



Environmental & Toxicity Related Diseases

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Environmental Diseases

- Refers to diseases caused by chemical or physical agents
 - Ambient (immediate surroundings)
 - Workplace
 - Personal Environment

- **Classification**
 - Personal exposures
 - Therapeutic drugs
 - Outdoor air pollution
 - Indoor air pollution
 - Industrial exposures
 - Agricultural hazards
 - Natural toxins
 - Radiation injury

Personal exposures

- Tobacco use
- Alcohol abuse
- Drug abuse

Tobacco use

- The different forms of tobacco use
 - Cigarettes
 - Snuff
 - Cigars
 - Pipes
 - Chewing

Smoking Epidemiology

- Multiple chronic conditions of premature death in the US
 - Accounts for ~20% of all deaths
 - Single preventable cause of cancer
- Percentage of US population that smokes ~25%
- Incidence of smoking is increasing in females and decreasing in males

Major Components of Cigarette Smoke

- Carbon monoxide
 - Damages endothelium which predisposes to atherosclerosis
- Carcinogens
 - Polycyclic Hydrocarbons, Benzopyrene, Nitrosamines, Vinyl Chloride, Hydrazine
- Chemical irritants/cilia toxins
 - Ammonia, Formaldehyde
 - Impaired tracheobronchial clearance
 - Increased susceptibility to pneumonia
 - Nicotine

Cigarette smoking is down, but almost
38 MILLION
American adults still smoke

Cigarette smoking remains high
among certain groups



Men



Adults 25-64
years old



Lower education



Below
poverty level



Midwest
and South



Uninsured
or Medicaid



Disabled



Serious
psychological
distress



American Indians,
Alaska Natives and
Multiracial



Lesbians, gays,
and bisexuals

Nicotine

- Alkaloid & Addicting agent
- MOA (Mechanism of Action)
 - Absorbed rapidly into the pulmonary circulation
 - Crosses the blood brain barrier and stimulates nicotinic receptors in the brain to produce the gratifying effects
- Acute pharmacologic effects are mediated by catecholamine release
 - Increased heart rate and blood pressure

Test used to document nicotine intake

- Plasma or urine level of cotinine
- Cotinine is derived from metabolism of nicotine
- Saliva test is considered the most sensitive way to detect cotinine, and it can detect it for up to 4 days.
- Hair testing is a reliable way to figure out long-term use of tobacco products and can be very accurate for as long as 1 to 3 months after you stop using tobacco.

Smoking and Diseases

- 1) Nonneoplastic diseases**
- 2) Neoplastic diseases**

Nonneoplastic Diseases

- **Pulmonary**
 - COPD – Chronic Obstructive Pulmonary Disease
 - Chronic bronchitis and emphysema
 - Recurrent infections
 - Pneumonia

Nonneoplastic Diseases

- **Cardiovascular system**
 - Acute MI
 - Peripheral vascular disease
- **Gastrointestinal tract**
 - GERD
 - Gastric and duodenal ulcers (delay in healing)

Nonneoplastic Diseases

- **Effect on pregnant women**
 - IUGR (Intra-Uterine Growth Retardation)
 - ↑risk of spontaneous abortions and stillbirths
 - Abruptio placenta
 - Placenta previa
 - Premature rupture of membranes

Nonneoplastic Diseases

- **Effect on women**
 - Early menopause
 - ↑ rate of postmenopausal osteoporosis

Nonneoplastic Diseases

- **Effect on children**
 - ↑ risk of SIDS (Sudden Infant Death Syndrome)
 - ↑ incidence of ASOM (Acute Suppurative Otitis Media)
 - ↑ incidence of URTI (Upper Respiratory Tract Infection)
 - ↑ risk of asthma

Neoplastic Diseases

- Smoking associated with 30% of all cancer deaths
- Cancers where smoking is the leading cause
 - Lung cancer
 - Squamous cell carcinoma and small cell carcinoma have the highest relationship to smoking
 - Adenocarcinoma to a lesser extent
 - Major cause of death due to cancer in both women and men

Neoplastic Diseases

Squamous Cell Carcinoma



Neoplastic Diseases

- **Gastrointestinal**
 - Oral - squamous cell carcinoma
 - Esophagus - squamous cell carcinoma
 - Pancreatic adenocarcinoma

Neoplastic Diseases

- **Others**

- Larynx – squamous cell carcinoma
- Transitional cell carcinoma of bladder
- Renal adenocarcinoma

Cigarette Smoking Additive or Synergistic Effects

- **Alcohol enhances carcinogenicity** by
 - solubilizing carcinogens in tissue
 - inducing liver or GI enzymes to activate tobacco carcinogens
 - Increased risk of oropharyngeal, esophageal and laryngeal cancer

- **Smoking + asbestos exposure markedly increase risk of lung cancer**
 - No association of smoking with mesothelioma
 - Whether the person is a smoker or not, lung cancer is the most common cancer associated with asbestos exposure.

Passive Smoking

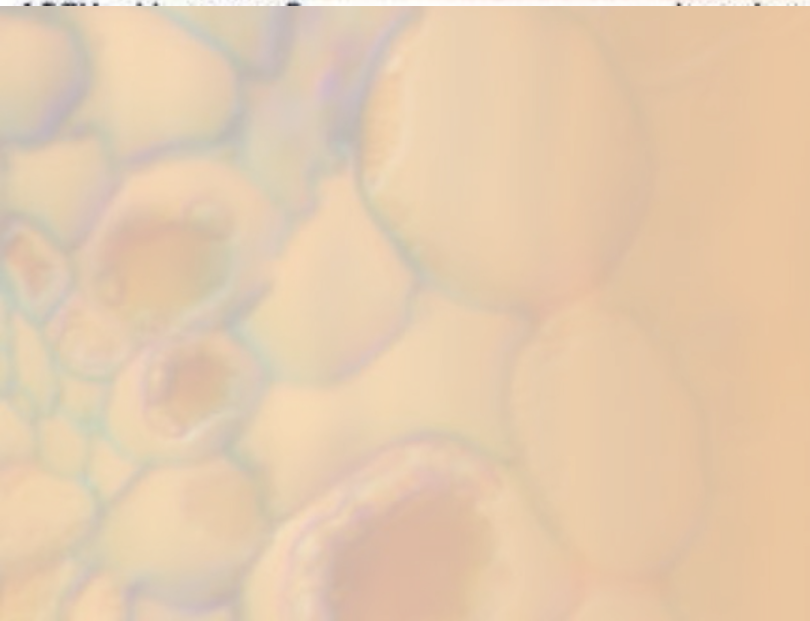
- Effect of cigarette smoke on bystanders ↑ risk of
 - Lung cancer
 - Acute myocardial infarction & ischemic heart disease
 - Respiratory illness

Passive Smoking

- **Children have ↑ risk for**
 - SIDS
 - Upper and lower respiratory infection
 - Ear infections (otitis media)
 - Exacerbates asthma

Effects of Smokeless Tobacco

- Snuff or chewing tobacco
 - Nicotine addiction
 - Oral leukoplakia /cancer
 - inside lip, under the tongue or cheek
 - Verrucose squamous cancers of oral cavity
 - Nasal cancer in snuff users
- Aggravation of cardiovascular disease



Alcohol Abuse

- Alcohol is of more widespread hazard and causes more deaths than cocaine & heroin addiction
- Western World Incidence Rate
 - 50% adult drink alcohol
 - 5-10% chronic alcoholics

Alcohol Abuse

- In USA
- >17 millions chronic alcoholics
- 1 in 12 adults are diagnosed with alcoholism
- Approximately 100,000 deaths per year
 - 50% DUI - drunken driving
 - 25% consequence of cirrhosis
 - Cost – \$100-130 billion per year

What is the diagnosis? “Drinking problem” or “Alcoholism”

- Excessive drinking is categorized by
 - heavy drinking
 - binge drinking
 - underage consumption
 - women who drink during pregnancy

Per National Institute of Alcohol Abuse

What is the diagnosis? “Drinking problem” or “Alcoholism”

- Heavy drinking for men is defined as more than five drinks in one sitting and more than 15 drinks per week.
- Heavy drinking for women is four drinks in one sitting and more than eight drinks in one week.
- **These individuals may be classified as “almost alcoholic.”**

Per National Institute of Alcohol Abuse

Definition of alcoholism

- Alcoholism is defined by alcohol dependence, which is the body's physical inability to stop drinking and the presence of alcohol cravings.

