

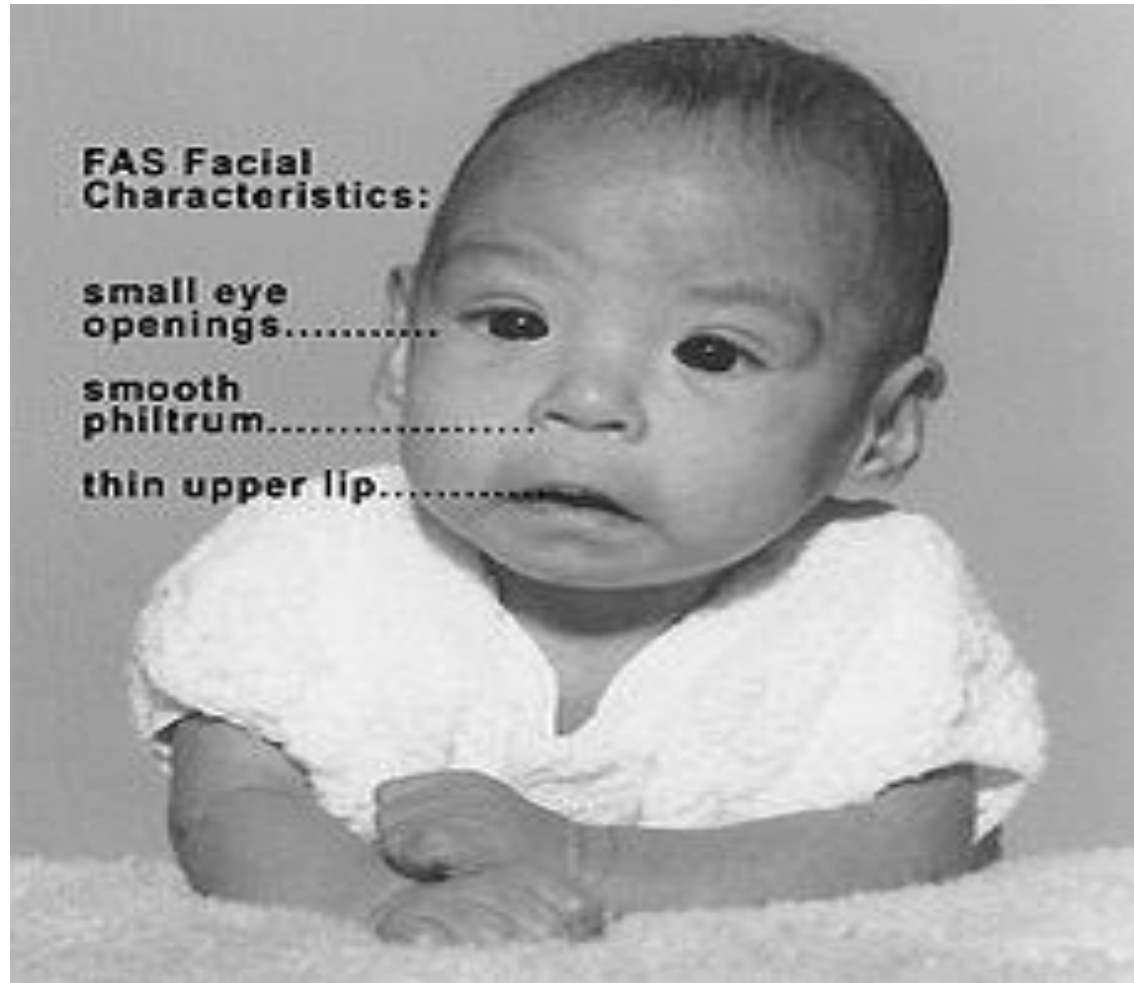
Alcohol

Rahul Kumar

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- Alcohol in low to moderate amounts relieves anxiety and gives a feeling of well-being or even euphoria.
- Alcohol is also the most commonly abused drug in the world.
- Each year thousands of children are born with **morphologic and functional defects** resulting from prenatal exposure to ethanol.

