Environmental and Nutritional Pathology

Reading:  Robbins Chapter 9

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Outline

I. Overview of Environmental Pathology

II. General Mechanisms of Toxicology
   Dose-response curve
   Metabolism

III. Air Pollutant Diseases
   Patterns of lung injury
   Indoor Air Pollutants and Occupational Lung Disease:
   Tobacco
   Radon
   Carbon Monoxide
   Asbestos
   Outdoor Pollutants

IV. Alcohol and Drugs of Abuse
   Alcohol Related Disease
   Cocaine
   Heroin

V. Adverse Drug Reactions
   Toxic versus Hypersensitivity
   Estrogens and Oral Contraceptives

VI. Non-therapeutic Agents: Metals and Disease
   Metals and Disease
   Lead
   Arsenic

VII. Injury from Physical Agents
   Mechanical Injury
   Thermal Injury
   Radiation Injury

VIII. Nutrition Related Disease
   Generalized Malnutrition
   Specific Deficiencies
   Obesity

*** Figure credits: Unless otherwise noted, all figures reproduced in this handout come from Robbins Pathologic Basis of Disease
I. Overview of Environmental Pathology

Defining Environmental Disease

Modes of Environmental Exposure:

AIRBORN: dusts, particles, aerosols

WATERBORN: dissolved gases and solids

FOODBORN: toxins in food chain, drugs, heavy metals

PHYSICAL AGENTS: mechanical, thermal, pressure, radiation

NATURALLY OCCURRING TOXINS: plant (poison ivy, mushrooms, aflatoxin)

arthropod/animal venoms

Effects of Environmental Agents:

Causality in Environmental Disease:

Acute versus Chronic Exposure

Research strategies: epidemiological, animal studies
1. General Mechanisms of Toxicology

Dose-response curves

Metabolism of Toxicants: many/most are LIOPHILIC
Phase I reactions:

eexample:

Phase II reactions:

eexample:

III. Air Pollutant Disease

A. Lung injury and Air Pollution

Patterns of Lung Injury:
B. Indoor Air Pollution and Occupational Lung Disease

Tobacco Related Disease

Epidemiological and Health Impact of Cigarette Smoking

Mechanisms of Tobacco-related Tissue Injury

Components of Cigarette Smoke

*Tobacco-Related Diseases*

*Chronic Obstructive Pulmonary Disease*

*Cancer*
Coronary Artery Disease

Other Smoking-related disease: Cerebrovascular Disease

Peptic ulcer disease

Gastroesophageal reflux

Maternal-Fetal Disease

Passive Smoking (environmental tobacco smoke ETS)

Other Indoor Air Pollutants and Occupational Lung Disease

Radon

Carbon Monoxide
Mineral Dusts (Pneumoconiosis)

Example: Asbestos

Origin:

Pathogenesis

Clinical features:

Outdoor Air Pollutants

Origin

Effects:

Ozone too little/too much

Greenhouse effect
IV. Alcohol and Drugs of Abuse

A. Alcohol-related Disease

1. Metabolism of Alcohol

2. Acute Alcohol Intoxication

3. Complications of chronic alcohol abuse

Alcoholic liver disease

fatty liver

alcoholic hepatitis

cirrhosis
Other effects:

Nervous System

Cardiac

Digestive and Pancreas

Fetal Alcohol Syndrome

Ethylene Glycol

Source

Metabolism and mechanism of tissue injury

Treatment
B. Drugs of Abuse

Classes: 
- Depressants
- Stimulants
- Narcotics
- Hallucinogens

Cocaine

origin

mechanism of action

pharmacologic effects

acute:

chronic:

fetal:

Effects of overdose
Other Stimulants:

*Methamphetamine* (“Meth”, “Ice”)

*Ecstasy* (*Adam, XTC, “Love Drug”)*

Intravenous Drug Abuse:  *Heroin*

*Drug effects*

*Effects of Intravenous use: Infection*

**V. Adverse Drug Reactions**

*Toxicity versus Hypersensitivity Reactions*

Examples:

- *sulfa*-related toxic epidermal necrolysis
- *protamine*-related anaphylactoid reaction
- *acetaminophen*-related hepatic necrosis
- *aminoglycoside*-related nephrotoxicity
Oral Contraceptives and Estrogen Replacement

Physiologic and Pharmacologic effects

Estrogens:

Progestins:

Exogenous Estrogen Replacement Therapy (ERT)

endometrial carcinoma

breast carcinoma

thromboembolism

cardiovascular disease

Oral Contraceptives

breast carcinoma

cervical and ovarian cancer

thromboembolism

cardiovascular disease

other: hepatic adenoma, cholestasis

VI. Non-therapeutic Agents and Disease
Metals and Disease

Lead Poisoning

a. Sources of environmental lead exposure

b. Pathophysiology of lead poisoning

binding to sulfhydryl groups

**major effects**: blood nervous system gastrointestinal tract kidneys
c. Children versus Adults
d. Laboratory Testing:

*blood lead levels*

*zinc and free erythrocyte protoporphyrin levels*
e. Treatment of Lead Poisoning
Arsenic

souces:

mechanism of action:

effects:

Laboratory testing for arsenic.

