

Environmental Pathology

Environmental Pathology

- Definition:
 - Study of diseases that are not entirely genetic

Comment: There are very few diseases that are purely genetic or environmental.

Environmental Pathology Classification

1. Air pollution by industrial waste and or the products of automobile exhaust
2. Use and abuse of drugs and physical agents, including radiation
3. Contamination of food and water by pesticides and industrial waste
4. Over- or under nutrition

Environmental Pollution

- A pollutant is an agent in the environment that can cause disease in those who are exposed and include agents that are naturally present but in abnormal quantities (ozone) and those that are not naturally present

ENVIRONMENTAL POLLUTANTS

- Substances that contaminate the soil, waters and the air can cause disease. Pollutants include
 - human, animal and plant waste.
 - Industrial vapors, heavy metals.
 - Dust.

AIR POLLUTANTS CAUSING MAJOR HEALTH THREATS

- Tobacco smoke.
- Smoke generated by burning wood.
- Exhausts from fossil fuels.
- Chemicals generated in industrial setting.
- Dust containing particulate matter.
- Normal gases present in excessive amounts – ozone, nitrogen, carbon monoxide, carbon dioxide.

HOW DO POLLUTANTS DAMAGE THE HUMAN BODY?

- **Direct effects:**

- Strong acids and alkali have a corrosive effect on the skin.
- Heavy metals, like mercury, have a direct toxic effect on cells of the gastrointestinal tract and renal tubules.

- **Indirect effects:**

- Intermediate metabolites that damage cells.
- Generation of new antigens, which stimulate the body to produce cytotoxic antibodies.

- **Late effects:**

- Cumulative effect seen only after a long period of time.
- Mutagenic effects of some chemicals or ultraviolet light become evident only many years after the initial exposure.
- E.g. radiation from radon leads to cancer after years of exposure

Pollution

Pollutant may produce

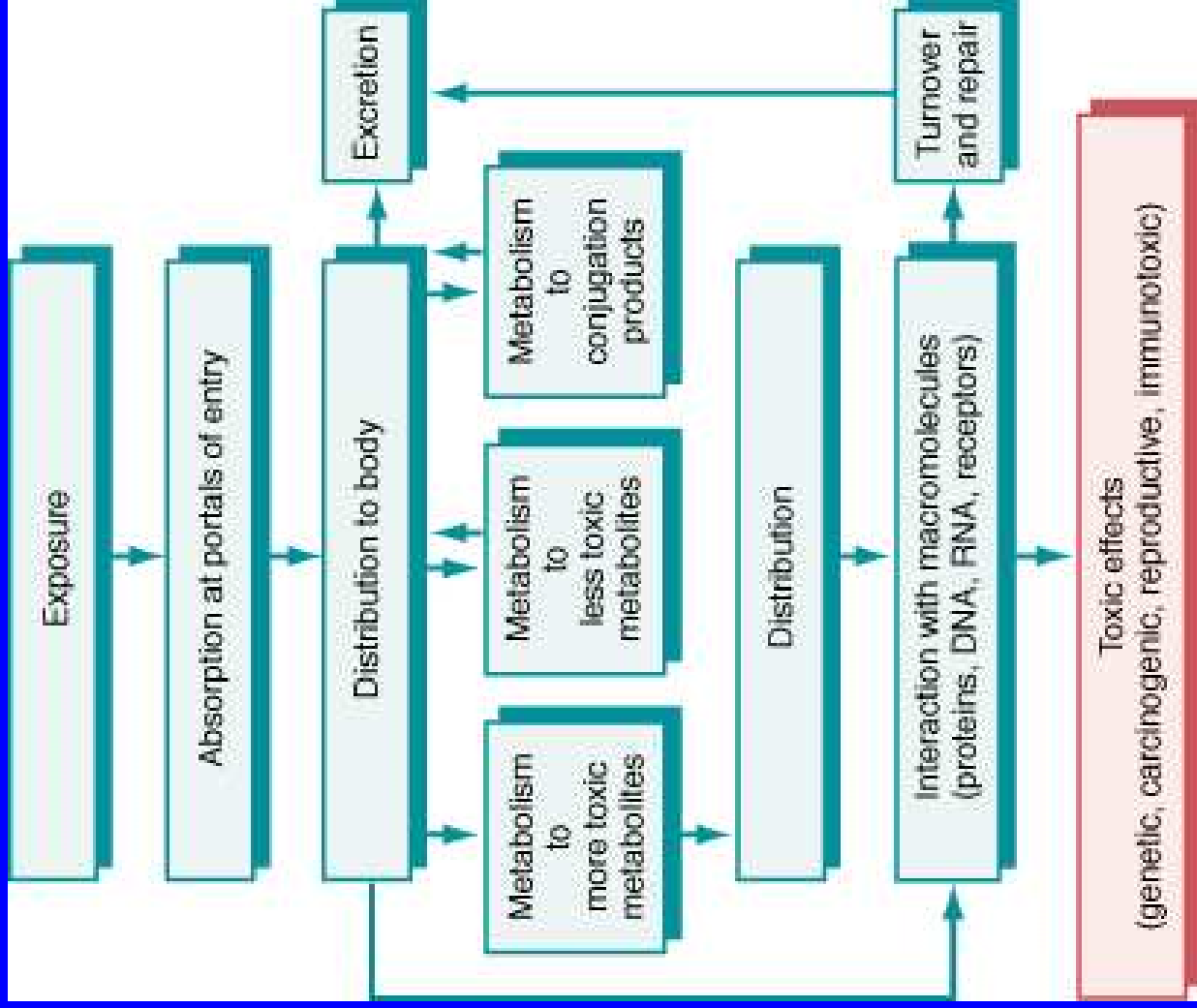
- **acute toxicity:**
 - directly through induction of inflammation or necrosis
 - indirectly through a hypersensitivity immune response
- **chronic effects:**
 - like sub clinical forms of chronic inflammation and fibrosis due to ongoing toxic effect, or degenerative changes (chronic lead toxicity)

EXAMPLES OF EFFECTS OF AIR POLLUTANTS ON LUNG

- **Acute toxicity**
 - Irritate the bronchi
 - Pulmonary edema
- **Allergic reaction.**
 - Asthmatic attacks.
- **Chronic lung disease**
 - Pneumoconiosis.
- **Cancer**

MAIN DETERMINANTS OF TOXICITY OF AIR POLLUTANTS

- Air pollutants do not affect all people equally. Depending on:
 - * **Physical and chemical properties:** Solubility in water (e.g., SO₂), particle size and airway anatomy (particles between 1 to 5 μm are most dangerous), and chemical reactivity
 - * Concentration of pollutant.
 - * Duration of exposure.
 - * Host's reaction to the pollutant and host clearance mechanisms



Tobacco Smoke

Tobacco Smoke

Use of tobacco products is associated with more mortality than any other personal, occupational or environmental exposure.

