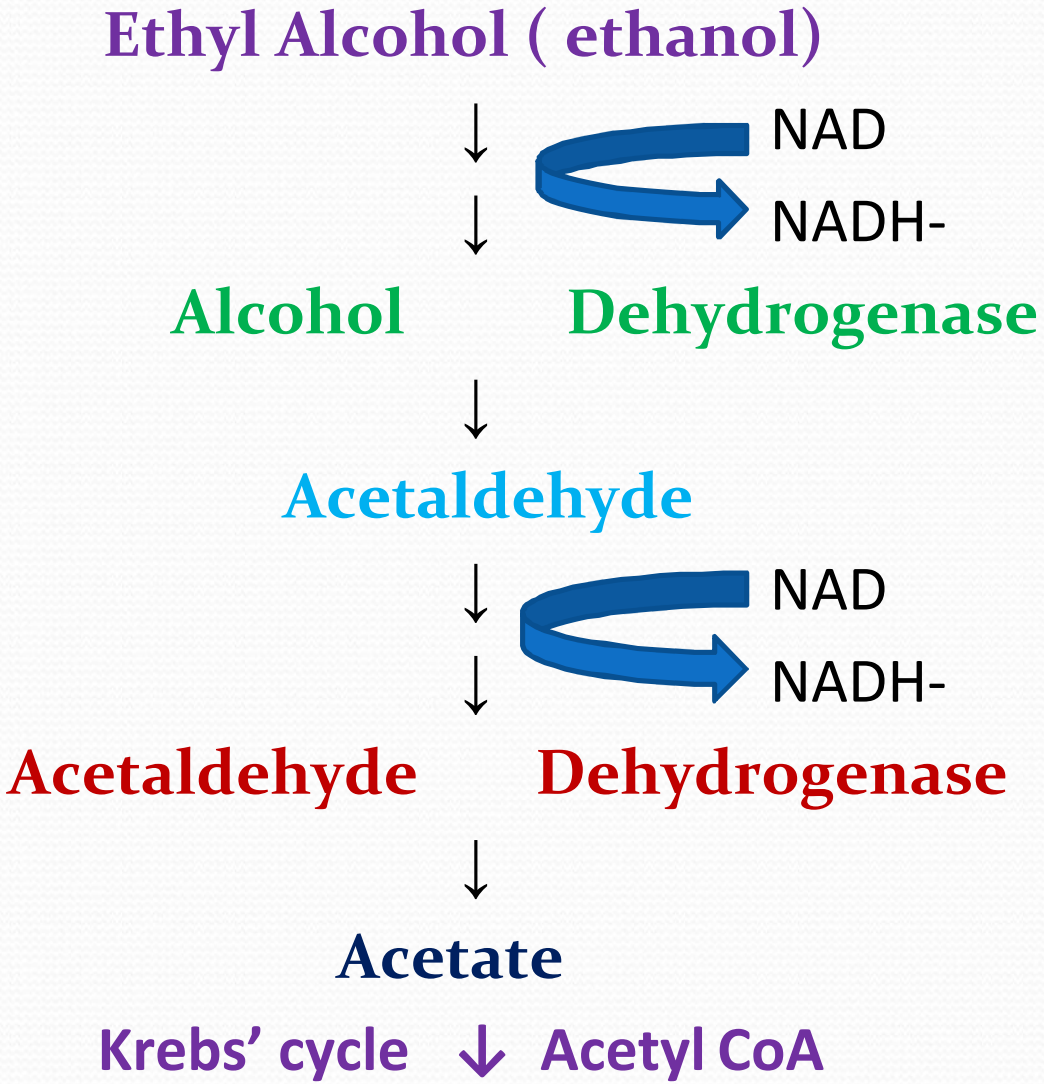
ETHYL ALCOHOL (ETHANOL)

—**3) CVS :-** Tachycardia, Hypertension, Cardiomyopathy, Cardiac arrhythmias.

—**4) Blood :-** ?HDL, ?LDL, Megaloblastic anaemia (Interference with folate metabolism).