Ethyl Alcohol

- Most widely used and abused agent throughout the world
- Leading contributor to death due to
 - Motor vehicle accidents and liver disease
- Legal drunkenness
 - Blood levels ≥ 80 mg/dL OR $\geq 0.08\%$ BAC (Blood Alcohol Concentration)

Signs and symptoms of alcohol toxicity

- 50 - 100 mg/dL **This is less than a pint !!!**
 - Euphoria
- 100 - 200 mg/dL
 - Slurred speech & ataxia – Legally drunk in most states
- 125 -150 mg/dL
 - Combativeness
 - Unrestrained behavior

- 200 - 300 mg/dL
 - Lethargy
- 300 - 400 mg/dL
 - Coma
- 500 mg/dL
 - Respiratory arrest and death
- Heavy drinkers can tolerate higher levels (up to 700mg/dL)

Ethyl Alcohol

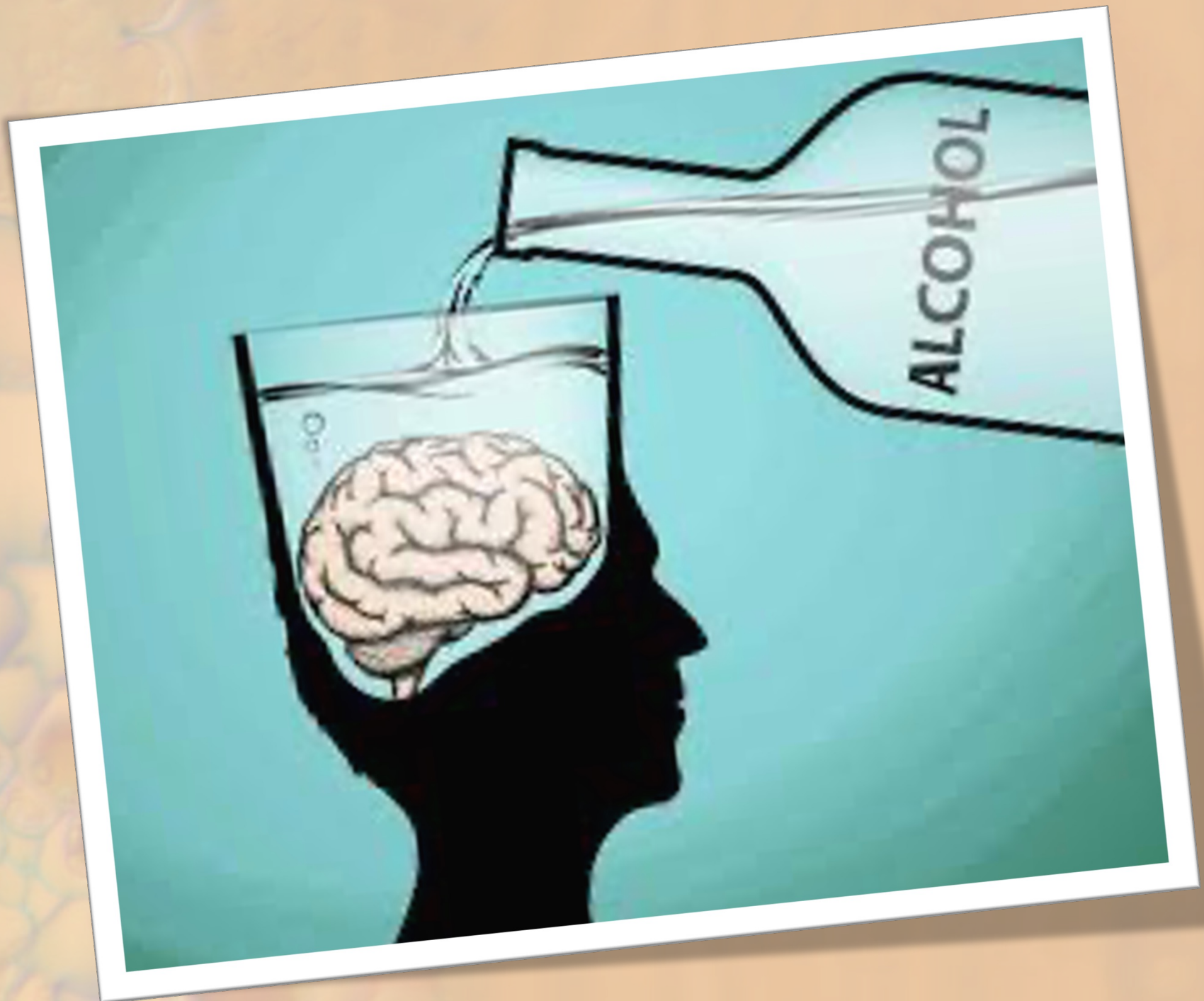
- Absorption occurs in
 - Small intestine and Stomach
- Metabolism occur in
 - Liver (95%) is primary site
 - Gastric mucosa
 - Partially metabolized by alcohol dehydrogenase

Conditions most commonly caused by alcohol abuse

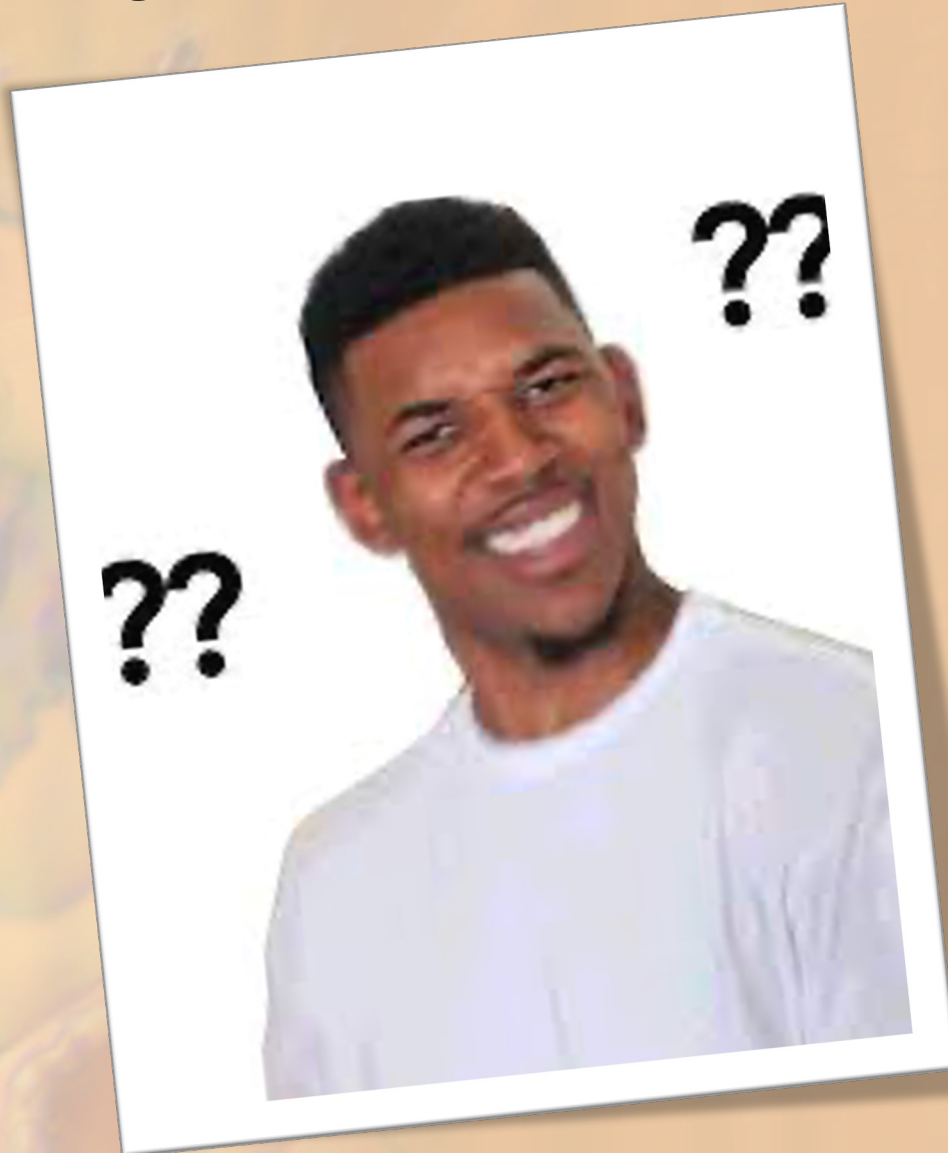
- Acute alcoholism
 - Primary effect on CNS
 - Acts as a CNS depressant
- Chronic alcoholism
 - Causes systemic effects due to
 - Direct toxic action and
 - Vitamin deficiency