Tobacco Smoke

- In Britain, it is estimated that about 50% of all regular cigarette smokers will die of smoking-related diseases
- Tobacco smoking is the single most common cause of preventable mortality
- Passive smoking is also injurious to health

Tobacco Smoke

- In USA , cigarette smoking contribute to 440,000 premature death per year.
- Death due to lung cancer, CVS disease, and chronic respiratory disease.
- Early exposure is associated with more risk of complications.
- Smoking interact with other occupational or environmental exposures in an additive or synergistic fashion.

Tobacco Smoke

- There are 0.3 to 3.3 billion particles per milliliter of mainstream smoke and more than 4000 constituents.
- At least 43 known carcinogens are present,
e.g. polycyclic aromatic hydrocarbon - lung CA & oral cavity
N-nitrosornicotine - esophagus & pancreas
4-Aminobiphenyl 2, naphthylamine - Bladder
- In addition to these chemical, smoking contains carcinogenic metals e.g. arsenic, nickel, cadmium & chromium, promoters e.g. acetaldehyde & phenol, cilia toxin e.g. hydrogen cyanide and irritant e.g. nitrogen dioxide & formaldehyde.

Tobacco Smoke

- Other substances:

- CO₂

- Nicotine

is an alkaloid that readily crosses the blood-brain barrier and stimulates nicotine receptors in the brain.

- It is responsible for the acute pharmacologic effects associated with tobacco use that are most likely mediated by catecholamines:

- increased heart rate and blood pressure

- increased coronary artery blood flow

- increased contractility and cardiac output

- mobilization of free fatty acids.

- Nicotine is responsible for tobacco addiction.

Tobacco Smoke: Selected Constituents

Substance	Effect
Tar	Carcinogenesis
Polycyclic aromatic hydrocarbons	Carcinogenesis
Nicotine	Ganglionic stimulation and depression, tumor promotion
Phenol	Tumor promotion and irritation
Benzopyrene	Carcinogenesis
Carbon monoxide	Impaired oxygen transport and utilization
Formaldehyde	Toxicity to cilia and irritation
Oxides of nitrogen	Toxicity to cilia and irritation
Nitrosamine	Carcinogenesis

Diseases related to smoking

Cause of Death	Number of Deaths	
	<i>Men</i>	<i>Women</i>
Cancer	102,812	54,664
Cardiovascular disease	90,906	57,699
Respiratory disease	53,713	44,429
Residential fires	589	377
Perinatal deaths	598	407
Lung cancer and heart disease attributable to passive smoking	15,517	22,536
Total	264,135	80,112

Diseases related to smoking

- **Cardiovascular system**
 - Atherosclerosis:
 - Cigarette smoking is a multiplicative risk factor with hypertension and hypercholesterolemia for development of coronary artery disease and arteriosclerosis.

Tobacco Smoke: CVS

– Myocardial infarction

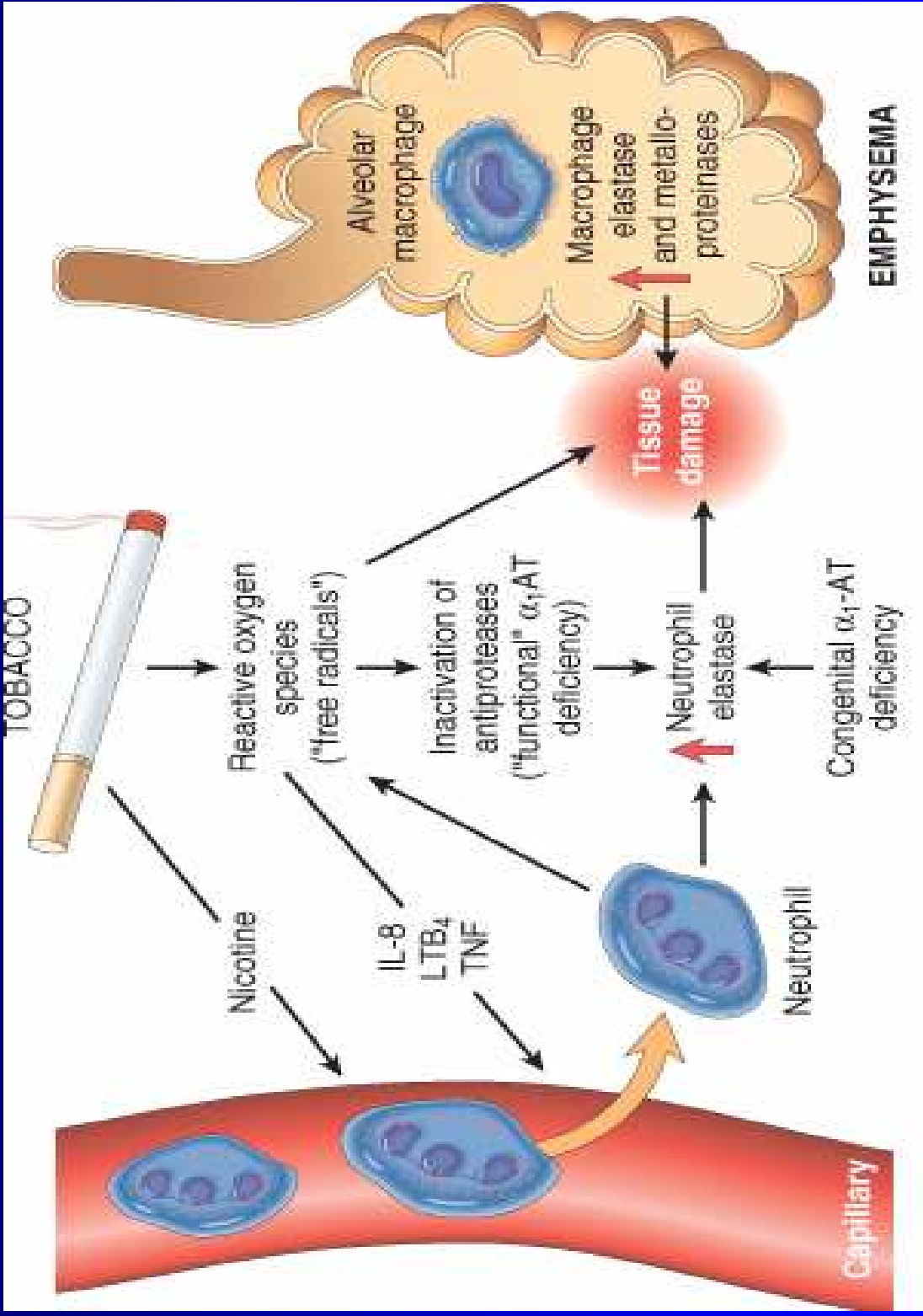
- Smoking is a multiplicative risk factor for acute myocardial infarction and stroke in women who take oral contraceptives.
 - Smoking may contribute to cardiac arrest by increasing platelet adhesion and aggregation, triggering arrhythmia, and by causing an imbalance between the demand for oxygen and supply to the myocardium.