—**5) Liver :-** ? Fatty acid synthesis à accumulation of protein à oxidative stress à cellular necrosis à acetaldehyde damages hepatocytes à ? lipid peroxidation à Glutathion depletion occurs à Vitamin + nutritional deficiency à Cirrhosis of Liver. (Fatty infiltration & Hepatomegaly) à Impaired Gluconeogenesis, Glycogen depetion,↓ albumin & transferrin synthesis, diminish fatty acid oxidation,↑ VLDL&TGs synthesis

Mechanism of Action of Ethanol



Pharmacokinetics of Ethanol

- Absorption from stomach and intestine is fast
- Widely distributed in body, crosses BBB & Placenta.
- Metabolized in liverà Follows Zero – Order Kinetics at higher Pl. Conc.(> 10mg/dl) (constant amountà 8 -12ml/hr is degraded in unit time, independent of Pl. Conc.).
- Excreted through Kidneys and Lungs (Conc. In exhaled air is 0.05% of Blood Conc.).

Uses of Ethanol

—1) Medicinal useà External application à feverà cooling effect & as vehicle for Vitamins liquid preparations.

—2) As an antiseptic (70%)

—3)Rubefacient & Counterirritant for sprains and strains

—4) To prevent bedsoresà hardens the skin

—5) Antiperspirant, Aftershave lotion

—6) Alcoholic sponges to reduce body temp. in fever

—7) Intractable neuralgias à by local inj. to destroy nerve

—8) As appetite stimulant & carminative (10%)

—9) Reflex stimulation in Hysteria / Fainting

—10) Methanol Poisoning.

Contraindications of Ethanol

1) Peptic ulcer, Hyperacidity, GERD
2) Epilepsy Pt.
3) Severe Liver Disease
4) Unstable personalities
5) Pregnant women à Produces Foetal Alcohol Syndrome à Intra-Uterine & Post-natal Growth Retardation, Low IQ, Facial & other abnormalities à Increase incidence of miscarriage, stillbirths and low birth weight babies.

Toxicities of Ethanol

(I) **Acute Alcoholic Intoxication :- (600ml of pure alcohol) à Hypotension, Hypoglycaemia, Respiratory Distress, Collapse, Coma, Death.**

—**Treatment :-** Supportive treatment

(Gastric lavage + Patent airways + Fluid and Electrolyte Balance), Correct Hypoglycaemia à by glucose 50%, 50 ml IV Infusion à Thiamine 100 mg (Bolus) IV à Magnesium sulphate 2-4 g IV over 1-2 hrsà Sedatives (if Not comatose but rowdy)à Haemodialysis.

(II) Chronic Alcoholism :-

Tolerance develops to subjective & behavioral effects of alcohol

Physical depedence on round the clock & heavy drinking

Nutritional deficiency & malnutrition, impaired mental & physical function

Neurological defects such as(polyneuritis, pellegra, tremors, seizures, encephalopathy)

Cirrhosis of liver, hypertension, cardiomyopathy, CHF, arrhythmias, stroke, hepatic malignancy.

Withdrawal syndrome à

8 Hrs : Tremulous syndrome à Tremors, anxiety, N,V

24 Hrs : Seizures syndrome à Hyper-excitability, insomnia, disordered perception, convulsions

2-5 days : (Delirium Tremens) à Excitement and confusion, tremors, hallucinations, disorientation , ANS over-activity.

Chronic Alcoholism (Contd…) :

Treatment :-

Detoxification : Nutrition + Vitamin B 50-100 mg Thiamine orally daily. Maintain hydration.

Psychological & medical supportive measures à chlordiazepoxide(25-50 mg) or diazepam (10mgo orally every 6 hrs on first day, then taper the dose for next 5 days.à Abatment of symptoms like anxiety and agitation occurs in 3-5 days.à In elderly with liver failure give Lorazepam or Oxazepam every 4 hrs.

Carbamazepine, Clonidine(0.1-0.4 mg qid) or Atenolol (50-100mg) daily to control autonomic hyperactivity

Opioid antagonist à Naltrexone (50-100 mg OD x 12-16 weeks)à prevents relapse of alcoholism à reduce alcohol craving à reduce number of drinking/day à reduce chances of resuming heavy drinking. (Free inhibitory GABA & block Dopamine release) -à Hepatotoxicity & Nausea

Nalmefene (Naloxone derivative) à longer acting, greater bioavailabilty , less Hepatotoxicity

NMDA antagonistà Acamprosate.(GABA-A receptor agonist & weak NMDA receptor antagonist) (2Tabs of 333mg each Twice Daily) à Reduces voluntary alcohol consumption and craving in alcohol withdrawal & early abstinence)

5-HT3 antagonist à Ondansetron.