Metabolic effects of alcohol abuse

- Deficiency of Thiamine (B1) deficiency predisposes to
 - Wernicke's encephalopathy
 - Characterized by confusion, ataxia, nystagmus
 - Korsakoff's psychosis
 - Characterized by memory loss
 - Inability to remember old and new information
- Cardiomyopathy may be not associated with B1 deficiency



Dr. M is having a “Senior Moment”. Where do you find liquefactive necrosis?

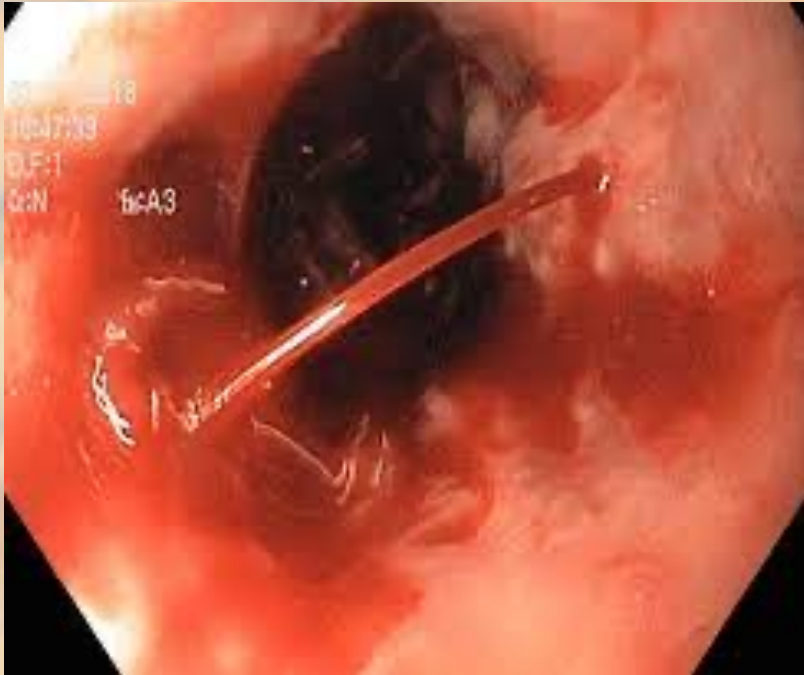


- Deficiency of Folate predisposes to
 - Macrocytic anemia



Gastrointestinal effects of alcohol abuse

- Esophageal varices - Secondary to Cirrhosis





- Acute gastritis and gastric reflux
 - Retching may result in
 - Mallory Weiss syndrome
 - retching causes esophageal tear at gastric-esophageal junction
 - Boerhaaves syndrome
 - retching causes esophageal rupture (distal esophagus)

Hepatobiliary effects of alcohol abuse

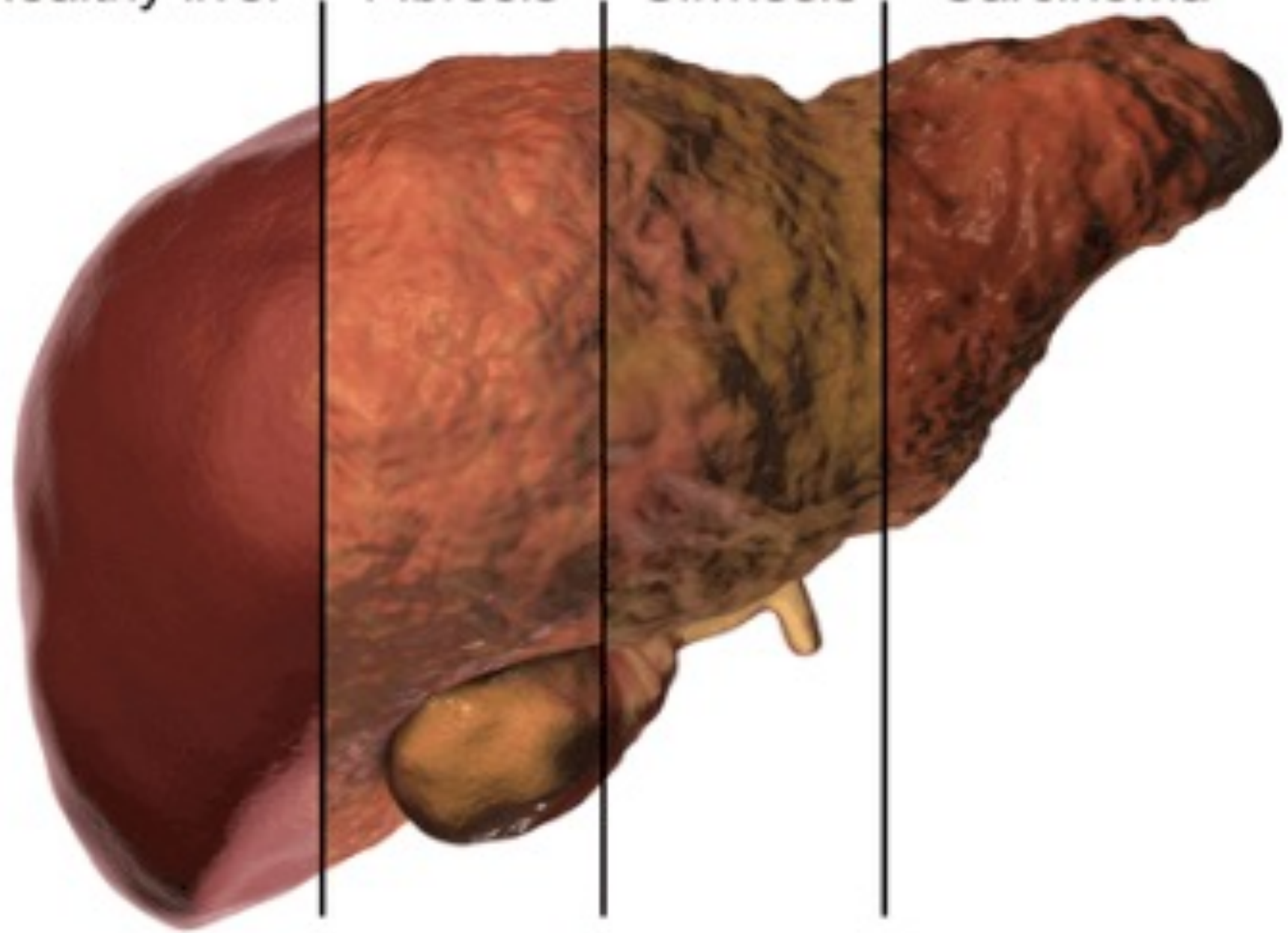
- The three major effects are
 - Fatty change (most common cause)
 - Cirrhosis (most common cause)
 - Acute alcoholic cirrhosis
- Other effects
 - Acute & Chronic pancreatitis
 - Hepatocellular carcinoma

