ALCOHOL

ETHYL ALCOHOL
(Ethanol)
ETHANOL

• **PHARMACOKINETICS**
  
  • absorption--more from intestine, peak level after 30 min from empty stomach
  
  • Vd----0.5 -0.7L/kg
  
  • High first pass by gastric& liver ADH, lower in females
  
  • Sequential hepatic oxidation to acetate 90-98%
  
  • Zero order metabolism, supply of NAD+ rate limiting step
• Induces CYP 2E1
• Vey small amount metab by catalase
PHARMACOLOGICAL EFFECTS

• CNS

• Exact mechanism not known, may be GABA receptor agonist, & blockade of NMDA recep
dose dependent CNS depression

• Relieve anxiety, euphoria

• Behavioral disinhibition
  uncontrolled mood swings & emotional outbursts that may have violent components

• Toxic doses resp depression, coma
CVS

HYPERTENSION

Incr prevalence of hypertension (5---11%) cessation more than 30 gm alcohol associated with 2 mmHg increase in systolic & diastolic BP,

i) increase in vascular reactivity due to release of Ca++

ii) inhibition of release of NO from endothelium
- **CARDIOMYOPATHY**
  
  dose related hypokinesis, free fatty acids react enzymatically with ethanol forming fatty acid ethyl esters
  
  50% patients of idiopathic cardiomyopathy are alcoholic
  
  abstinence reverses myopathy

- **CARDIAC ARRYTHMIAS**
  
  supraventricular tachycardia, atrial fibrillation, atrial flutter,
  
  alcohol–dependents resistant to cardioversion
• SERUM LIPOPROTEINS & EFFECT ON CVS

  20----30 gm/day cardioprotective,
  10---40% decreased risk of CHD & myocardial infarction

  increased HDL, tissue plasminogen activator, decreased fibrinogen consumption,

STROKE

  cardiac arrythmias lead to thrombus formation,
  hypertension, acute rise may cause bleeding,
  head trauma
• **SKELETAL MUSCLES**
• Myomathy, dec muscle strength,
• Heavy drinking may cause irreversible damage dec glycogen stores , reduced pyruvate kinase ,, reduction in muscle protein synthesis & type 11 fiber atrophy

**BODY TEMPERATURE** (hypothermia)

  i) Inc cutaneous & gastric blood flow, so a feeling of warmth
  inc sweating,

Rapid heat loss dec body temp

  ii) Heavy drinking depresses central temp-regulating center, in winters chance of death due to hypothermia
• **DIURESIS**

Inhibits release of ADH, volume loading complements diuresis
tolerance develops to diuretic effect

**GIT**

a) Esophageal reflux, barret’s esophagus, traumatic rupture, Mallory-Weiss tears, & esophageal cancer,

b) disrupt gastric mucosal barrier, inc gastric secretions due to stimulation of buccal & gastric nerves causing release of gastrin & histamine acute & chronic gastritis,

heavy drinking directly damages the mucosa
• C) **malabsorption**---leading to diarrheha, rectal fissures, pruritis ani

• Structural & functional changes in intestines, dec enzyme levels, flattened villi reversible after stopping alcohol

D) **acute & chronic pancreatitis** due to direct toxic metabolic effect on pancreatic cells

E) Fatty infiltration of liver, fibrosis,
• **VITAMINS & MINERALS**

Heavy drinkers have multiple nutritional deficiencies due to poor intake, malabsorption/poor absorption, and impaired utilization.

**B-complex deficiency** especially thiamine resulting in **peripheral neuropathy**, **Wernicke’s encephalopathy**, **Korsakoff’s psychosis**

**Vit A deficiency**, decreased intake, increased metabolism due to enzyme induction, daily supplementation

**Vit E** chronic alcohol intake inflicts oxidative stress, antioxidant effect of alpha tocopherol may ameliorate hepatotoxicity
• VIT D In liver cirrhosis not activated (hydroxylated) resulting in osteoporosis

Hypomagnesemia & dec intracellular levels of Mg disturb cytoplasmic & mitochondrial bioenergetic pathways, leading to Ca++ overload & ischemia

SEXUAL FUNCTION initially increased libido, excessive long term use causes

i) impotence (in about 50% of patients), it provokes the desire but takes away function

ii) Testicular atrophy & infertility (direct effect on Leydig cell & depressed hypothalamic function)

iii) gynaecomastia, in alcoholic liver disease due to accelerated metabolism of testosterone

iv) Small ovaries without follicular development, dec libido, dec vaginal lubrication
HEMATOLOGICAL & IMMUNOLOGICAL EFFECTS

- Microcytic anemia---blood loss & iron def
- Normocytic anemia
- Macrocytic anemia
- Reversible thrombocytopenia, below 20,000/mm³
- Dec T-cell production & migration, dec formation of immunoglobulins
- Dec IL2 function, inc replication of HIV
CLINICAL USES OAF ETHANOL

RELIEF OF LONG LASTING PAIN

LOCAL INJECTION

• Injection of dehydrated alcohol in close proximity to a nerve or sympathetic ganglia to relieve long-lasting pain e.g. trigeminal neuralgia, inoperable carcinoma

• Lumbar paravertebral injection may destroy sympathetic ganglia & produces vasodilation, relieve pain & promote healing of lesions in lower extremities of patients with peripheral vascular disease
TOLERANCE & DEPENDENCE

• Tolerance is defined as reduced behavioral or physiological response to the same dose of alcohol

• ACUTE TOLERANCE

• Tolerance can be demonstrated by measuring behavioral impairment at the same BAL (blood alcohol level) on the ascending limb of BAL-time curve (minutes after ingestion of alcohol) and on the descending limb of the curve as BALs are lowered by metabolism
• **CHRONIC TOLERANCE**
  • seen in long term heavy drinkers & is due to induction of metabolizing enzymes & is mainly due to induction of metabolizing enzymes

• **PHYSICAL DEPENDENCE**
  • Elicitation of withdrawal syndrome when alcohol consumption is terminated

• **SYMPTOMS**
  • **Immediate**: Sleep disturbance, sympathetic stimulation, tremors and maybe seizures
  • **Late**: *delirium tremens* characterized by hallucination, delirium, fever & tachycardia, may be fatal
PSYCHOLOGICAL DEPENDENCE

Craving & drug seeking behavior. This may be due to impairment of dopaminergic reward system thus resulting in increased intake in an attempt to regain activation of the system.

Prefrontal cortex is sensitive to alcohol abuse, influencing decision making & emotion. This lack of judgement and control causes obsessive alcohol consumption.

Increase in NMDA-receptor function after chronic use & may contribute to CNS hyperexcitability & neurotoxicity after withdrawal.
• **SYSTEMIC ADMINISTRATION**
• Methanol & ethylene glycol poisoning, methyl alcohol is metabolized to formaldehyde by the enzyme ADH (alcohol dehydrogenase). As ethyl alcohol has more affinity ADH, it competes & replaces methyl alcohol from enzyme binding site thus decreasing the rate of production of formaldehyde.
ACUTE ALCOHOL INTOXICATION

• (Depends upon the level of tolerance, chronic alcoholics can tolerate high dose which may be fatal in non-addicts)

• **Intoxication** at blood levels of 80mg/dl, motor vehical accidents greatly reduced at levels <50-80 mg/dl

• **20---30mg/dl** increased reaction time, diminished fine motor control, impaired judgment

• >**150mg/dl**

• >**400 mg/dl** resp depression & death