

Environmental and Toxicity Related Diseases

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Environmental diseases

- Refers to diseases caused by chemical or physical agents
 - Ambient, 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

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
- A 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

- Nonneoplastic diseases
- Neoplastic diseases

Nonneoplastic diseases

- Pulmonary
 - COPD – Chronic Obstructive Pulmonary Disease
 - Chronic bronchitis and emphysema
 - Recurrent infections
 - Pneumonia
- Cardiovascular system
 - Acute MI
 - Peripheral vascular disease
- Gastrointestinal tract
 - GERD
 - Gastric and duodenal ulcers (delay in healing)

Nonneoplastic diseases

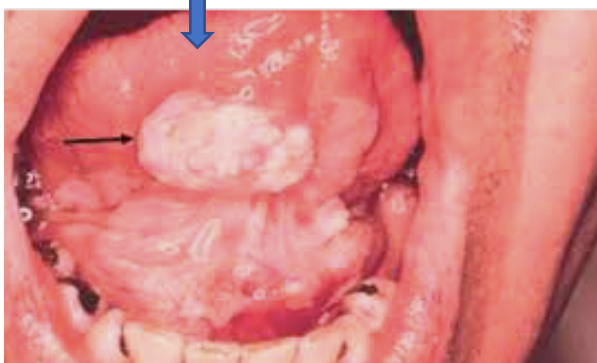
- Effect on pregnant women
 - IUGR (Intra-Uterine Growth Retardation)
 - ↑ risk of spontaneous abortions and stillbirths
 - Abruptio placenta, Placenta previa, Premature rupture of membranes
- Effect on women
 - Early menopause
 - ↑ rate of postmenopausal osteoporosis
- Effect on children
 - ↑ risk of 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
 - Gastrointestinal
 - Oral - squamous cell carcinoma
 - Esophagus - squamous cell carcinoma
 - Pancreatic adenocarcinoma
 - Others
 - Larynx – squamous cell carcinoma
 - Transitional cell carcinoma of bladder
 - Renal adenocarcinoma



Squamous Cell Carcinoma
Lung Oral



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
 - AMI & ischemic heart disease
 - respiratory illness
- 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



Leukoplakia



Verrucose oral cancer

Alcohol Abuse

- Alcohol is of more wide spread hazard and causes more deaths than cocaine & heroin addiction
- Western World Incidence Rate
 - 50% adult drink alcohol
 - 5-10% chronic alcoholics
- In USA
- >10 millions chronic alcoholics
- Approximately 100,000 deaths per year
 - 50% DUI - drunken driving
 - 25% consequence of cirrhosis
 - Cost – \$100-130 billion per year

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
 - 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
- Deficiency of Folate predisposes to
 - Macrocytic anemia

Gastrointestinal effects of alcohol abuse

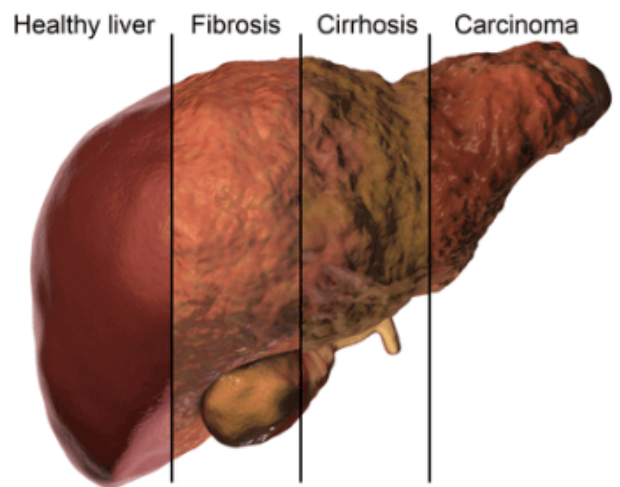
- Esophageal varices
 - Secondary to Cirrhosis
- Acute gastritis and gastric reflux
 - Retching may result in
 - Mallory Weiss syndrome
 - retching causes esophageal tear at gastric-esophageal junction
 - Boerhaaves syndrome
 - retching causes esophageal rupture (distal esophagus)