Fetal alcohol syndrome

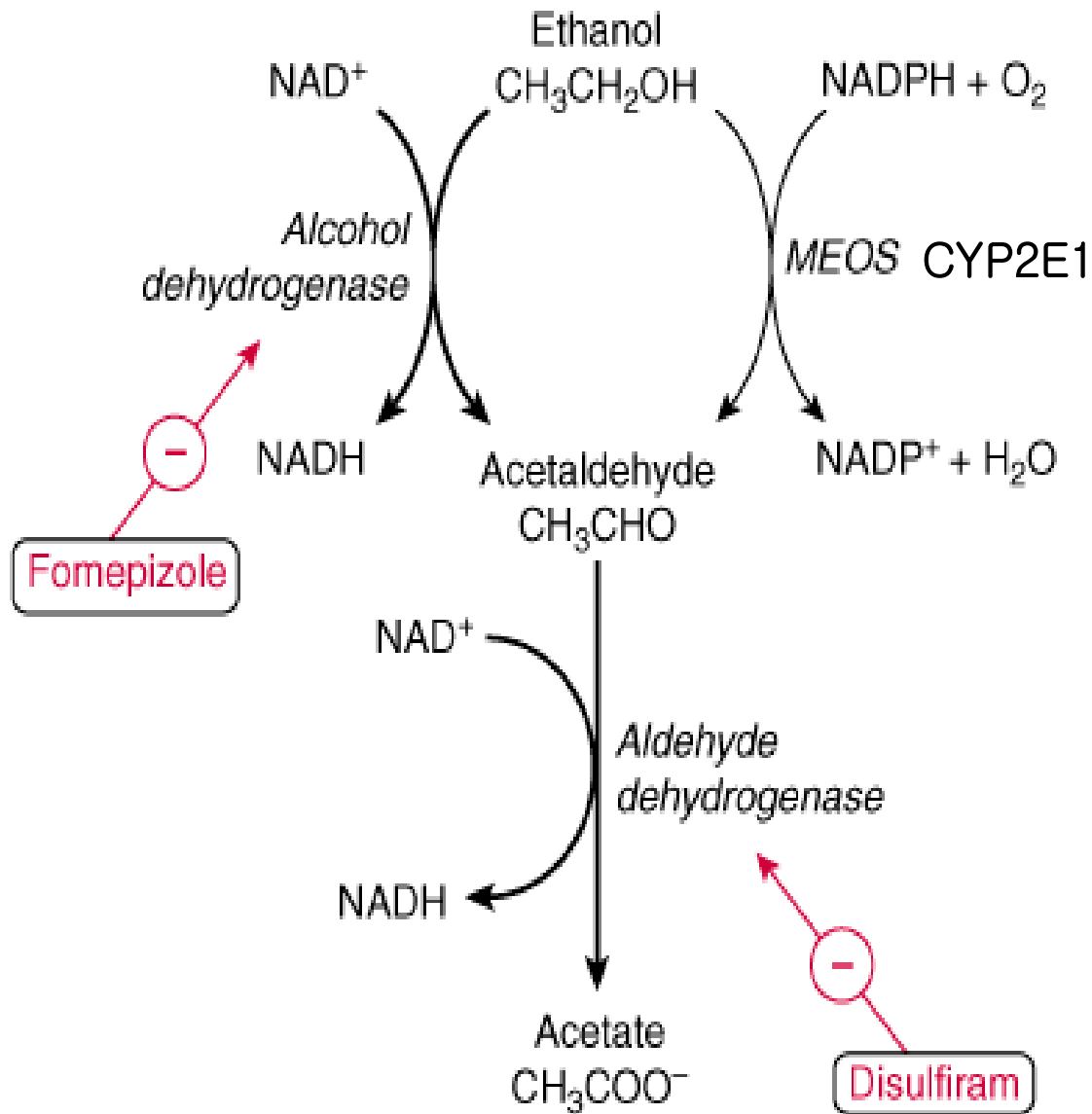


Growth retardation
Low IQ
Microcephaly

Pharmacokinetics

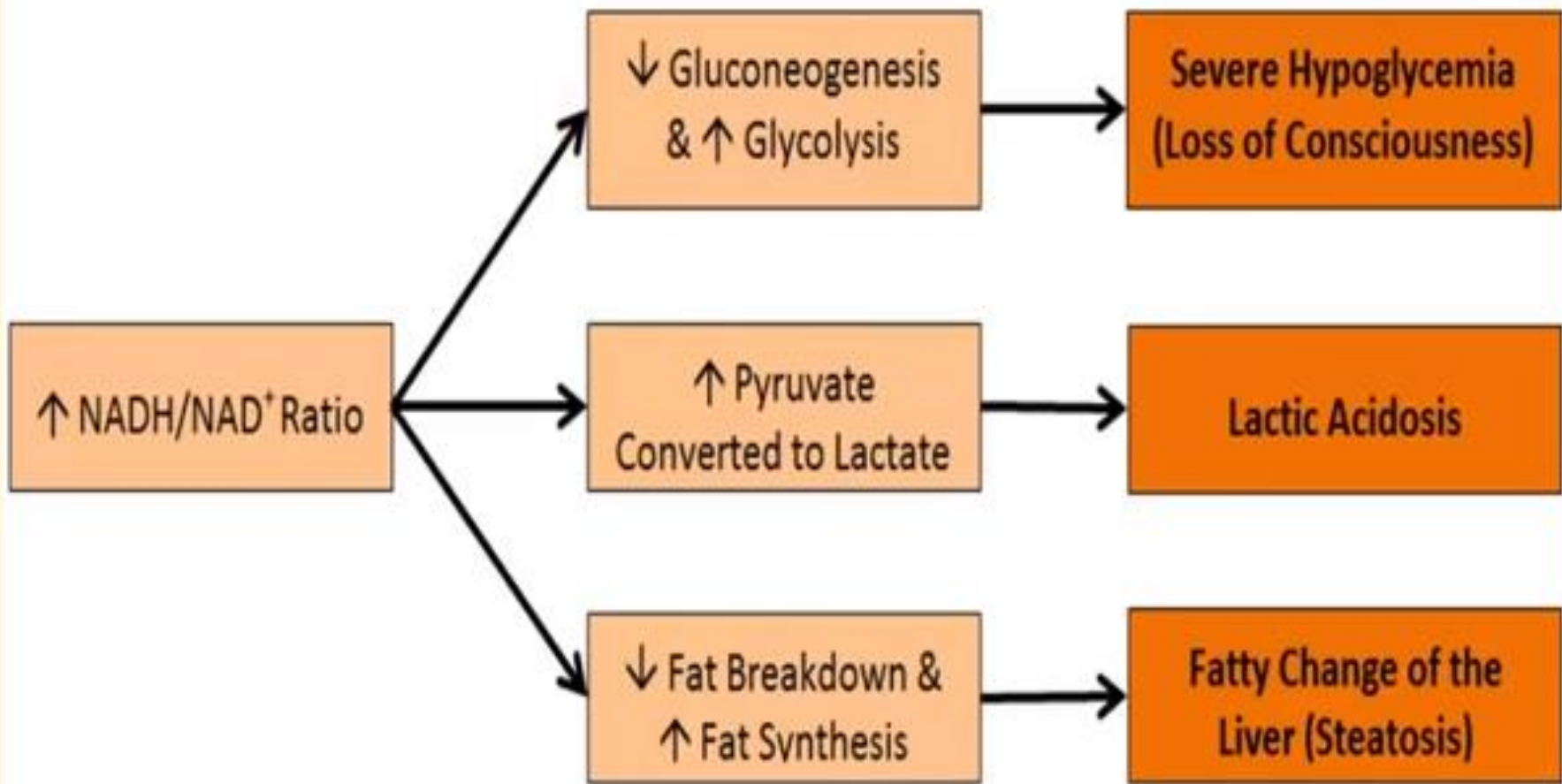
- Over 90% of alcohol consumed is oxidized in the liver. Much of the remainder is excreted through the lungs and in the urine.
- Rate of oxidation follows zero-order kinetics.
- The typical adult can metabolize approx. **8g** of alcohol **per hour**, the equivalent of approximately **one "drink" (300 mL beer, 105 mL wine, or 30 mL whisky)**.