Diseases related to smoking

- **Lung:**

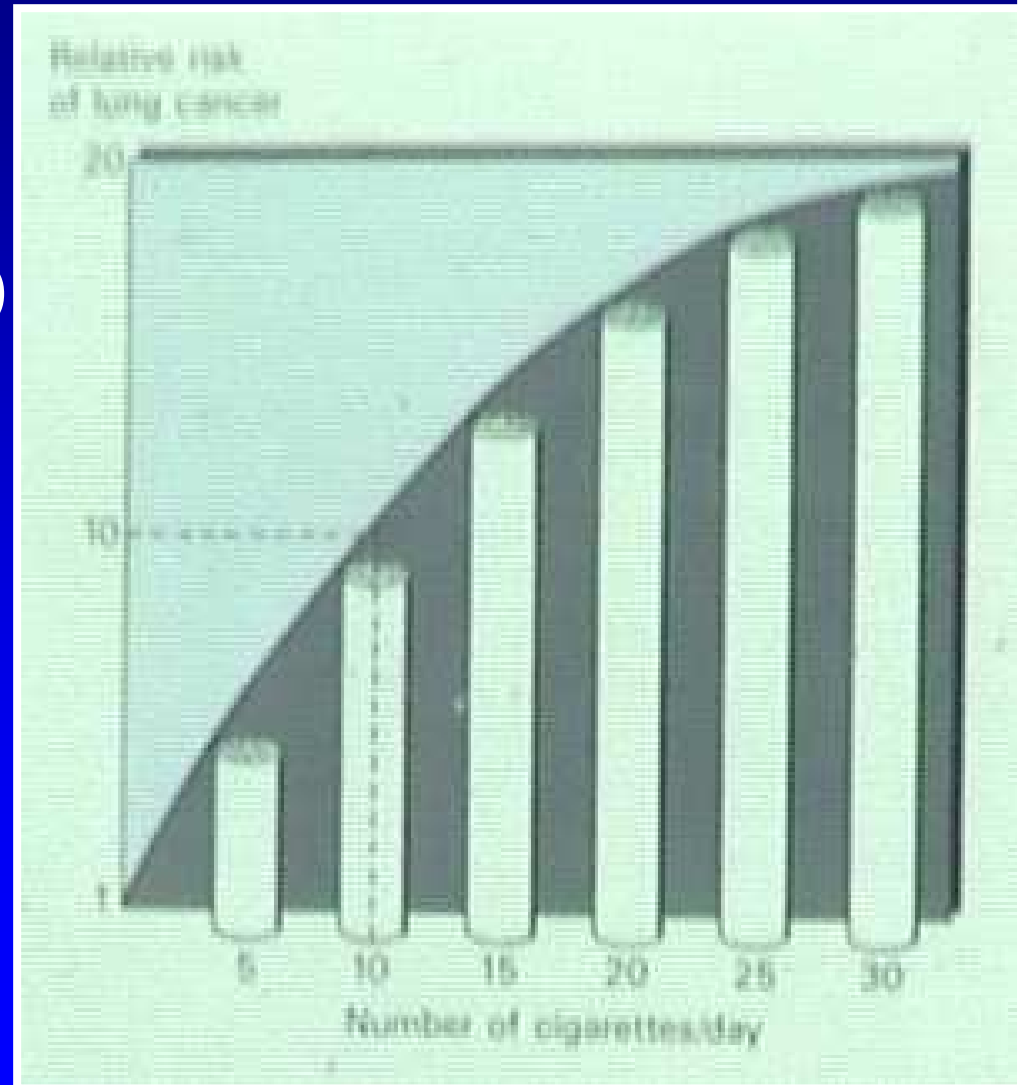
(dose related: “pack years”)

- Chronic bronchitis (irritation & ↑ mucus production)
- Emphysema (recruitment of leukocytes with ↑ local elastase production)
- Cancer of lung, bronchogenic carcinoma (mutagens and cancer promotion)



Diseases related to smoking

- **Lung:**
 - Cancer of lung (bronchogenic carcinoma)
 - (mutagenic and cancer promotor)



Tobacco Smoke: Cancer of lung

- It is estimated that 30% of all cancer deaths and up to 90% of all lung cancer deaths are attributable to cigarette smoking.

Tobacco Smoke: respiratory tract

- Smokers also suffer from increased morbidity due to **acute respiratory tract infections**, including influenza, and acute and chronic sinusitis.
 - Ciliotoxins in cigarette smoke impair tracheobronchial clearance
 - many of the gas phase constituents of smoke are direct irritants of the respiratory epithelium.

Tobacco Smoke: peptic ulcers

- Tobacco use also increases the prevalence of peptic ulcers
- smoking impairs healing of ulcers and increases the likelihood of recurrence
- Smoking may also increase pyloric reflux and decrease bicarbonate secretion from the pancreas.

Tobacco Smoke: effect on fetus

- The fetus is especially vulnerable to the consequences of maternal smoking.
- Even 10 cigarettes per day can cause fetal hypoxia; fetal carboxyhemoglobin levels are higher than maternal levels.
- Consequences of fetal hypoxia:
 - low birth weight
 - prematurity
 - increased incidence of spontaneous abortion.
- Serious complications at the time of delivery include:
 - premature rupture of the membranes
 - placenta previa
 - abruptio placentae

Tobacco Smoke: Environmental tobacco smoke

Passive smoking environmental tobacco smoke (ETS)