Healthy liver

Fibrosis

Cirrhosis

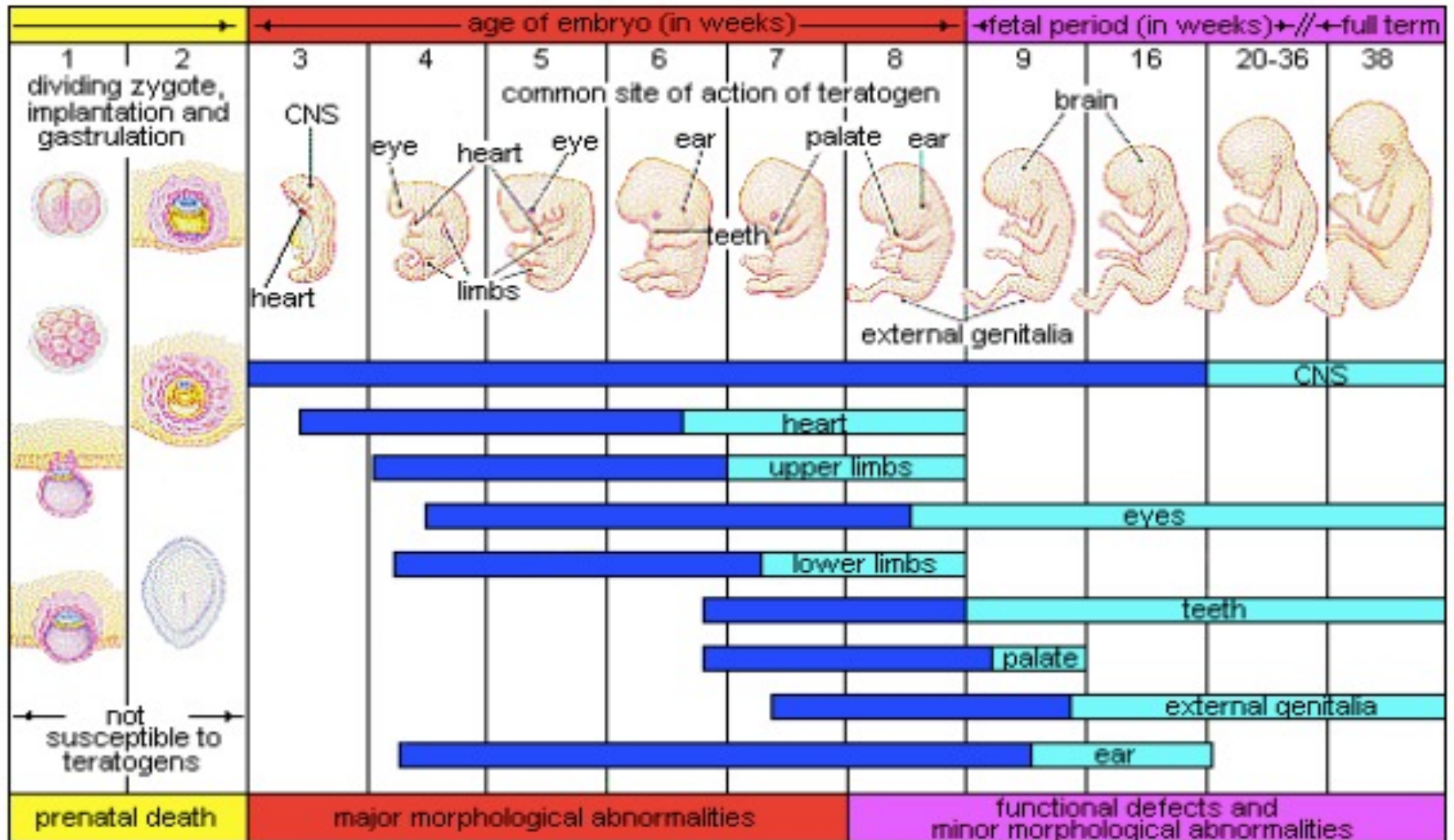
Carcinoma



Hematologic effects of alcohol abuse

- Macrocytic anemia
 - Folate deficiency
- Thrombocytopenia
 - Direct toxicity to bone marrow, hypersplenism
- Leukopenia
 - Hypersplenism
- Acquired Sideroblastic Anemia

What is a teratogen?

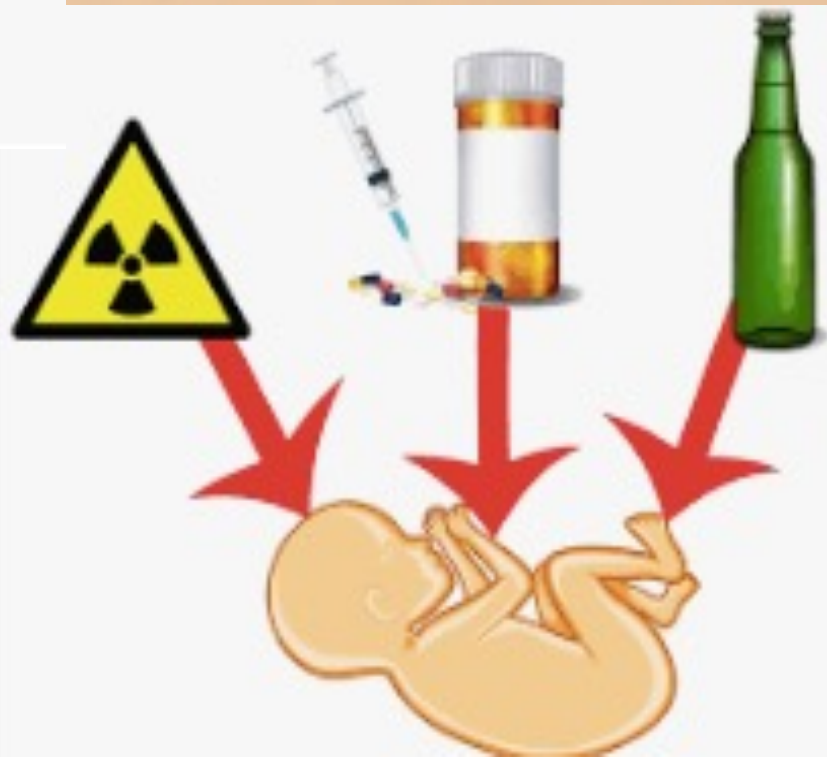


radiation



fetus

- ← alcohol
- ← drugs
- ← hormones
- ← cigarettes
- ← german measles
- ← lead
- ← mercury



Fetal Alcohol Syndrome

- Characterized by defect in growth and development
- Clinical features
 - Microcephaly
 - Short palpebral fissure
 - Maxillary hypoplasia
 - Mental and growth retardation