- Beers- 4-8%
- Wines- 9-12%
- Rum, Gin, Whiskey, Brandy, Vodka- 42.8% v /v
or 37% w /w.



MEOS -microsomal ethanol oxidizing system (by CYP2E1)

- Each metabolic step requires NAD⁺
- Thus oxidation of 1 mol ethanol (46 g) to 1 mol acetic acid requires 2 mol NAD⁺ (approximately 1.3 kg)
- NAD⁺ availability limits ethanol metabolism
- In a 70-kg adult
 - **8 g or 10 ml or 170 mmol alcohol per hour**
- Approximately 120 mg/kg per hour.
- For individuals with normal hepatic function, ethanol is metabolized at a rate of **one standard drink every 60 minutes.**



Breath alcohol test

- The **excretion** of a small but **consistent proportion of alcohol by the lungs** can be quantified with breath alcohol tests.
- **Alcohol exceeding 30 mg per 100 ml of blood** as detected in a test by a **Breath Analyzer** is liable to be charged for impaired driving under Section 185 MVA'88.

Blood concentration after ingestion of three standard drinks

- empty stomach -67 to 92 mg/dl in men
- after a mixed meal -30 to 53 mg/dl in men

Concentrations will be higher in women because,

- smaller than men
- have less body water per unit of weight
- have less gastric ADH

Avoid these drugs with alcohol

- **Aspirin** - increases ethanol bioavailability by **inhibiting gastric ADH** (alcohol dehydrogenase)
- **Paracetamol**
- Antihistaminics, hypnotics, opioids

ETHANOL TOXICITY

- **Moderate drinking**

- nausea, vomiting, hangover, traffic accidents

- **Acute alcohol intoxication**

- gastritis, stupor,

- hypotension, hypoglycaemia,

- respiratory depression, collapse, coma ,death

ETHANOL TOXICITY

Treatment

- Fluid, electrolyte balance
- Glucose (with Thiamine) to treat hypoglycaemia

Comatose patients with respiratory depression -

- intubated and ventilatory assistance
- Stomach lavage
- Hemodialysis
- Sedatives and antipsychotic agents to quiet patients
(Some individuals may display extremely violent behaviour)

ACUTE ETHANOL INTOXICATION

CNS manifestation

- 20 - 30 mg/dl in the blood
 - increased reaction time
 - diminished fine motor control
 - Impulsivity
 - impaired judgment
- 30 -100/dl - excitation and euphoria
- 100 - 150 mg/dl -mental clouding, disorganization of thought, impairment of memory
- 150-200 mg/ dl - ataxic and drunk
- 200-300 mg/ dl -stupor
- 300 - 400 mg/dl - fatal

Effects of Alcohol

Local effects

- **Astringent**-precipitates surface proteins and hardens skin
- **Antiseptic**
The antiseptic action increases with concentration from 20 to 70%

Effects of Alcohol

CNS

- Ethanol primarily is a **CNS depressant**
- But there is little margin between the anaesthetic actions and lethal effects (usually owing to respiratory depression).

Chronic Alcoholism

- Deficits in cognitive functioning and judgment
- Dementia
- **Shrinkage of the brain** (loss of both white and gray matter)
- Polyneuritis, **pellagra**, tremors, seizures,
- **Wernicke's encephalopathy** (confusion, ophthalmoparesis, ataxia)
- Korsakoff's psychosis
- Megaloblastic anemia

Cardiovascular System

- **Moderate doses - tachycardia and mild BP rise**
- **Large doses - increased incidence of arrhythmias, cardiomyopathy, and haemorrhagic stroke.**
- Alcohol has a **J-shaped dose-mortality curve**.
Reduced risks for CHD are seen at intakes as low as one-half drink per day ([Maclure, 1993](#))([Libby, 2007](#)).