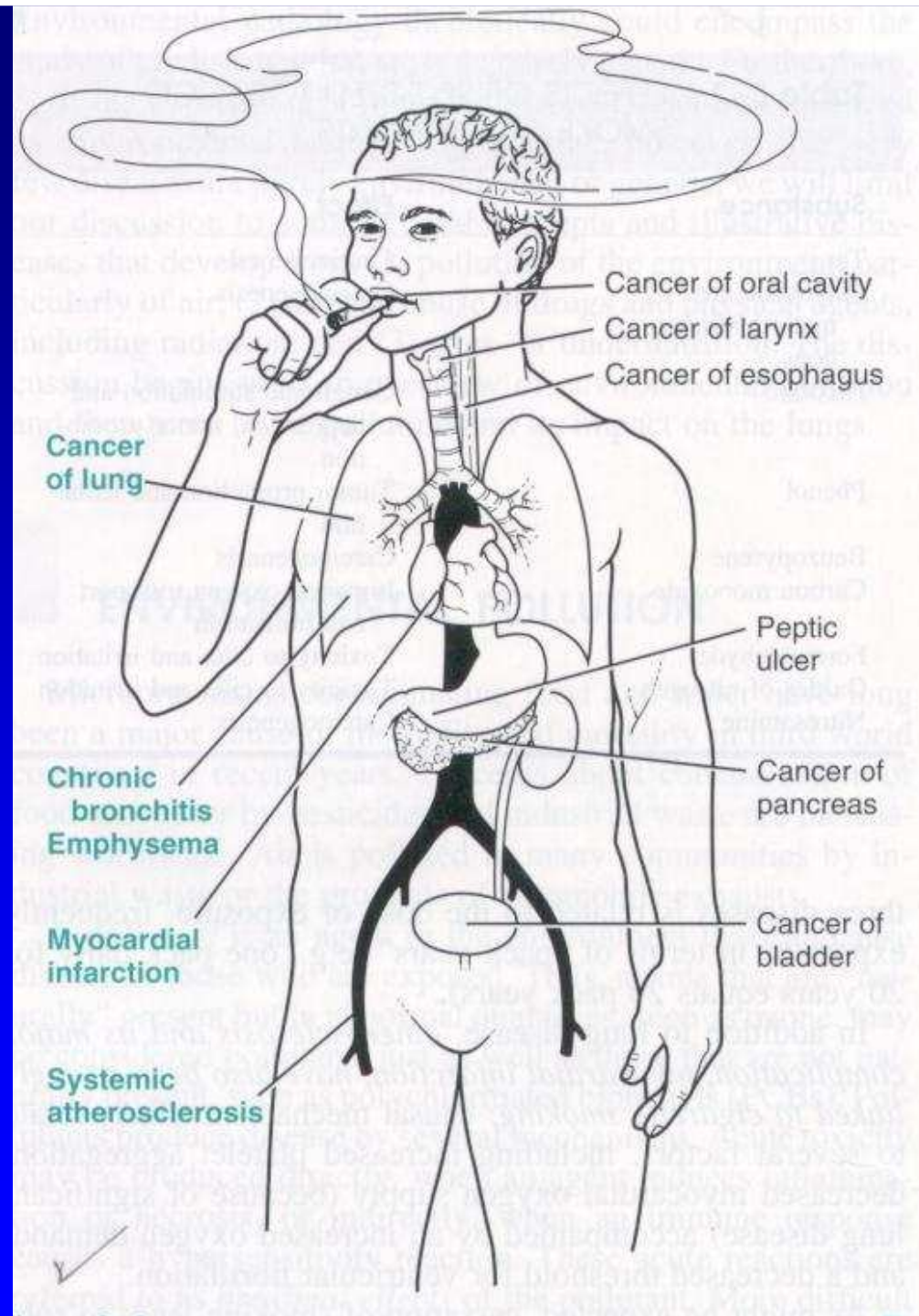
- In 1986, two reports issued by the National Research Council and the Surgeon General concluded that ETS increases the risk of :
 - lung cancer
 - ischemic heart disease
 - exacerbation of asthma attacks in children
 - chronic bronchitis
 - acute myocardial infarction.

Tobacco Smoke

- The Environmental Protection Agency classified ETS as
 - a known human carcinogen .
 - is especially hazardous for infants and young children.
 - Young children in households of cigarette smokers suffer from an increased incidence of respiratory and ear infections and exacerbation of asthma.

Diseases related to smoking

Cessation of smoking leads to substantial benefits



WHICH CANCERS OCCUR AT A HIGHER RATE IN SMOKERS?

- Directly linked to the action of carcinogens in smoke are:
 - * Bronchial carcinoma.
 - * Oral cancer.
 - * Carcinoma of the larynx.
- The incidence of the following cancers is increased significantly in smokers:
 - * Carcinoma of the esophagus.
 - * Carcinoma of the urinary bladder.
 - * Carcinoma of the uterine cervix.
 - * Carcinoma of the kidney.
 - * Carcinoma of the pancreas.

Alcohol

Alcohol

- Ethanol is the most widely used and abused agent throughout the world.
- There are 15 to 20 million alcoholics in the United States.
- Approximately 100,000 deaths in the United States are attributed to alcohol abuse per year.

Alcohol

- A blood alcohol concentration of 80 to 100 mg/dL is the legal definition for driving under the influence of alcohol
- Approximately 3 ounces (44 ml) of ethanol are required to produce this blood alcohol level in a 70-kg person.
- This is equivalent to 12 ounces of fortified wine
 - 8 bottles of beer (12 ounces each)
 - 6 ounces of 100-proof whiskey

Alcohol

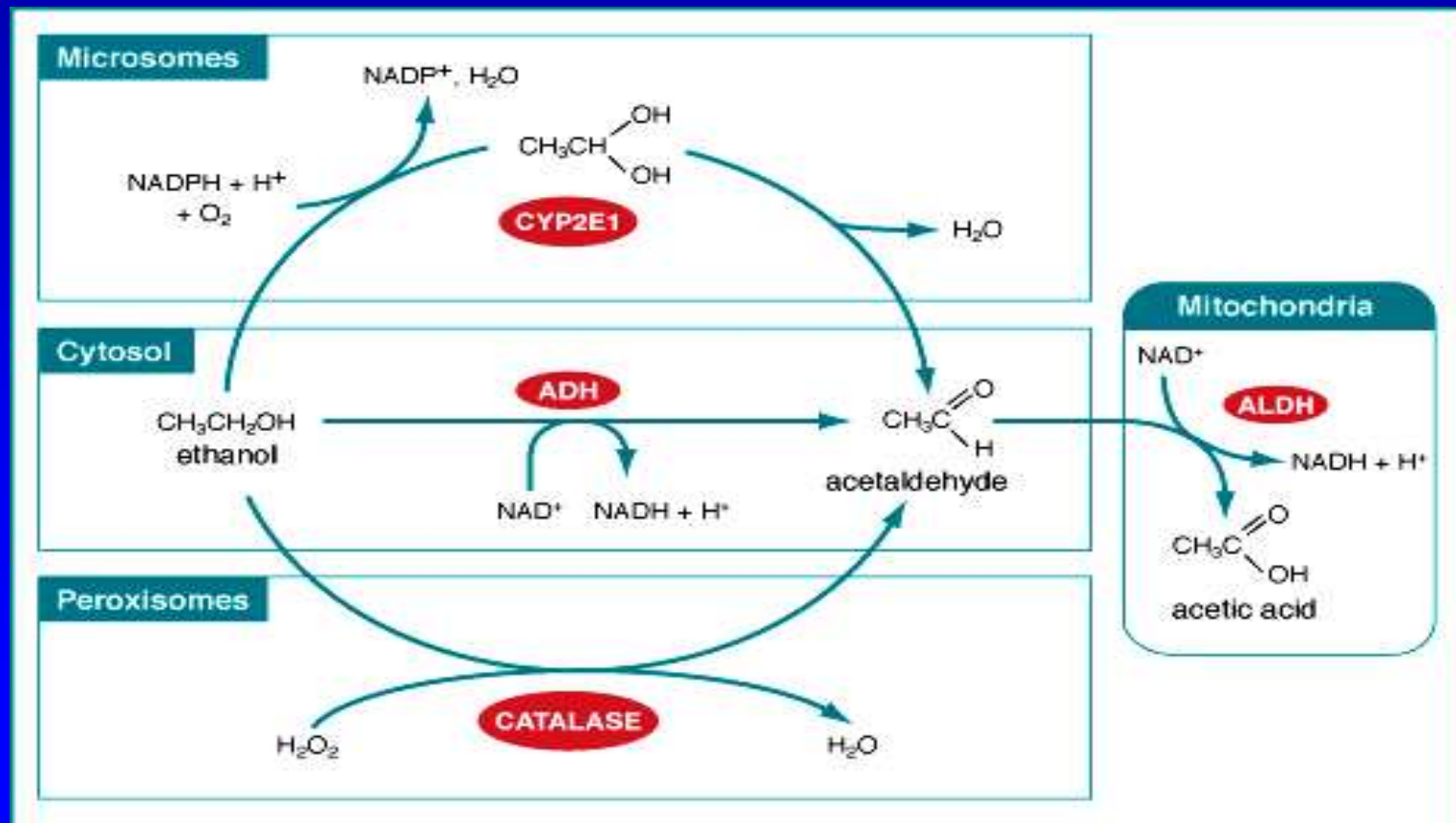
- Habitual drinkers can tolerate blood alcohol levels up to 700 mg/dL.
- This metabolic tolerance is partially explained by a fivefold to tenfold induction of the cytochrome P-450 xenobiotic-metabolizing enzyme CYP2E1.
- Such induction increases the metabolism of ethanol as well as that of other drugs and chemicals, including cocaine and acetaminophen.