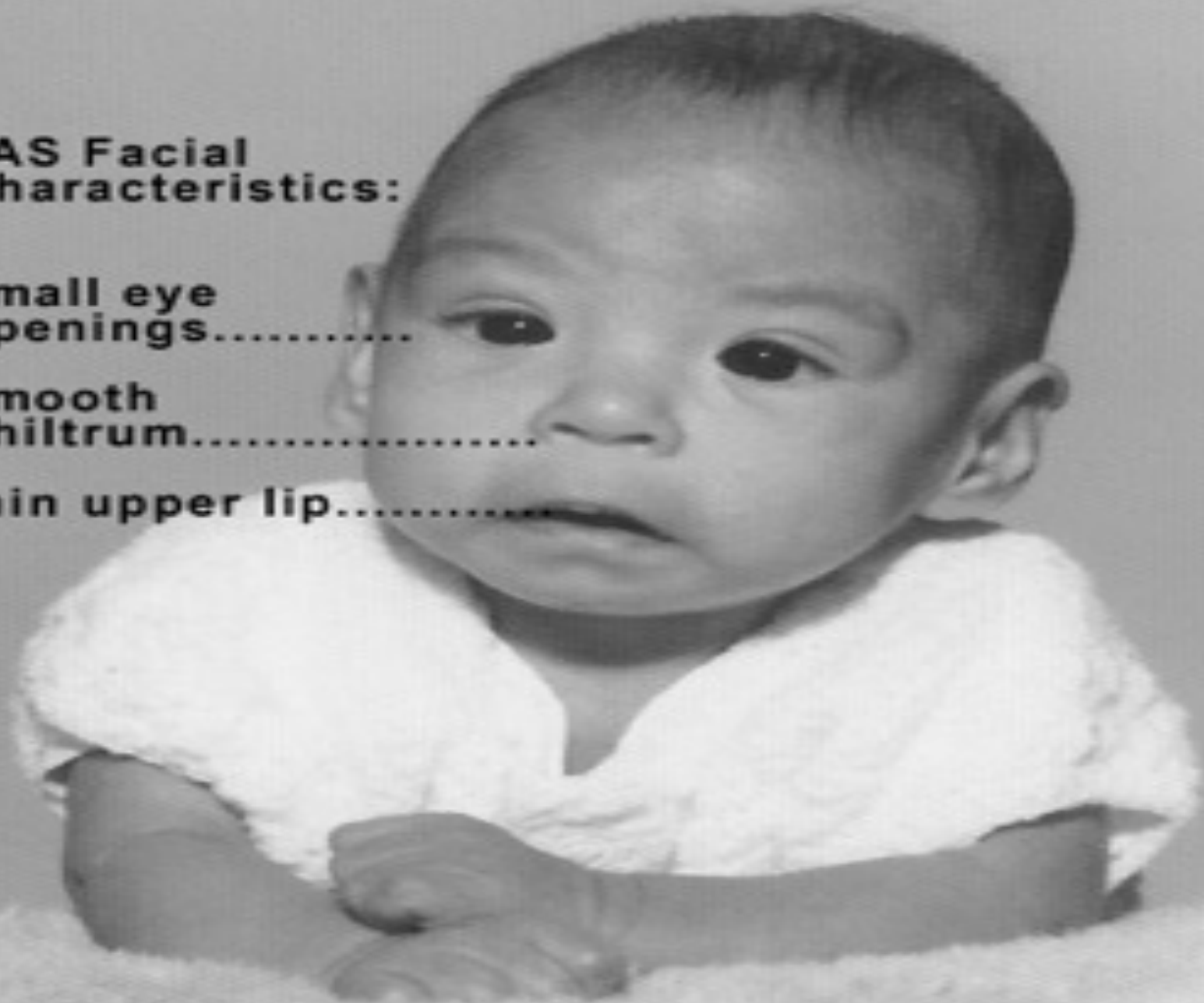
Baby with Fetal Alcohol Syndrome

FAS Facial Characteristics:

small eye openings.....

smooth philtrum.....

thin upper lip.....



- The MOST COMMON type of preventable mental retardation in the U.S.
- Mechanism of pathophysiology
 - Acetaldehyde crosses the placenta and damages the fetal brain

Methanol Poisoning

- Present in
 - Window shield washer fluid
 - Solvents for paints
- Ingestion
 - Accidental
 - As a substitute for ethanol
- Metabolized in liver by alcohol dehydrogenase into formic acid
 - Damages the optic nerve (optic neuritis)
 - Blurred vision
 - Could lead to permanent blindness

Ethylene Glycol (Antifreeze)

- Liver converts it into glycolic acid and oxalic acid.
- Oxalic acid causes calcium oxalate crystals which obstructs renal tubules causing renal failure



Calcium Oxalate Crystals in Urine



Drug Abuse

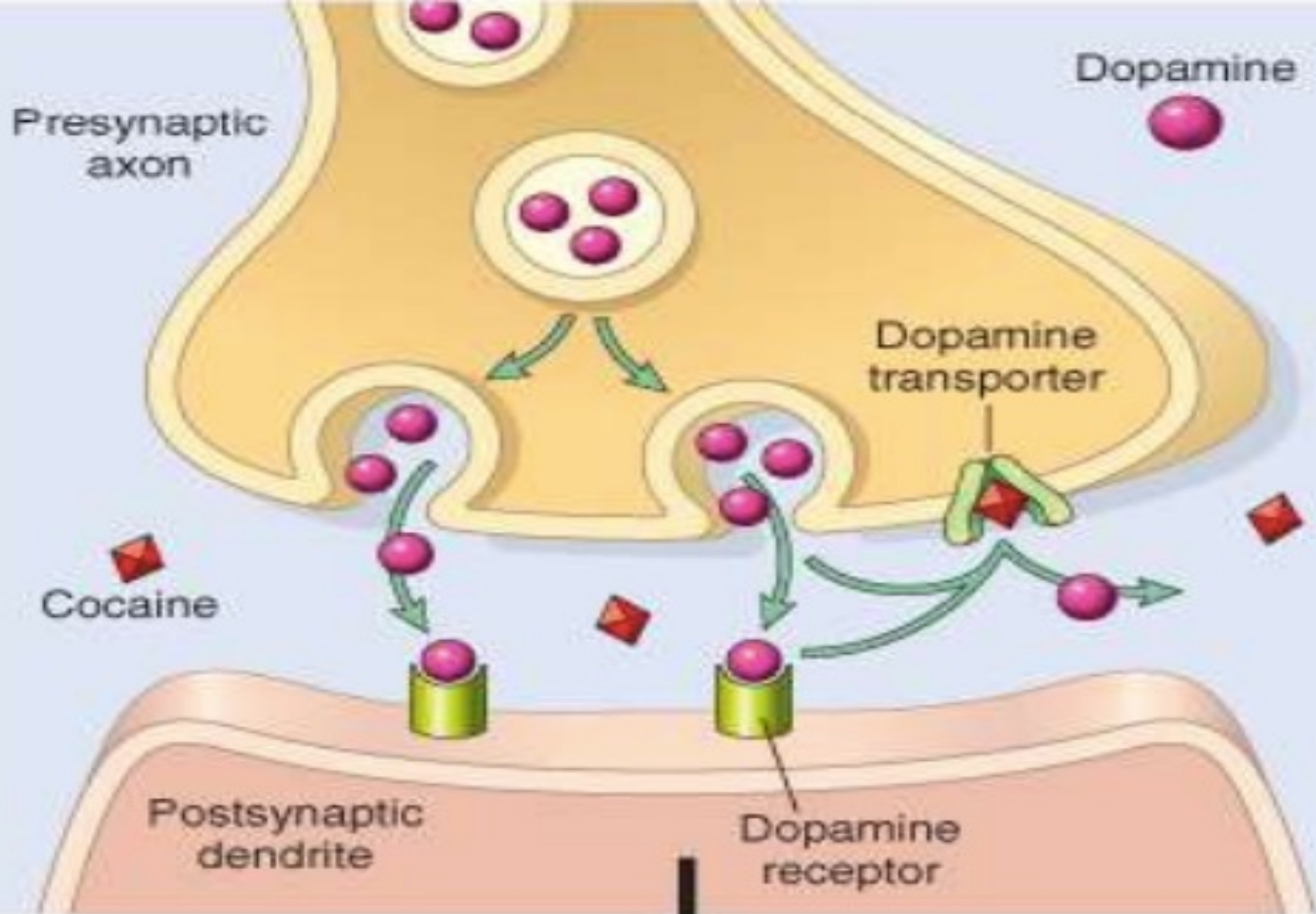
- Commonly abused drugs
 - CNS depressants
 - barbiturates (Pharmacology)
 - CNS stimulants
 - Cocaine
 - Tricyclic Antidepressants (Pharmacology)
 - Narcotics or hallucinogens
 - Heroin
 - Marijuana