Cardiovascular System

Possible mechanism of cardio protective effect of low dose alcohol-

- Elevates HDL
- Elevates tPA (tissue plasminogen activator)
- Inhibit platelet activation
- Flavonoids (in red wine) have additional antiatherogenic role

GIT

- Vomiting, mucosal congestion and gastritis
- Lower esophageal sphincter tone is reduced
- Acute pancreatitis

Liver

- Fatty Liver-increases fat synthesis in liver
- Oxidative stress / cellular necrosis / fibrosis

Skeletal muscle

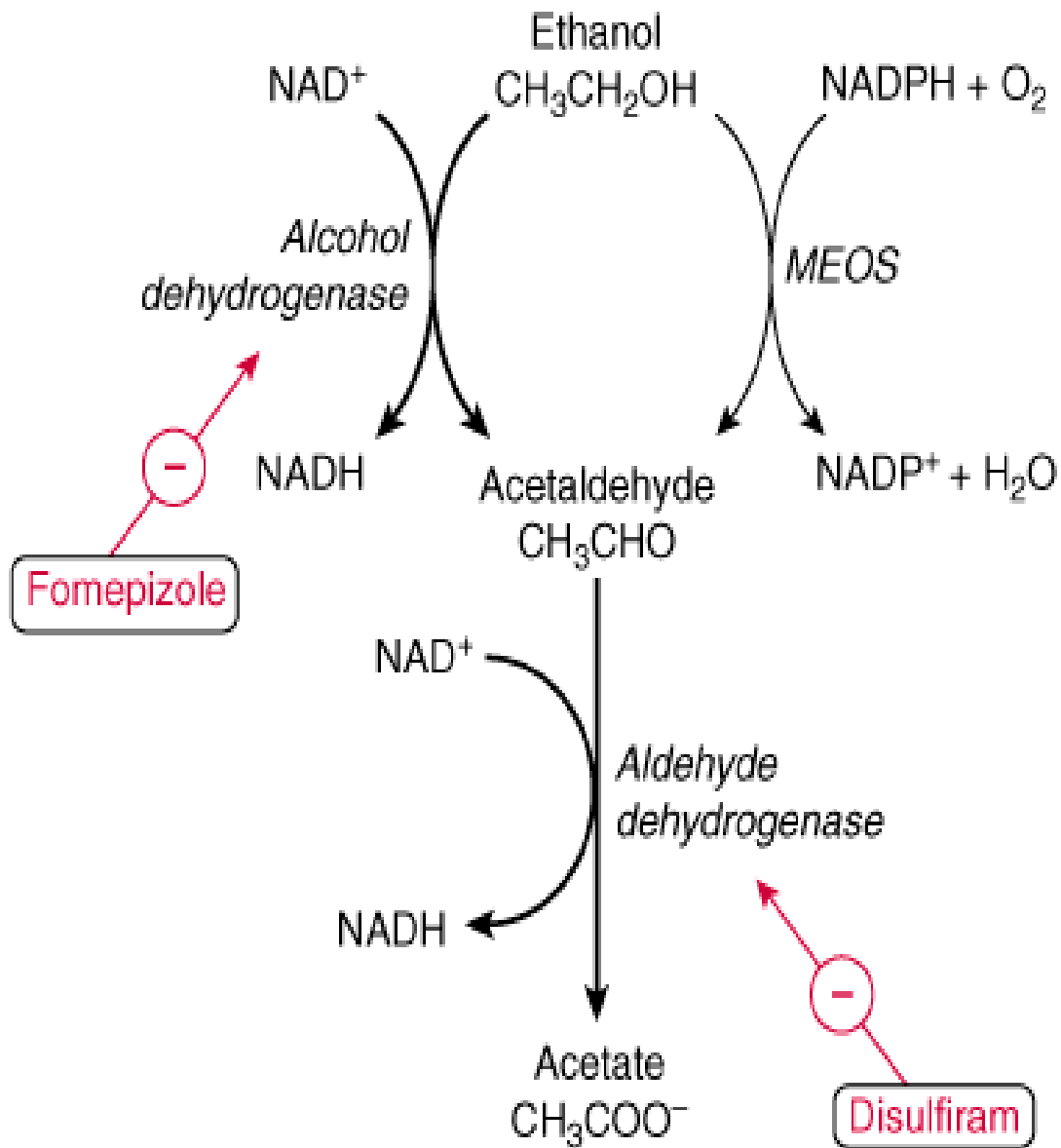
- Weakness and myopathy

Sex

- Aphrodisiac
- Loss of restraint and inhibition
- Performance is impaired
- Impotence
- Testicular atrophy
- Gynaecomastia
- Infertility