Esophageal Varices

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

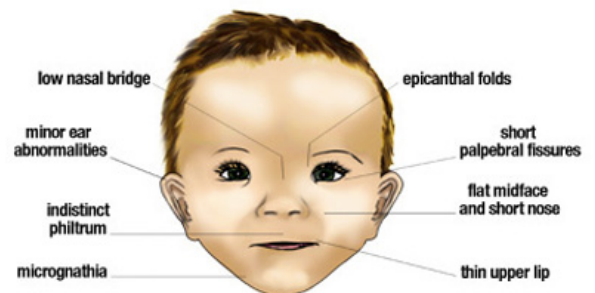


Hematologic effects of alcohol abuse

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

Fetal Alcohol Syndrome

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



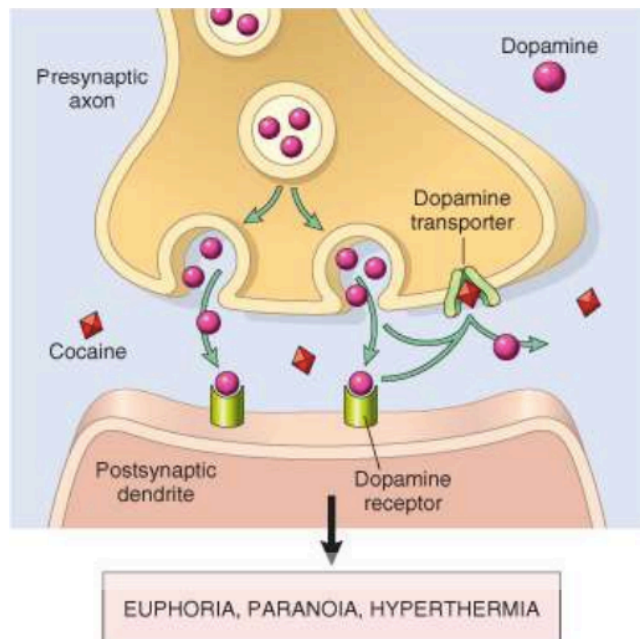
Calcium oxalate crystals in urine

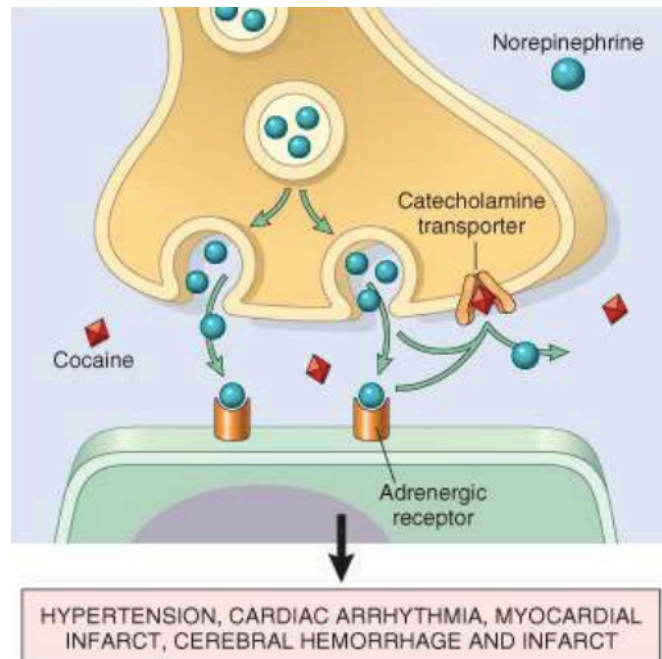
Drug Abuse

- 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





Cocaine Effects

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

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
- 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

Chronic toxicity (salicylism) - continued

- Miscellaneous complications
 - Triad asthma
 - Aspirin sensitivity
 - Asthma
 - Nasal polyps
- Reye syndrome
 - Child with flu/chickenpox takes aspirin
 - Encephalopathy
 - Fatty liver

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
 - 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 (< 50µg/day of estrogen) associated with much lower risk of side effects.
- Increase malar eminence pigmentation
 - Pregnancy mask = Chloasma
- 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

- MCC 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
- 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