Cocaine

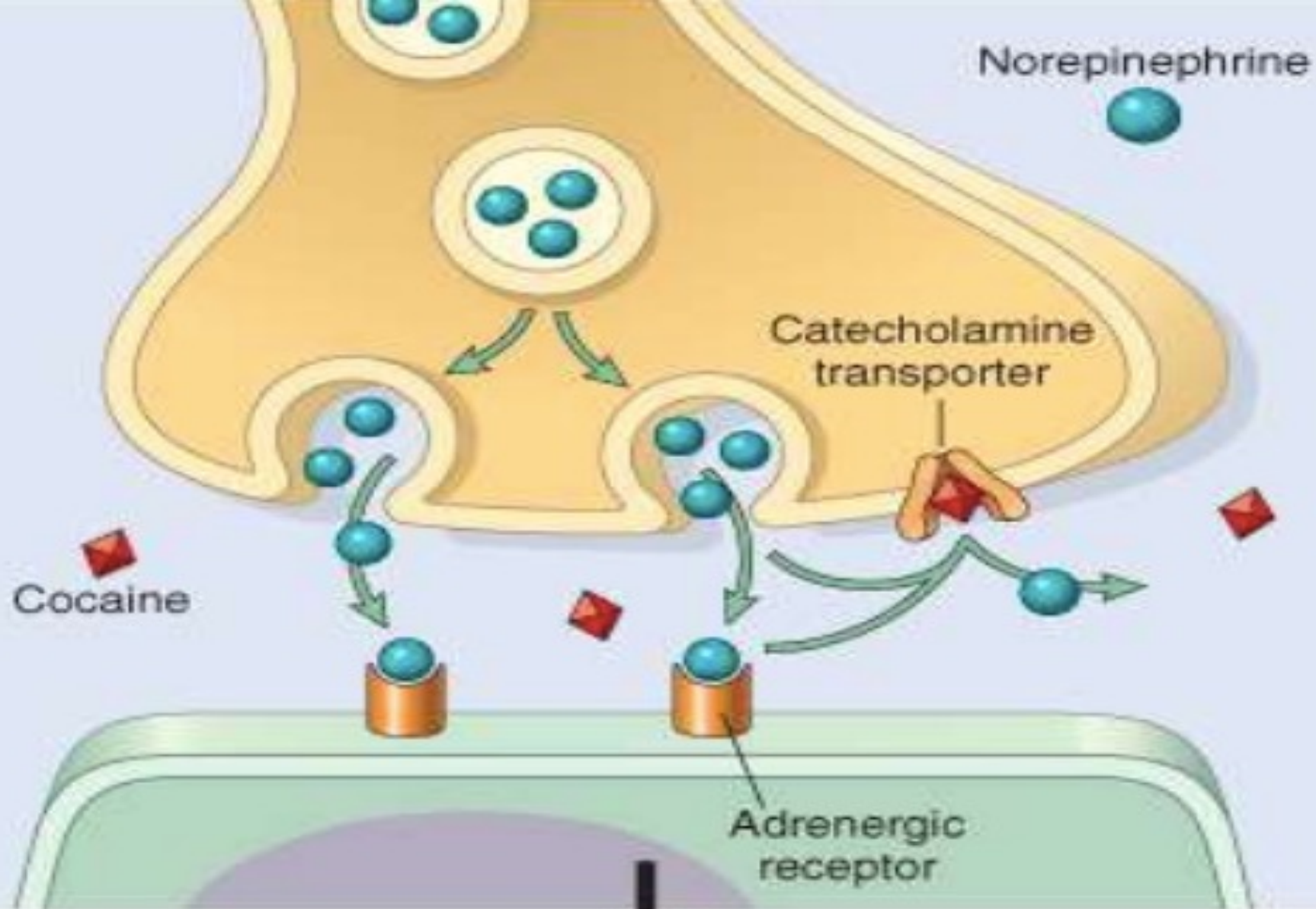
- Most common cause of death due to an illicit drug in USA
- An alkaloid from leaves of *Erythroxylon coca*



- Can be
 - Smoked
 - Sniffed (may cause nasal septum perforation)
 - Ingested
 - Injected
- A sympathomimetic drug
 - Blocks reuptake of Dopamine, Serotonin, Epinephrine and Norepinephrine by presynaptic axons resulting in
 - Excessive excitation of postsynaptic fibers or effector cells



EUPHORIA, PARANOIA, HYPERTHERMIA



HYPERTENSION, CARDIAC ARRHYTHMIA, MYOCARDIAL INFARCT, CEREBRAL HEMORRHAGE AND INFARCT

Cocaine Effects

- Intense euphoria
- Predisposes to
 - Acute MI/stroke
 - Pulmonary edema
 - Ventricular arrhythmias

Cocaine Effects

- Signs and symptoms of cocaine overdose
 - Mydriasis (prolonged abnormal dilatation of pupils)
 - Tachycardia and hypertension
 - Perforated or ulcerated nasal septum
 - CNS infarction

Opioid Narcotics

- General comments
 - Prescribed to relieve pain
 - Are depressant drugs
- Can cause sedation and mood changes

Opioid Narcotics

- Either isolated from opium or synthesized from morphine
 - Heroin
 - Morphine (derivative of heroin)
 - Meperidine
 - Methadone
 - Codeine

Heroin

- Diacetylmorphine
- Derived from poppy plant
- Modes of administration
 - Usually self-administered intravenous or subcutaneous
 - Snorting or smoking
 - Usually “cut” with some agent (quinine, talc) to lessen its potency
 - Granulomatous reaction occur in the skin and lungs from the cutting agent

Signs and symptoms of heroin overdose

- Miotic pupils
- Noncardiogenic pulmonary edema
- Frothing from mouth is common
- Focal segmental glomerulosclerosis
- Respiratory depression

Complications of Heroin

- Skin abscess from Staph aureus
- Granulomatous reaction to cutting agent
- Viral hepatitis (Hep B, Hep C, Hep D)
 - most common systemic infection in addicts
 - Hepatitis B most common

Complications of Heroin

- Infective endocarditis
 - Involves tricuspid or aortic valve
 - Staph. aureus is the most common cause
 - 2nd most common systemic infection in addicts
- AIDS
- Noncardiogenic pulmonary edema
- Focal segmental glomerulosclerosis causes nephrotic syndrome
- Thrombophlebitis, tetanus