Alcohol

- Although no specific receptor for ethanol has been identified, chronic use results in psychologic and physical dependence. The biologic basis for ethanol addiction is unknown.

Alcohol

- Ethanol is metabolized to acetaldehyde by alcohol dehydrogenase in the gastric mucosa and liver, and by cytochrome P-450 (xenobiotic-metabolizing enzyme CYP2E1) and catalase in the liver. Acetaldehyde is converted to acetic acid by aldehyde dehydrogenase.



BLOOD ALCOHOL CONCENTRATION (BAC) OF 80 MG/DL

- Is federally mandated upper limit. This BAC may be reached at different rates depending on:
 - * Amount of alcohol ingested
 - * Rate of intake
 - * Rate of absorption
 - * Rate of metabolism –150mg/kg/hr
 - * Rate of excretion in urine and air

ACUTE EFFECTS OF ALCOHOL

- Euphoria – irresponsible behaviour, uncritical thinking, slurred speech, motor incoordination.

Ethanol

Acute alcoholism:

- Central nervous system:

- alcohol is a depressant.
- First affecting the subcortical structures (high brain stem reticular formation) that modulate cerebral cortical activity
→ stimulation and disordered cortical, motor and intellectual behaviour.

At progressively higher blood levels, cortical neurons and then lower medullary centers are depressed, including those that regulate respiration. Respiratory arrest may follow.

Chronic Alcoholism

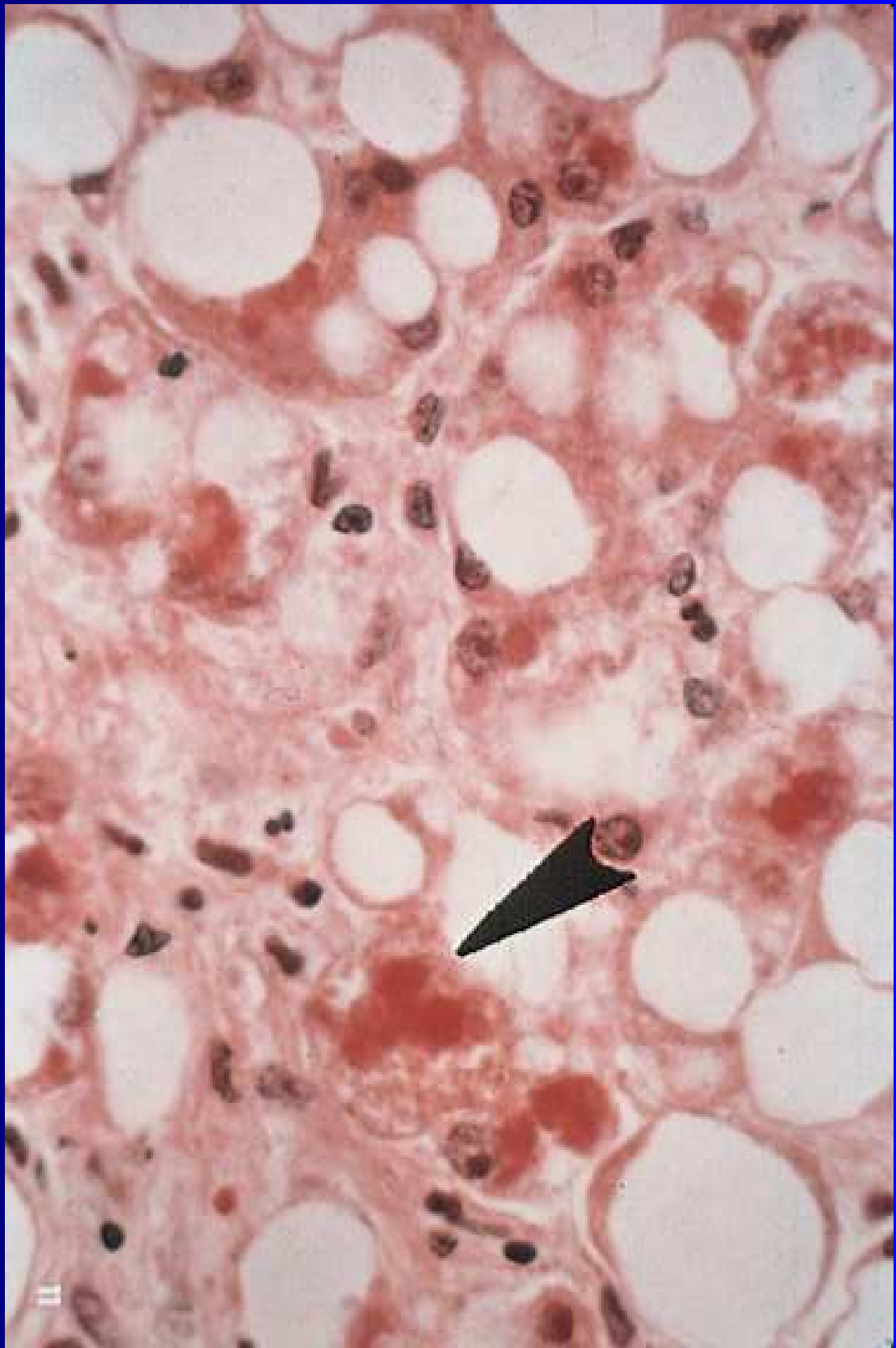
GI tract:

- bleeding from gastritis, gastric ulcer, or esophageal varices
- reflux esophagitis (Mallory-Weiss syndrome).