VII. Injury from Physical Agents

A. Mechanical Force (trauma)

1. Soft tissue injuries:

   abrasions               contusions

   laceration             incised/stab wounds
2. Penetrating injury: Gunshot wounds

Type of firearm: rifled versus shotgun

Entrance vs. Exit Wounds

B. Temperature-Related Injury

Hyperthermia

Localized Burns

Classification of burns

Pathophysiology of severe burns

Body fluid shifts

Airway injury

Infection

Hypermetabolic state
Generalized hyperthermia

Definitions:

Hyperthermia

Heat stress

Heat exhaustion

Heat stroke and multiorgan dysfunction syndrome

Hypothermia

Systemic

Definition of hypothermia

Pathophysiology

Frostbite and Trenchfoot
D. Radiation Injury

1. Mechanism of Radiation Effect and Tissue Injury

   direct versus indirect effects

   principle target: DNA

2. Factors affecting Radiation Effect

   Source factors

   Target factors

3. Acute effects of Radiation

   Variable radiosensitivity of tissues

   **Hi** sensitivity:

   **Lo** sensitivity:
**Acute** whole body exposure

Hematopoietic

Gastrointestinal

Central Nervous System

**Specific** acute effects:

radiation *dermatitis*

radiation *gastroenteritis*

radiation *pneumonitis*

4. **Delayed Effects of Radiation**

Chronic tissue injury:  blood vessels

  skin

  heart and lungs

  gastrointestinal tract

  eyes and CNS
5. Other radiation: ultraviolet

electromagnetic

“Latent” effect: Neoplasia
VIII. Nutrition Related Diseases

• Environmental (Primary) versus Conditioned (Secondary) Malnutrition

A. Generalized Malnutrition

The spectrum of Protein-Calorie Malnutrition

1. Marasmus

Calorie Malnutrition

2. Kwashiorkor

Protein malnutrition

3. Laboratory Testing for Nutritional Status

albumin
thyroxine-binding prealbumin (TBPA)
retinol binding protein
C. Deficiency of Specific Nutrients: Vitamins

1. *Fat Soluble Vitamins*: D, A, K, E

Causes of Fat-soluble vitamin deficiencies

**Vitamin D**

Vitamin D and bone mineralization

Metabolism of Vitamin D

Causes of Vitamin D deficiency

Deficiency diseases: *rickets* and *osteomalacia*
**Vitamin A**

Sources of Vitamin A and Vitamin A metabolism

Vitamin A and maintenance of epithelia, visual pigment

Vitamin A deficiency: keratomalacia

night blindness

**Vitamin K**

Sources of Vitamin K

Vitamin K and coagulation

Origin of Vitamin K deficiency
Vitamin E

Function of Vitamin E

Deficiency state

2. Water Soluble Vitamins: C, B-complex

Vitamin C

Sources of Vitamin C

Vitamin C and collagen synthesis

Other functions of Vitamin C

Vitamin C deficiency: poor wound healing

bone changes (scurvy)
B COMPLEX VITAMINS

Thiamine

Normal function of thiamine

Deficiency state: dry and wet beri beri

Wernicke encephalopathy

Niacin

Normal function of niacin

Niacin deficiency:  
Pellagra : 3 “Ds” 
  dermatitis 
  diarrhea 
  dementia

Vitamin B-12 and Folate

Megaloblastic anemia, neurologic sequelae
D. Consequences of Overnutrition

**Obesity**

*defining* obesity

*etiology* of obesity:

*Complications* of obesity:

- insulin resistance
- hypertriglyceridemia
- low HDL
- coronary artery disease
- hypoventilation syndrome
- osteoarthritis
- cholelithiasis
STUDY QUESTIONS

1. How are acute and chronic exposures to environmental agents different: clinical effect? Epidemiological considerations?
2. What is the threshold dose for a toxicant?
3. How do Phase I and Phase II reactions differ?
4. How does the methylation of mercury affect its toxicity?
5. What different mechanisms are involved in tobacco smoke related tissue injury?
6. What is the most common cause of smoking related death?
7. Name 4 cancers associated with cigarette smoking
8. Name 2 agents which are synergistic with tobacco in causing lung cancer
9. What is ozone? what effect does ozone depletion/excess have?
10. How is alcohol metabolized?
11. What are the 3 major types of alcoholic liver disease?
12. What effect(s) does alcohol have on the CNS, heart?
13. Is there a safe amount of alcohol consumption during pregnancy?
14. What effect does cocaine have on the cardiovascular system?
15. What are some complications of intravenous drug abuse? Which heart valve(s) is/are most commonly involved by IVDA associated endocarditis?
16. What are the preferred specimens for drug testing?
17. What is the difference between a toxic and hypersensitivity (idiosyncratic) drug reaction?
18. What association is there between estrogen therapy and endometrial cancer?
20. Hepatic adenoma is associated with what medication?
21. What are the major pathologic effects of lead exposure?
22. How do adults and children differ in the effects of lead exposure?
23. Name 2 tests used for assessing lead exposure.
24. What is the significance of the skeletal system in chronic lead exposure?
25. What specimens are useful for assessing arsenic levels?
26. How does a laceration differ from an incised wound?
27. Compare the appearance of an entrance versus exit gunshot wound.
28. How does a gunshot wound reflect the proximity of the gun to the victim?
29. What are the major pathophysiologic sequelae of severe burns?
30. What organ systems are particularly sensitive to radiation? Which are relatively resistant?
31. What effect does radiation have on skin, GI tract, bone marrow, lungs?
32. How does malnutrition differ in developed versus developing countries?
33. How does radiation injury increase the risk of cancer?
34. What are 3 lab tests used in assessing nutritional status?
35. What are the major features of deficiencies of the fat and water soluble vitamins discussed in lecture?
36. Which vitamin is currently used in treatment of leukemia?
37. What is the definition of obesity? How is it assessed?
38. Name 3 metabolic consequences of obesity.
39. What are some pathologic complications of obesity?