Skin “popping scars” of heroin addict





Needle Tracks



**Injection site infections
with Staph aureus**

Marijuana

- Contains tetrahydrocannabinol (THC)
- Smoking rapidly delivers THC to the brain, producing a state of relaxation and heightened sensation
 - greater effect than oral intake
- Urine test (+) for metabolites > 1 week
- Hashish is the extracted resin of marijuana
 - 5 to 10 times more potent

Marijuana

- Clinical uses
 - Cancer decreases post-chemotherapy nausea & vomiting in cancer patients
 - Lower intraocular pressure in glaucoma
 - Analgesia

Marijuana

- Signs and symptoms of marijuana use
 - Reddening of conjunctiva
 - Delayed reaction time
 - Inability to judge speed or distance
 - Euphoria
 - Uncontrollable laughter

Therapeutic drugs Aspirin (acetylsalicylic acid) overdose

- MOA (Mechanism of Action)
 - Irreversibly acetylates cyclooxygenase
- Toxicity
 - Accidental overdose common in children and arthritics
 - High concentration in oil of wintergreen
 - Directly stimulates respiratory center
 - Primary respiratory alkalosis
 - Produces increased anion gap metabolic acidosis

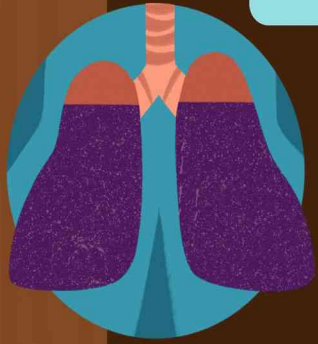
- Mechanism of toxicity
 - Respiratory alkalosis followed by
 - Metabolic acidosis
- Acute toxicity
 - Headache, tinnitus, vomiting, tachypnea and confusion

Chronic toxicity (salicylism)

- Dose: > 3 g daily
- Acute erosive gastritis and upper GI bleed
- Bleeding tendency due to reduced platelet aggregation
- Analgesic nephropathy
 - Can cause renal papillary necrosis if combined with acetaminophen

- Miscellaneous complications
 - Triad asthma
 - Aspirin sensitivity
 - Asthma
 - Nasal polyps