Chronic Alcoholism

Liver:

- hepatic injury leading to chronic liver disease including
 1. fatty liver
 2. alcoholic hepatitis
 3. cirrhosis (15-20%).



Alcoholic hepatitis

- Alcoholic hepatitis can produce fever, liver tenderness, and jaundice.
 - On histologic examination, there are focal areas of hepatocyte necrosis and cell injury manifest by fat accumulation and alcoholic hyalin, or Mallory bodies. Neutrophils accumulate around foci of necrosis.

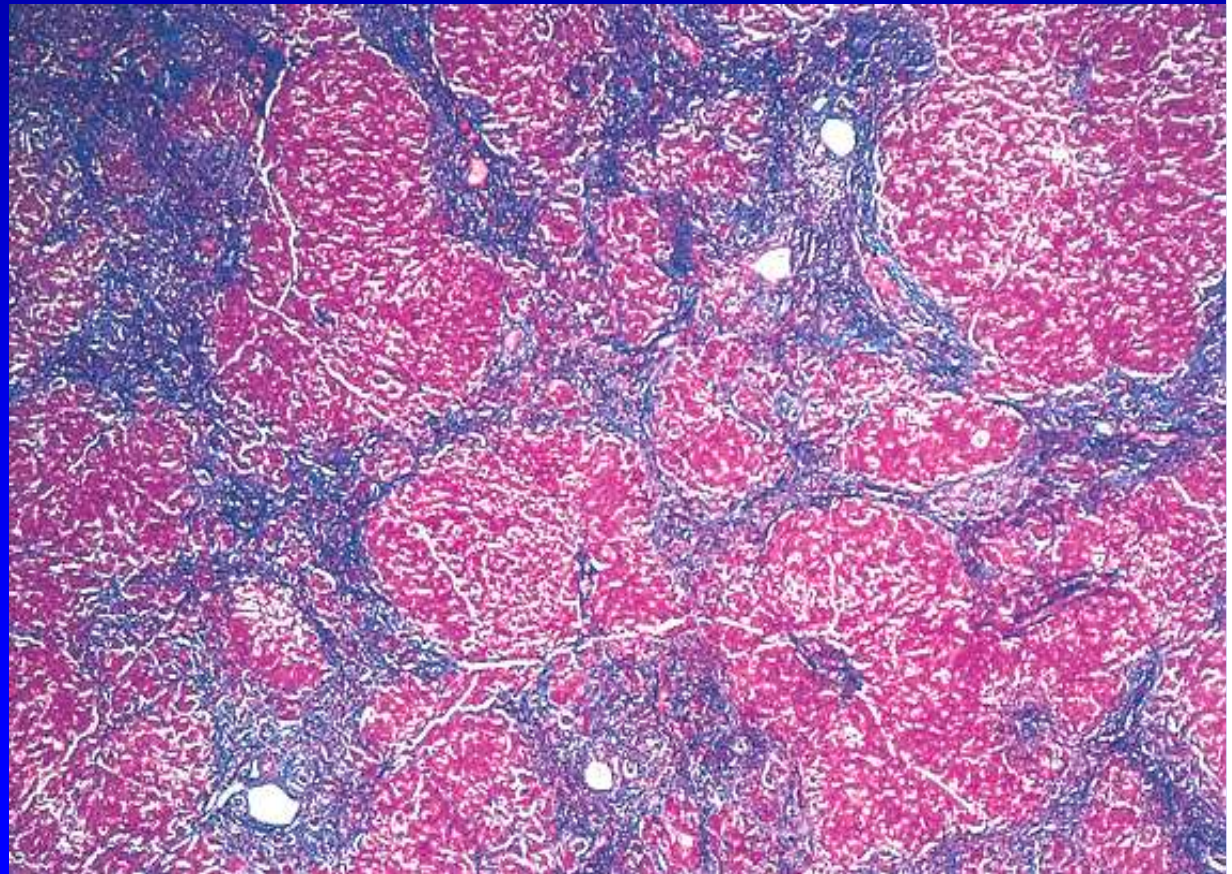
Alcoholic cirrhosis

- Ethanol and its metabolites are directly toxic to hepatocytes with chronic ethanol use
- 10% to 15% of alcoholics develop irreversible liver damage, or alcoholic cirrhosis

Alcoholic cirrhosis

- characterized by a hard, shrunken liver with formation of micronodules of regenerating hepatocytes surrounded by dense bands of collagen.

- Perisinusoidal fibrosis occurs initially, with deposition of collagen by perisinusoidal stellate cells (Ito cells) in the spaces of Disse,
- This may be mediated by cytokines.



Alcoholic cirrhosis

- Alcoholic cirrhosis is a serious, potentially fatal disease accompanied by:
 - weakness
 - muscle wasting
 - Ascites
 - gastrointestinal hemorrhage
 - coma.

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Chronic Effect on Nervous System

- *Wernicke syndrome:*
 - ataxia, disturbed cognition, ophthalmoplegia, and nystagmus.
 - Chronic thiamine deficiency contributes to degeneration of nerve cells, reactive gliosis, and atrophy of the cerebellum and peripheral nerves.

Chronic Effect on Nervous System

Korsakoff syndrome:

- Some alcoholics with poor nutrition develop the severe memory loss.
 - This is believed to result from a combination of direct toxicity and thiamine deficiency.

Effect on Cardiovascular System

- Chronic ethanol abuse can cause cardiomyopathy, a degenerative disease of the heart muscle, resulting in dilation of the heart.
 - due to direct toxicity rather than thiamine deficiency
- Hypertension is also more common in chronic alcoholics
 - secondary to the vasopressor effects of ethanol triggered by increased release of catecholamines.
- Moderate consumers (one to two drinks per day) show a protective effect of ethanol on the cardiovascular system.
 - At this level of consumption, drinkers show increased levels of high-density lipoprotein and decreased platelet aggregation.

Effect on Gastrointestinal Tract

- Acute gastritis is a direct toxic effect of ethanol use.
- Chronic users are vulnerable to acute and chronic pancreatitis, which may lead to destruction of pancreatic acini and islets.
 - Pancreatic acinar destruction leads to impaired intestinal absorption of nutrients and contributes to vitamin deficiencies

Effect on Skeletal Muscle

- Direct ethanol toxicity can also injure skeletal muscles, leading to muscle weakness, pain, and breakdown of myoglobin.