Drug Interactions of Ethanol

1) **Alcohol + Insulin/sulphonulureas à** Enhances hypoglycaemia
2) **Alcohol + Aspirin à** ↑ Gastric Bleeding
3) **Alcohol + Paracetamol à** ↑ PCM Toxicity
4) **Alcohol + Cefoperazone/Metronidazole/ Sulphonylureas à** Disulfiram like reaction
5) **Alcohol + CNS depressants/antihistaminics à** CNS depression with motor impairment à increase accident chances

DISULFIRAM- Aldehyde Dehydrogenase Inhibitors

Disulfiram

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Inhibits Aldehyde Dehydrogenase

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Inhibit Active Metabolic Conversion

- Disulfiram + Alcohol à ? Aldehyde Dehydrogenase levels in blood & tissues à **Aldehyde syndrome** (Flushing, burning sensation, throbbing headache, perspiration, uneasiness, tightness in chest, dizziness, vomiting, visual disturbances, mental confusion, postural fainting & circulatory collapse).

DISULFIRAM – USES & ADVERSE EFFECTS

1) As an Aversion technique in chronic alcoholics à motivated & sincerely desire to leave the habit.

2) After abstaining from alcohol overnight à give Disulfiram 1 gm on 1st day, 0.75 gm on 2nd day, 0.5 gm on 3rd day & 0.25 gm on daily for 1-2 weeks followed by 0.125- 0.25 g/day. Sensitization to alcohol develops after 2-3 hrs of 1st dose and lasts for 7-14 days after stopping it. Subject resolve not to drink is reinforced by distressing symptoms.

3) Adverse Effects :- rashes, metallic taste, nervousness, malaise & abdominal upset.

Tab. Antabuse : 250 mg.

METHANOL POISONING

—Unscrupulous mixing of methylated spirit with alcohol à **Methanol poisoning** (Pl. levels > 50mg/dl).

Methyl Alcohol (Methanol)

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Alcohol ↓ Dehydrogenase

↓

Acetaldehyde

↓

Acetaldehyde ↓ Dehydrogenase

↓

Formaldehyde + Formic acid (Blindness, acidosis)

(Vomiting, Headache, epigastric pain, uneasiness, dyspnoea, bradycardia, hypotension, acidosis, delirium, Respiratory failure & death)

Treatment of Methanol Poisoning

- Keep pt. in dark room à protect eyes from light.
- Gastric Lavage, Activated Charcoal
- Maintain ventilation, BP
- Combact acidosis with I.V Na_2HCO_3 infusion à prevent retinal damage
- Kcl if Hypokalaemia occur
- Inhibition of Methanol Metabolism :
- (i) Ethanol 10% IV; 0.6 g/kg loading dose followed by 10 g/ Hr infusion à saturates alcohol dehydrogenase à retards ethanol metabolism.
- Ethanol 10% in water is administered through nasogastric tube à loading dose of 0.7ml/kg à followed by 0.15ml/kg/hour drip. Continue treatment for long time.

Treatment of Methanol Poisoning

- **(ii) Fomepizole à 100 mg diluted in 250 ml isotonic saline and infused slowly over 45mins à** specific **inhibitor of alcohol dehdrogenase à** retards methanol metabolism.**(Orphan Drug)**
- (A loading dose of 15 mg/kg i.v. followed by 10 mg/ kg every 12 hrs till serum methanol levels falls below 20 mg/dl).

TO Promote Metabolic Degradation of Folate :

- **Folate Therapy à** Calcium Leucovorin injected repeatedly à enhances folate metabolism à reduces blood folate levels
- Folinic acid 1mg/kg (Max 50mg) IV with Folic acid 1mg/Kg IV 4 hrly for 6 doses
- Diuretics, urine alkanization
- **Haemodialysisà hastens recovery.**