Aspirin-Induced Asthma (AIA) Symptoms



Shortness of breath



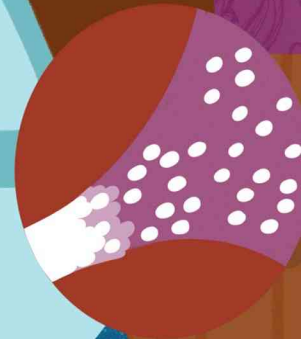
Hives



Wheezing



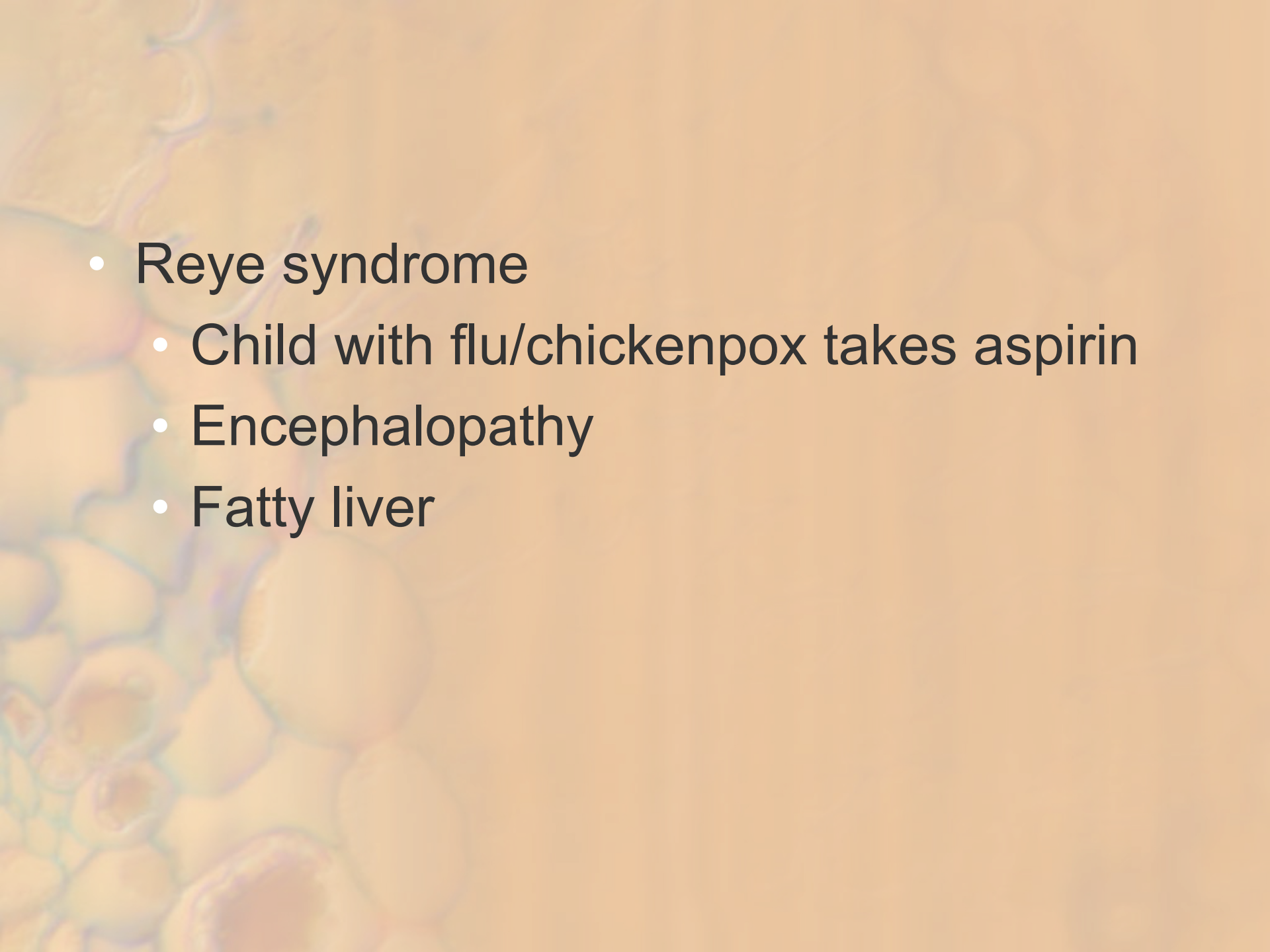
Coughing



Congestion

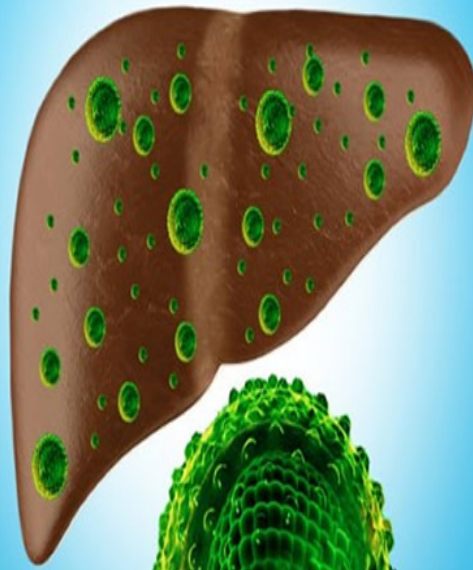
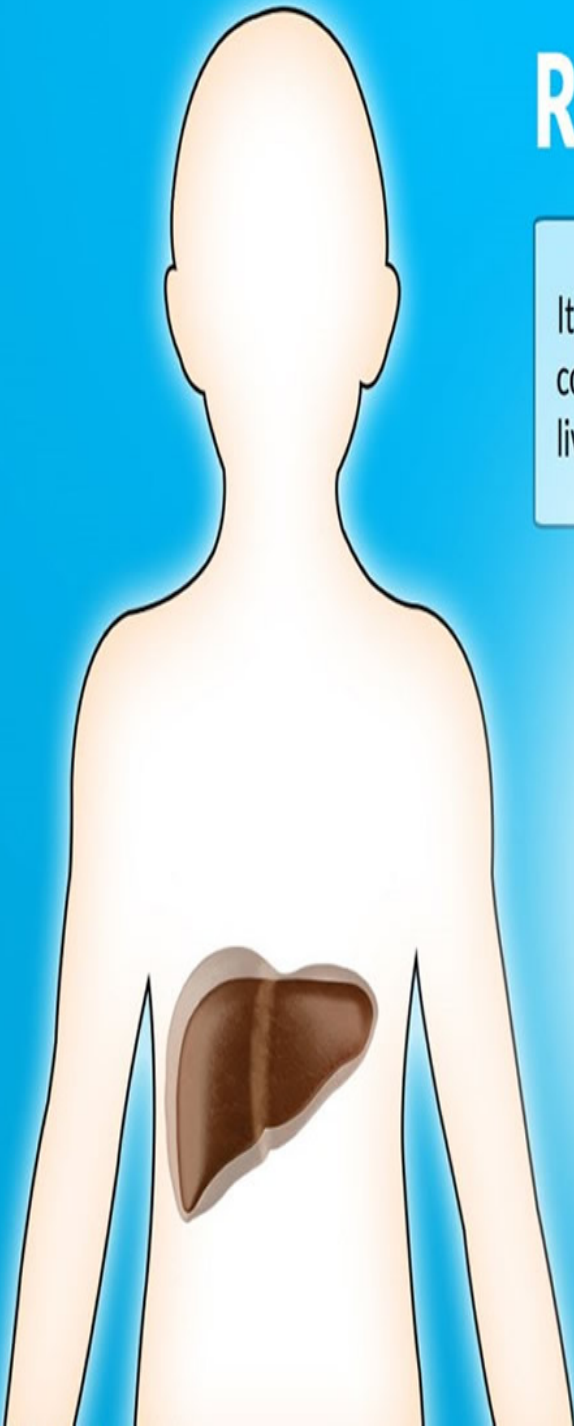


Facial flushing

- 
- A microscopic image of liver tissue, likely from a patient with Reye syndrome, showing characteristic features such as fatty liver and encephalopathy. The image displays a dense network of cells with prominent nuclei and surrounding cytoplasm, typical of liver parenchyma. The overall appearance is consistent with the clinical presentation of Reye syndrome, which involves acute liver failure and encephalopathy in children, often following a viral infection like flu or chickenpox, and the use of aspirin.
- Reye syndrome
 - Child with flu/chickenpox takes aspirin
 - Encephalopathy
 - Fatty liver

Reye Syndrome

It is an extremely serious pathological condition associated with swelling of liver and brain

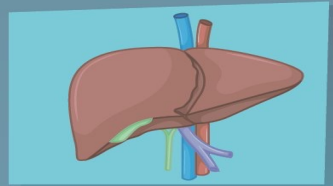


Viral Infection



What is Reye's Syndrome?

It is a rare, serious condition that causes swelling in the liver and brain. It most often affects children and teenagers recovering from a viral infection, commonly the flu or chickenpox.



Therapeutic drugs Acetaminophen (Tylenol) overdose

- Conversion to free radicals in the liver may result in
 - Damage to the liver (fulminant hepatitis)
 - Kidneys (renal papillary necrosis)

Therapeutic drugs

Chloramphenicol (Antibiotic)

overdose

- Adults – Causes reversible aplastic anemia
- In newborns: dose-related toxicity
- (Gray Baby Syndrome)
 - Cannot be degraded well by the liver due to immature glucuronic acid conjugation which accumulates in body



Gray baby syndrome is a rare, life-threatening condition that can develop in infants and premature babies up to the age of 24 months.

The condition has been linked to

overdoses of chloramphenicol

administered either to the mother or the infant, and the drug is one of the potentially inappropriate medications included in the KIDS List.

- **Gray Baby Syndrome**
 - Cyanosis (gray skin)
 - Hypothermia
 - Bradycardia
 - Diarrhea
 - Hypotension



Exogenous Estrogens

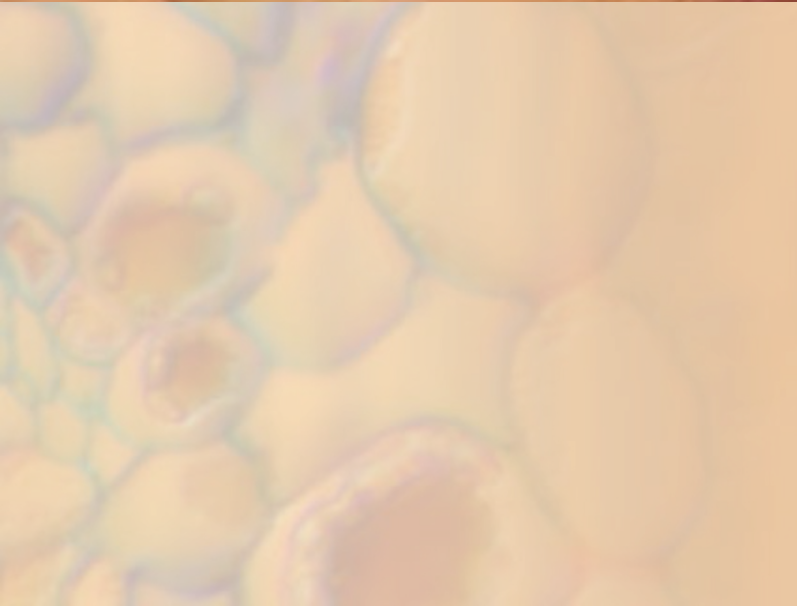
- Exogenous estrogen without progestin may result in
 - Cancer
 - ↑ risk of ovarian, endometrium, breast carcinomas
 - Venous thromboembolism
 - Intrahepatic cholestasis
 - Cardiovascular effects: MI and stroke

Therapeutic drugs - Oral Contraceptives overdose

- Contain synthetic estrogen (estradiol) and progesterone
- New dose formulations ($< 50\mu\text{g}/\text{day}$ of estrogen) associated with much lower risk of side effects.
- Increase malar eminence pigmentation
 - Pregnancy mask = Chloasma



Chloasma
Pregnancy mask



Therapeutic drugs - Oral Contraceptives overdose

- Venous Thromboembolism
- Increased liver synthesis of angiotensinogen
 - Hypertension in young women
- Liver disorders
 - Hepatic adenoma : tendency to rupture
 - Increase gallstone formation
- Cancer risk
 - Breast (disputed) and cervix

Carbon Monoxide

- Most common cause of death due to poisoning in the USA
 - Common accidental injury or method of suicide
 - Odorless, colorless gas
- Sources of CO
 - Automobile exhaust
 - Smoke in fires, cigarette smoke, space heaters and wood stoves with blocked vent

Carbon Monoxide

- Pathogenesis
 - High affinity for hemoglobin
 - Competes with O₂ for Hb binding sites
 - Forms carboxyhemoglobin (HbCO)
 - Shifts the oxygen dissociation curve to the left
 - Decreased O₂ release by Hb causes tissue hypoxia

- Clinical Symptoms depend on the concentration of CO in blood
 - 10% - asymptomatic
 - 30% - headache (1st sign)
 - 50% - loss of consciousness , convulsions and coma
 - > 60% : death • Cherry-red color to the skin , mucosal membrane and blood (not a reliable sign)
- Treatment: 100% O₂