PHARMACOTHERAPY OF ALCOHOLISM

- DNA-(*D*isulfiram, *N*altrexone, *A*camprosate)



Disulfiram

- inhibits ALDH activity
- increase blood acetaldehyde concentration
- Effects within 5 to 10 minutes
- Facial flush
- Intense throbbing or pulsating headache
- Respiratory difficulties, nausea, copious vomiting, sweating, thirst, chest pain, considerable hypotension, uneasiness, weakness, vertigo, blurred vision, confusion
- Facial flush changes to pallor, and BP may fall to shock levels

Disulfiram

- Alarming disulfiram reactions may result after ingestion of even small amounts of alcohol
- Disulfiram use should be attempted only **under medical and nursing supervision**
- **Patients must be warned** that as long as they are taking disulfiram, the ingestion of alcohol in any form will make them sick and may endanger their lives.
- Patients must learn to **avoid disguised forms of alcohol**
 - sauces
 - fermented vinegar
 - cough syrups
 - after-shave lotions

Disulfiram-like reactions

- sulfonyleureas (chlorpropamide)
- Cephalosporins (cefoperazone, moxalactam, cefamandole)
- Metronidazole

Naltrexone

- It reduced alcohol craving, number of drinking

Acamprosate

- NMDA-receptor antagonist
- Modest GABA_A receptor agonistic activity
- Maintenance therapy of alcohol abstinence

Methanol Poisoning

- Methanol is metabolized to formaldehyde and formic acid
- Toxic effects of methanol are largely due to **formic acid**
- 15 ml of methanol has caused blindness and 30 ml has caused death; fatal dose is regarded to be 75-100 ml.
- **Retinal damage**, Blurring of vision, congestion of optic disc followed by **blindness** always precede death which is due to respiratory failure.

Methanol Poisoning Treatment

- **Dark room**
- protect the eyes from light
- Gastric lavage with sod. bicarbonate
- **i.v. Sod. bicarbonate** infusion-the most important measure
- **Ethanol** (10% in water) by nasogastric tube (saturate ADH and retard methanol metabolism)
- Haemodialysis
- **Fomepizole** (4-methylpyrazole)- iv infusion
- **Folate/Calcium leucovorin** (50 mg iv 6 hourly)- reduce formic acid level by enhancing its oxidation

Psychostimulants

- **Amphetamine & Methylphenidate**
(release NA & DA in brain) -**ADHD**
- **Modafinil-**
inc **alertness** & keep awake
- **Caffeine-**
Migraine, allay fatigue, treat apnoea in
premature infants

Alzheimer's disease

- Progressive **memory loss**
- Disordered cognitive functions
- Reduced verbal fluency
- Bedridden as disease progresses
- Complications of immobility

Alzheimer's disease

- **Amyloid plaque** (extracellular deposits of β -amyloid protein)
- **Intraneuronal neurofibrillary tangles** (aggregates of highly phosphorylated neuronal protein)
- **Loss of cholinergic neurons** in brain (originates from nucleus basalis in forebrain and project to frontal cortex and hippocampus)

Alzheimer's disease Tx

- Anticholinesterases
 - Donepezil
 - Rivastigmine
 - Galantamine
 - Tacrine (hepatotoxic)
- NMDA antagonist
 - Memantine
- Nootropics
 - Piracetam
- Anti-oxidants
 - Vit. A, C,
 - Zinc, Selenium
- Miscellaneous
 - Statins
 - Ibuprofen
 - Ginkgo biloba

Thanks