Effect on Reproductive System

- Chronic ethanol use leads to testicular atrophy and decreased fertility in both men and women.
- Women who drink alcohol also have an increased risk of spontaneous abortion.
 - The mechanisms responsible for these adverse reproductive effects are unknown.

Fetal Alcohol Syndrome

- A tragic consequence
- characterized by growth and developmental defects, including microcephaly; facial dysmorphism; and malformations of the brain, cardiovascular system, and genitourinary system
- This is the most common type of preventable mental retardation in the United States, and it affects at least 1200 children per year.
 - The pathogenesis of fetal alcohol syndrome is not entirely clear. It is hypothesized that acetaldehyde, a metabolite of ethanol crosses the placenta and damages the fetal brain.

Ethanol and Cancer

- Use of alcoholic beverages is associated with an increased incidence of cancer of the oral cavity, pharynx, esophagus, liver, and possibly the breast.
- Although ethanol is not a direct-acting carcinogen, one of its metabolites, acetaldehyde, may act as a tumor promoter.

Ethanol and Cancer

- Heavy alcohol use synergizes with chronic hepatitis B or C infection in predisposing to the development of hepatocellular carcinoma

CONSEQUENCES OF CHRONIC ALCOHOL ABUSE

- Testicular atrophy.
- Megaloblastic anemia.

DRUG ABUSE

DRUG ABUSE

- Drug abuse has been defined as “the use of any substance in a manner that deviates from the accepted medical, social or legal patterns within a given society:
 - * CNS depressants –alcohol, diazepines
 - * CNS stimulants – cocaine, amphetamine
 - * Narcotics – morphine
 - * Hallucinogens – marijuana, lysergic acid diethylamide (LSD)

HOW DO SUBSTANCES OF ABUSE CAUSE DISEASE?

- Direct effect. Sympathomimetic effects and may cause severe hypertension.
- Side effects from contaminants.
- Long term effects:
 - e.g. Marijuana irritate the bronchi and cause chronic inflammation.

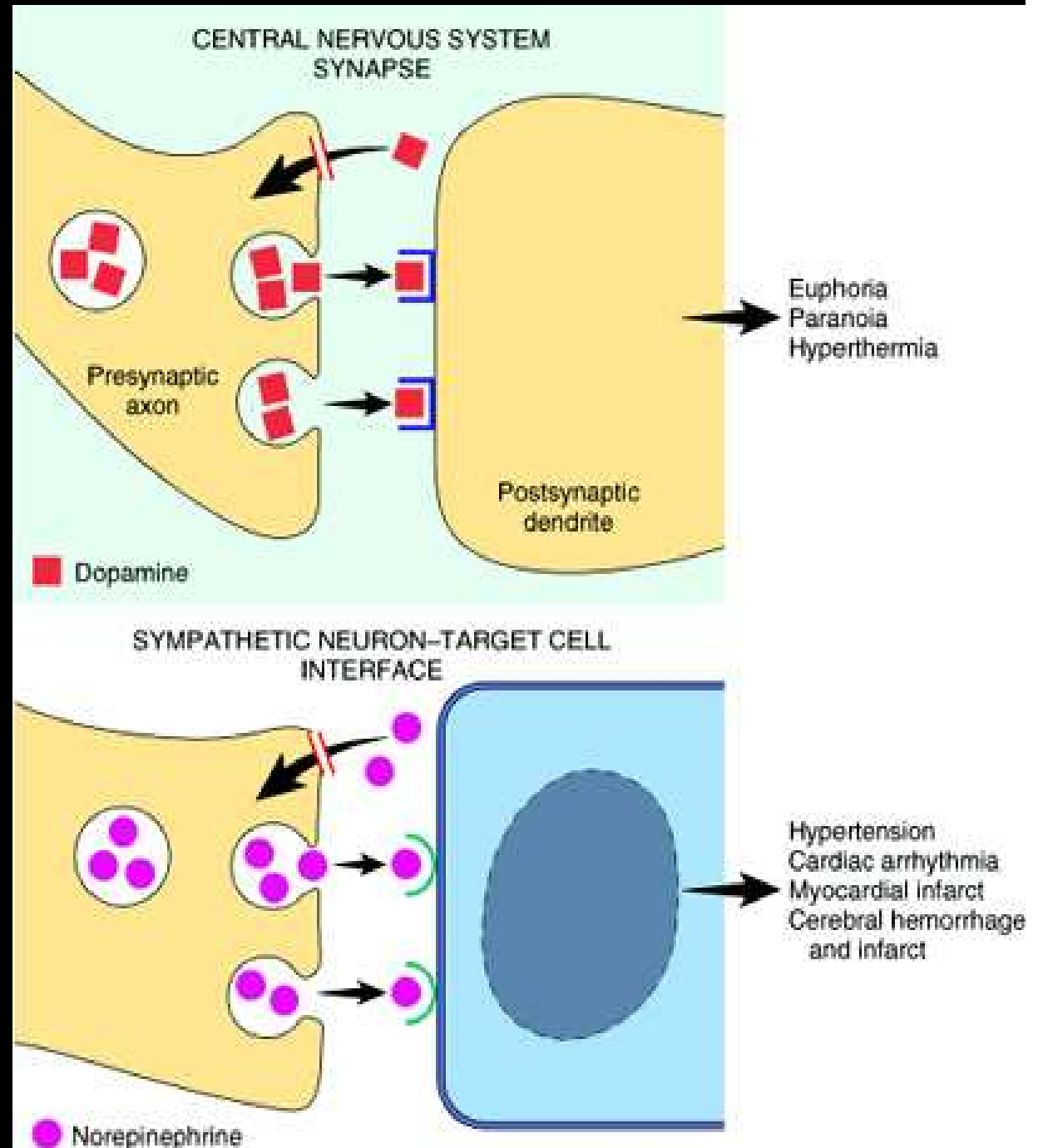
COMMON COMPLICATIONS OF INTRAVENOUS DRUG ABUSE

- Local infections at the site of injection.
- Systemic infections such as endocarditis and AIDS.
- Viral hepatitis.
- Glomerulopathy.
- Narcotic lung.

Cocaine

- An alkaloid extracted from the leaves of the coca plant.
- Very addictive.
- Acute cocaine toxicity:
 - Sympathetic nervous system stimulation, resulting in dilated pupils, vasoconstriction, increased arterial pressure, tachycardia, lethal arrhythmias and myocardial infarction.
 - Central nervous system: Cerebral infarction and intracranial hemorrhage, hyperpyrexia, seizures.
 - Rhabdomyolysis, which may lead to renal failure.

Effect of cocaine



Cocaine

- Chronic cocaine use may result in:
 - Perforation of the nasal septum in cocaine snorters.
 - Decreased lung diffusing capacity in those who inhale the smoke of cocaine.
 - Rarely, the development of dilated cardiomyopathy.
 - Effects on pregnancy and fetus: abruptio placenta, premature labor, intrauterine growth retardation.

CONSEQUENCES OF COCAINE OVERDOSE

- Cocaine has sympathomimetic effects and may induce tachycardia, hypertension, profound sweating, agitation, dilated pupils and hallucinations.
- Severe intoxication is accompanied by seizure, cardiac, arrhythmia and hypertension, or respiratory arrest.
- Cardiac arrhythmia may cause sudden death.
- Hypertension may be complicated by cerebral bleeding.

Heroin

- Closely related to morphine.
- Derived from the poppy plant.
- It is sold diluted with an agent (often talc or quinine) → dose unknown.
- Is usually self-administered intravenously or subcutaneously.

Heroin: Complications

- **Sudden death**

usually related to overdose, due to profound respiratory depression, arrhythmia and cardiac arrest, and severe pulmonary edema.

- **Pulmonary complications:**

edema, septic embolisms, lung abscess, opportunistic infections, and foreign body granulomas.

- **Infectious complications:**

skin, heart (endocarditis), viral hepatitis, AIDS.

- **Kidney disease:**

amyloidosis, focal glomerulosclerosis

- **Heroin overdose will cause hypothermia, bradycardia, hypotension and coma**

Marijuana: Complications

- Functional and organic CNS consequences: cognitive and psychomotor impairment → inability to judge time, speed, and distance → automobile accidents.
- Laryngitis, pharyngitis, bronchitis, asthma-like symptoms, increased tar inhalation.
- Increases heart rate and sometime increases blood pressure.
- Chromosomal damage.

HEAVY METALS

POTENTIALLY TOXIC IN THE HUMAN ENVIRONMENT

- Lead – found in old house paint used up to the 1940s, is a source of poisoning in children who eat it. Industrial contamination of waters next to foundries and smelters. Car batteries contain lead.
- Mercury – an industrial contaminant. Contamination of waters with mercury caused Minimata disease in Japan.
- Aluminum.

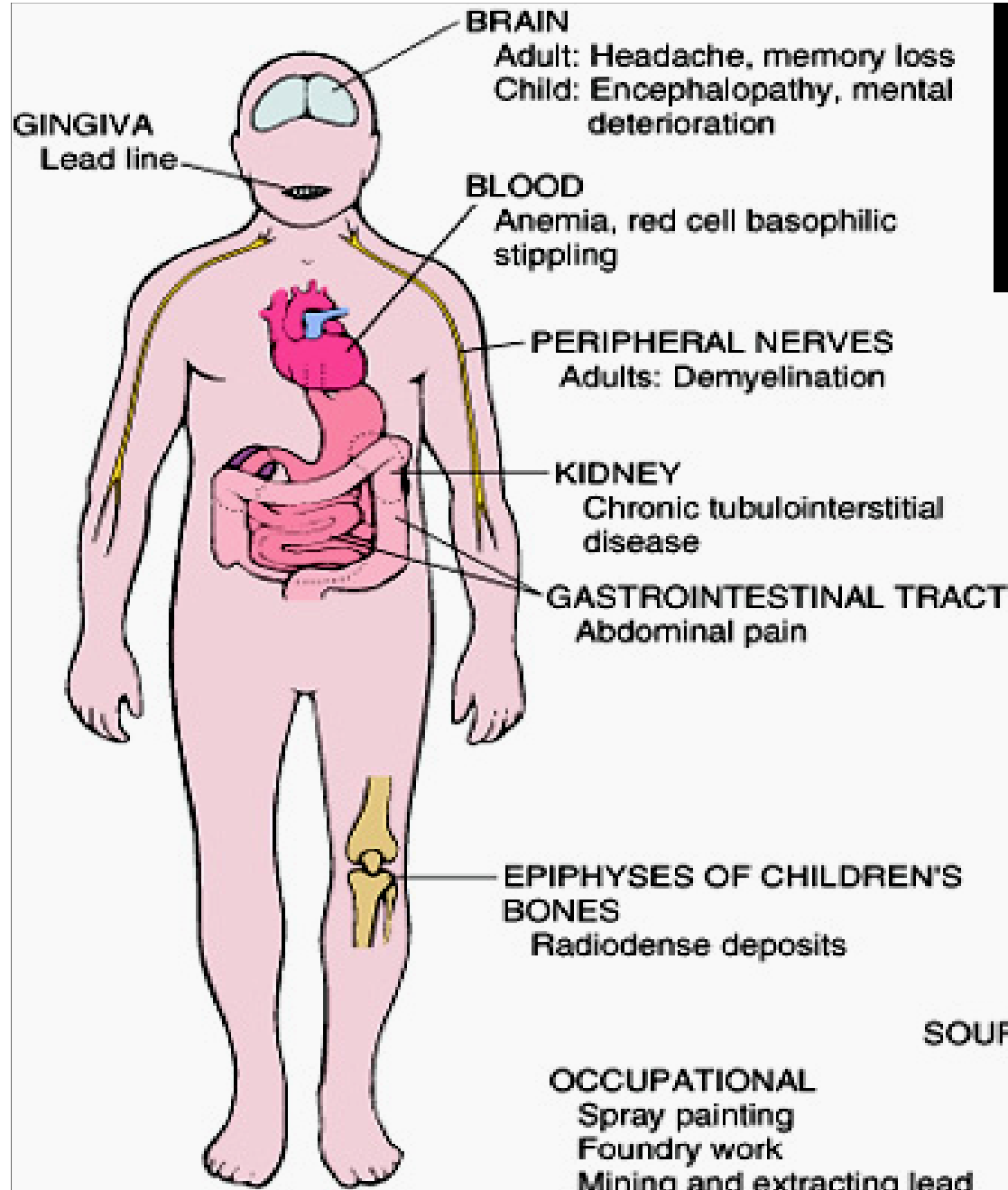
WHAT ARE THE SIGNS OF LEAD POISONING?

- Chronic accumulation of lead in the body has many consequences:
 - * Lead lines on the gums.
 - * Lead lines in the epiphyses of long bones.
 - * Anemia develops due to the inhibition of hematopoiesis (basophilic stippling).
 - * Renal toxicity. Lead damages proximal renal tubules causing aminoaciduria and glycosuria. Diagnostic intranuclear inclusions are seen in proximal renal tubules.

WHAT ARE THE SIGNS OF LEAD POISONING?

- Gastrointestinal colics.
- Lead encephalopathy:
 - CNS cell necrosis and demyelination with astrocytosis.
 - Peripheral nerve demyelination.
- In children, lead poisoning retards mental development.

LEAD POISONING



SOURCES

OCCUPATIONAL

- Spray painting
- Foundry work
- Mining and extracting lead
- Battery burning

NONOCCUPATIONAL

- Water supply
- Paint dust and flakes
- House dust
- Urban soil
- Newsprint
- Automotive exhaust